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DergiPark tarafından yürürlüğe konulan kurallar çerçevesinde yazarların
"Etik İlkeler ve Yayın Politikası" ile "Yazım Kuralları" na uyulması konusunda ilgili başlıkları
dikkatlice incelemesi tavsiye edilmektedir.

Dergi 2022 yılından itibaren sadece İngilizce yazı kabul etmeye başlayacaktır.

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Değerli Bilim İnsanları,

Biyoteknolojik ve Stratejik Sağlık Araştırmaları Dergisi (JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH), Deneysel, Biyoteknolojik, Klinik ve Stratejik Sağlık Araştırmaları Derneği'nin uluslararası, bağımsız, önyargısız ve çift-kör hakemlik ilkeleri çerçevesinde yayın yapan açık erişimli, bilimsel yayın organıdır. Dergi, Nisan, Agustos ve Aralık aylarında olmak üzere yılda 3 sayı yayınlanır. Dergi ağırlıklı olarak İngilizce yayın kabul etmektedir.

Derginin amacı; etik kurallara uyumlu hazırlanmış biyoteknolojik, kritik, stratejik sağlık araştırmaları ile ilgili bilimsel makaleleri, klinik ve deneysel çalışmaları, derleme, olgu sunumu, editöre mektup ve editöryel yorum türündeki yazıları yayınlayarak literatüre ve sağlık alanındaki tüm disiplinlerde katkı sağlamaktır.

Derginin hedef kitlesi; sağlık alanındaki tüm disiplinlerde çalışan araştırmacılardır.

Dergimizin 6. Yılı, Nisan'2022 sayımızda da yine birbirinden ilginç derleme ve araştırma yazıları ile karşınızdayız. Makalelerini gönderen değerli yazar arkadaşlarımıza ve zaman ayıran hakemlerimize teşekkür eder, bilginin kullanılarak toplum sağlığına değerli katkılar sağlamasını temenni ederiz.

DergiPark tarafından yürürlüğe konulan kurallar çerçevesinde yazarların "Etik İlkeler ve Yayın Politikası" ile "Yazım Kuralları" na uyulması konusunda ilgili başlıkları dikkatlice incelemesi tavsiye edilmektedir.

Editör
Prof. Dr. Mustafa ALTINDİŞ
Editor in Chief

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YAZARLARA BİLGİLER

MAKALE YAZIM KURALLARI

Derginin Kapsamı

JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH, yılda üç kez Deneysel, Biyoteknolojik, Klinik ve Stratejik Sağlık Araştırmaları Derneği tarafından yayımlanmakta olup tıp alanında ve sağlık bilimlerinin ilgili konularında yazılmış İngilizce veya Türkçe makaleler kabul edilmektedir. Dergiye kabul edilecek yazı türleri deneysel araştırmaları, klinik ve laboratuvar çalışmalarının sunulması amaçlı özgün makaleler, vaka sunumları, derleme makaleleri ve editöre mektuplardır.

A. Genel Bilgiler

➢ Etik Kurallar

Dergiye gönderilen makalelerin daha önce başka bir dergide değerlendirme sürecinde olmaması, yayım için kabul edilmemiş ve de yayınlanmamış, olması, bilimsel ve etik kurallara uygun şekilde hazırlanması gereklidir. Yazarlar, makalelerin bilimsel ve etik kurallara uygunluğundan sorumludur. (http://www.icmje.org/about-icmje/faqs/conflict-of-interest-disclosure-forms/).

Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda "Yöntem" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklarasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH'ne gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir. Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin "Yöntem" bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır. Sonuç olarak, etik kurul kararı gerektiren klinik ve deneysel insan ve hayvanlar üzerindeki çalışmalar için etik kurul onayı alınmış olmalı, bu onay makalede "Etik Kurul Onay Numarası" ile belirtilmelidir ve belgelendirilmelidir.

Dergide çıkan yazıların tüm hakkı dergiye aittir. Yazılar için yazarlara telif hakkı ödenmez. Makaleye ek olarak yukarıdaki şartları kaşif taramalarına dayalı yazılarda Anabilim Dalı (Bilim Dalı) Başkanlığı, Başhekimlik veya Servis Şefliği tarafından arşivde çalışılmasına izin verdiğine dair bir belgenin çalışmaya eklenmesi zorunludur. Prospektif klinik çalışmalar için resmi gazetenin 29.01.1993 tarih ve 21480 sayılı nüshasında yayımlanan yönetmeliğe uygun bir şekilde Etik Kurulu onayı alınmalıdır. Dergide yer alan makalelerin etik sorumluluğu yazarlarına aittir.

Dergiye gönderilen makalelerden hakeme gönderilmesi uygun görülen makaleler konunun uzmanı hakemlere gönderilir. Makalenin yayımlanabilmesi için iki hakemin de olumlu görüş bildirmesi gerekmektedir. Değişikliğe gerek görüldüğü takdirde, istenilen değişiklikler yazarlarca 15 gün içerisinde yapıldıktan sonra yayın tekrar incelemeye alınır, yazım ve dil bilgisi hataları makalenin içeriğine dokunulmaksızın yayın kurulu tarafından düzeltilir.

Derleme yazılarında, tüm yazarların derleme konusu ile ilgili en az bir SCI/SCI-expanded indekse giren yayınının bulunması gerekmektedir.

Sonucu desteklemek için istatistiksel analiz genellikle gereklidir. İstatistiksel analiz, tıbbi dergilerdeki istatistik verilerini bildirme kurallarına göre yapılmalıdır (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). İstatistiksel analiz ile ilgili bilgi, Yöntemler bölümü içinde ayrı bir alt başlık olarak yazılmalı ve kullanılan yazılım kesinlikle tanımlanmalıdır.

Dergi İntihal İlkesi

JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH'de makale göndermeden önce uygun intihal yazılım programlarıyla (iThenticate, Turnitin: Tezler için vb.) makalenizdeki benzerlik durumunu belirlemeniz beklenir. Benzerlik oranlarının dergimiz için kaynaklar hariç % 20'un altında olması istenmektedir.

Simgeler, Birimler ve Kısaltmalar

Dergimiz, İngilizce makalelerde Scientific Style and Format, The CSE Manual for Authors, Editors, and Publishers, Council of Science Editors, Reston, VA, USA (7th ed.) uzlaşılarını; Türkçe makalelerde ise TDK Yazım Kılavuzu, Türkiye Bilim Terimleri ve TÜBA Türkçe Bilim Terimleri Sözlüğü'nü esas almaktadır. p, ×, μ, η, or v gibi karakterler, sözcük işlem uygulamasının simge menüsünden seçilerek kullanılmalıdır. Sayılarla birimler arasında bir boşluk bırakılmalı (örn. "3 kg"), sayılarla yüzde simgesi arasında boşluk bırakılmamalıdır (örn. "%45"). Tüm kısaltma ve kısa adlar, ilk kez kullanıldıklarında tanımlanmalıdır. Canlıların ve mikroorganizmaların jenerik isimleri, tür adını değiştirmeden, uygun şekilde kısaltılmalı ve yatık olarak yazılmalıdır.

Makale Hazırlama Şekli ve Biçimi & Gönderim

Makale gönderimi çevrimiçi olarak http://dergipark.gov.tr/bshr adresine Microsoft Word dosyası olarak eklenmelidir. "Öz", "Ana Metin ve Kaynaklar (Çizelgeler dahil)" Microsoft Word dosyası (.doc veya .docx uzantılı) olarak, 12 yazı tipi boyutunda, Times New Roman karakterleriyle, 1,5 satır aralığıyla ve paragraflar iki yana yaslanmış olarak yazılmalıdır. Makalelerin değerlendirilmeye alınabilmesi için, başvuru esnasında 'Telif Hakkı devir formu' doldurulmalıdır. Bu formu içermeyen yazılar değerlendirmeye alınmaz. Makaleler, Ana metnin sayfa numaraları, her sayfanın sağ alt köşesinde belirtilmelidir.

Makaleler, Türkçe veya İngilizce yazılabilir.

B. Yazım Kuralları

Metin içi ve metin sonu kaynak gösterimi için, AMA (Amerikan Tıp Birliği/American Medical Association) Stili kullanılmalıdır (http://library.nymc.edu/informatics/amastyle.cfm; https://drive.google.com/drive/folders/1hzvgxnau1lBPUBYfKN1vTBKbPE31LBXQ) .

Dergide kör hakemlik uygulaması söz konusu olduğundan makale ana metin üstünde yazarlara ilişkin herhangi bir bilgi bulunmamalıdır.

Tüm makale yazarlarının, ORCID iD (Open Researcher and Contributor ID) numaraları başlık sayfasına eklenmelidir.

B. 1. Başlık Sayfası

Yazılar başlık sayfasından başlanarak numaralandırılmalı, sayfa numaraları sağ alt köşeye yazılmalıdır.Başlık sayfasında; yazının başlığı (Türkçe ve İngilizce), başlık altında tüm yazarların ad ve soyadları, kurumları yer almalıdır. Sorumlu yazarın adı ve soyadı, telefon numarası, e-posta ve yazışma adresleri bulunmalıdır. Makale başlığı, 25 kelime ile sınırlı, Türkçe ve İngilizce dillerinde verilmelidir. Kısa başlık (running title, running head) 50 karakterle (boşluk dahil) sınırlı şekilde Türkçe ve İngilizce olmalıdır.

B. 2. Öz Sayfası

Öz (Abstract), Türkçe ve İngilizce olarak en fazla 250 sözcük olacak şekilde; 'Amaç (Objective)', 'Yöntem (Methods)', 'Bulgular (Results)' ve 'Sonuç (Conclusion)' bölümlerinden oluşmalıdır. Derleme ve olgu sunumunda öz sayfası bölümlere ayrılmadan yazılmalıdır.

Öz'ün altına "anahtar kelimeler" (en az 3, en fazla 6) verilmelidir. Anahtar kelimeler Türkçe ve İngilizce yazılmalıdır. İngilizce anahtar kelimeler Index Medicus'da "Medical Subjects Headings" listesine uygun olmalıdır (Bkz: www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler Türkiye Bilim Terimleri, uygun olarak verilmelidir (Bkz: www.bilimterimleri.com). Bulunamaması durumunda bire bir Türkçe tercümesi verilmelidir.

B. 3. Ana Metin

B. 3. 1. Özgün Araştırma

Sırasıyla ve kesin sınırlarla ayrılmış "Giriş", "Yöntem", "Sonuç" ve "Tartışma" bölümlerinden oluşmalıdır. Sonuç kısmı, ayrı bir bölüm olarak veya Tartışma'nın son paragrafı olarak yazılabilir. Tartışma kısmının son paragrafında çalışmanın sonuçları ifade edilebilir, ek bir başlık açılmasına gerek yoktur.

En çok 15 sayfa (öz, teşekkür ve kaynaklar hariç) olmalıdır.

Sistematik derleme ve meta-analiz özgün araştırma makalesi kapsamındadır. Yazarlar, taslaklarını gönderirken sistematik derleme ve meta-analiz için, PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) beyanatı (http://www.prisma-statement.org/). yönergesine uyduklarını gösteren standart kontrol listelerini kullanmalı ve istendiğinde sunmalıdır.

Sözcük sayısı öz, teşekkür ve kaynaklar hariç en çok 5 000 olmalıdır. Kaynak sayısı, 50'yi geçmemelidir(derleme hariç). Metin boyunca bilimsel terimler yatık olarak yazılmalıdır.

B.3.2. Derleme

En çok 20 sayfa (öz ve kaynaklar hariç) olmalıdır. Derlemeler, standart yazı şeklinden farklıdırlar. Yazı yazmanın evrensel formatı IMRAD derleme yazılarında uygulanmamaktadır. Ana hatlarıyla "Giriş" bölümü daha geniş olmakta ve derlemenin amacını ve yazı gerekçesini açıklamaktadır.

"Yöntem" ve "Bulgular" kısmı bulunmamaktadır. Tartışma kısmı yine geniş tutulacak ve kişisel deneyimler doğrultusunda aynı konuda yapılmış çalışmalar ve onların sentezi yapılacaktır. Sonuç anlamında bir yorum ve değerlendirme paragrafı bulunmalıdır. Kaynaklar ise tüm yazılara göre daha fazla sayıda olacaktır. Ancak mutlaka yazarın kendi çalışmaları da bulunacaktır.

B.3.3. Olgu Sunumu

En çok 10 sayfa (öz, teşekkür ve kaynaklar hariç) olmalıdırr. Olgu sunumlarında ise sırasıyla giriş, olgu sunumu ve tartışma bölümlerini içermelidir.

B.3.4. Editöre Mektup

En çok 5 sayfa (öz ve kaynaklar hariç) olmalıdır. Çizim ve çizelge içermez. Bir makaleye ithaf olarak yazılmış ise sayı ve tarih verilerek belirtilmeli ve metnin sonunda yazarın ismi, kurumu ve adresi bulunmalıdır.

B.4. Çizim ve Çizelgeler

Metin içerisinde kullanılan fotoğraf, grafik, şekil, resim gibi görsel sunum araçları 'Çizim' olarak tanımlanır. 'Tablo' ise sınıflandırılmış verilerin yer aldığı görsel sunum araçlarıdır. Tablolar kaynaklardan sonra başlıklarıyla birlikte verilmelidir. Tablolar, başlığın alt ve üstünde, ayrıca alt satırın altında yatay kenarlık ve sol sütunun sağ dikey kenarlığı olacak şekilde düzenlenmelidir.

Figür ve Tablolar, numaraları ile metin içinde geçtiği yerlerde ilgili cümlenin sonunda ayıraç içinde belirtilmeli; sırayla numaralandırılmalıdır.

Örnek tablo:

Tablo 1. Araştırmaya katılanların ilk başvurularını birinci basamakta çalışan hekime yapmama nedenleri

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YAZARLARA BİLGİLER

Başvurmama Nedeni	*n	%
Sadece psikiyatri uzmanı ruh sağlığı hizmeti sunabilir		
Birinci basamakta çalışan hekimin bu hizmeti sunduğunu bilmemem		
Ebeveyn kararıydı		
Birinci basamakta çalışan hekime güveniyorum ancak tercih etmedim		
	47	53,4
	17	19,3
	12	13,6
	12	13,6

* Toplam hasta sayısı

Tablolar, metne dahil edilmemeli ve sistem üzerinden "Görseller" başlığı seçilerek yüklenmelidir. Görseller; JPG, GIFF, PNG veya TIFF formatında gönderilmelidir. Metine ek olarak sisteme yüklenen tüm çizim başlıkları, "Çizim Başlığı" altında, kaynaklardan sonra listelenmelidir. Kullanılan kısaltmalar çizim ve çizelgelerin altındaki açıklamada 10 yazı boyutunda belirtilmelidir. Ondalıklı sayıların belirtilmesinde Türkçe metinlerde virgül işareti, İngilizce metinlerde nokta işareti kullanılmalıdır. Yüzde ile belirtilen sayılarda Türkçe metinlerde sayı önünde, İngilizce metinlerde ise sayı arkasında % işareti kullanılmalıdır.

B. 5. Açıklamalar

Çalışmada teşekkür, daha önce sunulduğu kongre, çıkar çatışması olmadığı, maddi destek, bağış ya da teknik yardım gibi konular metnin sonunda kaynaklardan önce belirtilmelidir. Çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazı yazılmalıdır. Araştırma desteği (Üniversite Bilimsel Araştırma projeleri , TÜBİTAK projeleri ve benzeri kurumlardan) alınmışsa, proje numarası belirtilmelidir.

C. Kaynak Gösterimi

Dergimiz, kaynak gösteriminde AMA stilini kullanılmaktadır ve kaynak yazımında atıf düzenleme programlarının kullanımını tavsiye edilmektedir (EndNote, Mendeley, Zotero vb.).

C. 1. Metin İçinde;

Kaynaklar, metinde geçiş sırasına göre numaralandırılmalıdır ve kaynak numaraları üst simge olarak verilmelidir. Örneğin,"… belirtilmektedir8. , bildirilmiştir8,13,18. , şeklindedir8-10

C. 2. 'Kaynaklar' Başlığı Altında;

Kaynaklar ayrı bir liste olarak metin içindeki sıralamalarına göre numaralandırılarak verilmelidir. Kaynak sayısı özgün araştırmalarda en çok 50, olgu sunumlarında en çok 20, editöre mektuplarda ise en çok 5 olmalıdır.

Kaynaktaki yazar sayısı 3 veya daha az ise tüm yazarlar belirtilmeli; 3'den fazla ise, Türkçe kaynak gösteriminde sadece ilk 3 isim yazılmalı "ve ark." şeklinde, İngilizce kaynak gösteriminde ise ilk 3 isim yazılmalı ve "et al." şeklinde gösterilmelidir.

Dergi isimleri Index Medicus/Medline/PubMed'de yer alan dergi kısaltmaları ile uyumlu olarak kısaltılmalıdır. Index Medicus'ta indekslenmeyen bir dergi kısaltılmadan yazılmalıdır. Çevrimiçi yayınlar için DOİ (digital object identifier) numarası verilmelidir.

Örnek:

1. Gage BF, Fihn SD, White RH. Management and dosing of warfarin therapy. The American Journal of Medicine. 2000; 109(6): 481-488. doi:10.1016/S0002-9343(00)00545-3.

Örnekler:

1. Debes-Marun CS, Dewald GW, Bryant S, et al. Chromosome abnormalities clustering and its implications for pathogenesis and prognosis in myeloma. Leukemia. 2003; 17: 427–436.
2. Ozcelik F, Oztosun M, Gülsün M, ve ark. İdiopatik trombositopenik purpura ön tanılı bir olguda EDTA'ya bağlı psödotrombositopeni. Turk J Biochem. 2012; 37(3): 336–339.

Örnek:

1. Yoldas O, Bulut A, Altindis M. Hepatit A Enfeksiyonlarının Güncel Yaklaşımı. Viral Hepatit J 2012; 18: 81-86.
2. Bir derginin ek sayısı (Supplement) kaynak gösterileceği zaman; İngilizce makalelerde (Suppl.) ve Türkçe makalelerde ise (ES) şeklinde gösterilmelidir.

Çevrimiçi makale ise tam yayın tarihi kullanılır. Genellikle cilt ve dergi sayıları, sayfa numaraları yoktur. Makaleye doğrudan ulaşım adresi ve erişildiği tarih verilmelidir.

Örnek:

5. Frederickson BL (2000, Mart 7). Cultivating positive emotions to optimize health and well-being. Prevention & Treatment 3, Makale 0001a. http://journals.apa.org./prevention/volume3/pre003000-1a.html adresinden 20 Kasım 2000'de erişildi.

Kitabın kaynak gösterimi ise yazarların adı, kitabın adı, birden çok basımı varsa kaçıncı basım olduğu, basımevi, basım yeri, basım tarihi belirtilmelidir

Örnek:

2. Strunk W Jr., White EB. The Elements of Style (4. baskı). Longman, New York, 2000.

Kaynak çok yazarlı bir kitabın bölümü ya da bir makalesi ise bölümün ya da makalenin yazarı, bölümün ya da makalenin adı, kitabın adı, kaçıncı baskı olduğu, cildi, kitabın yayın yönetmenleri, basım yeri, sayfaları, tarih yazılmalıdır.

Örnek:

3. Meltzer HY, Lowy MT. Neuroendocrin function in psychiatric disorders. American Handbook of Psychiatry, 2. Baskı, cilt 8, PA Berger, HKH Brodie (Ed), New York. Basic Books Inc, 1986; s. 110-117.

Çeviri kitaplar aşağıdaki şekilde kaynak olarak gösterilmelidir.

Örnek:

4. Liberman RP. Yetiyitiminden İyileşmeye: Psikiyatrik İyileştirim Elkitabı. American Psychiatric Publishing Inc. Washington DC. 2008. Çev. Mustafa Yıldız, Türkiye Sosyal Psikiyatri Derneği, Ankara, 2011.

Kaynak çevrimiçi (internette yer alıyor) ise erişim tarihi ile birlikte yazılmalıdır.

MAKALE SÜREÇ YÖNETİMİ

A. Çift-Kör Hakemlik

JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH (J of BSHRS), yılda 3 kez yayınlanan ve çift-kör hakemlik sürecinden geçen bilimsel makalelerin yayınlandığı ulusal/uluslararası ve hakemli bir akademik dergidir. Yayınların incelenmesi için çalışmaların içeriğine ve hakemlerin uzmanlık alanlarına göre en az iki hakem, makale alan editörü/leri tarafından atanır. Bu süreçte hakem değerlendirme raporları elektronik ortamda isimsiz olarak gönderilir. Değerlendirmeyi yapan hakemlerin isimleri çift-kör yöntemi gereği raporlarda ve dergide belirtilmemektedir. Talep edilmesi halinde, hakem olarak dergiye katkı sağladığına ilişkin yazılı bir belge hakemlere verilebilir. Yazarlar, hakemlerle doğrudan iletişime geçemez, değerlendirme ve hakem raporları dergi yönetim sistemi aracılığıyla iletilir. Bu süreçte değerlendirme formları ve hakem raporları editör aracılığıyla sorumlu yazara iletilir.

B. Karar Alma Süreçleri

Yayınlanmak üzere gönderilen tüm çalışmalar, değerlendirme için alanlarında uzman en az iki hakeme gönderilir. İnceleme sürecinin tamamlanmasının ardından editör, söz konusu çalışmanın doğruluğu, araştırmacı ve okuyucular için önemi, hakem raporları, telif hakkı ihlali ve intihal gibi yasal düzenlemeleri de göz önünde bulundurarak hangi çalışmaların yayınlanacağına karar verir. Editör, bu kararı verirken diğer editörlerden veya hakemlerden de tavsiyeler alabilir.

C. İvedilik

Hakem değerlendirmesi yapmak üzere davet alan bir hakem, ilgili çalışma için hakemlik yapıp yapamayacağını yedi gün içinde editöre bildirmelidir. Kabul edilen hakemlik değerlendirme süreci onbeş, sorumlu yazara bildirilen değişikliklerin tamamlanması için, yazarlara verilen süre ortalama onbeş gündür. Sorumlu yazara son okuma için gönderilen metnin değerlendirme süresi ise üç gündür. Değerlendirme için hakemlere gönderilen çalışmalar gizli belge olarak tutulmalıdır. Çalışmalar başkalarına gösterilmemeli, içerikleri tartışılmamalıdır. Gerekli durumlarda editörün izni dahilinde hakemler başka meslektaşlarından tavsiye isteyebilirler. Editör, bu izni ancak istisnai bir koşul olması durumda verebilir. Gizlilik kuralı, hakemlik yapmayı reddeden kişileri de kapsamaktadır.

E. Tarafsızlık İlkesi

Değerlendirme sürecinde yazarlara yönelik kişisel eleştiri yapılmamalıdır. Değerlendirmeler, nesnel ve çalışmaların geliştirilmesine katkı sağlayacak şekilde olmalıdır.

F. Kaynak Belirtme

Hakemler, çalışmada atıf olarak belirtilmeyen alıntılar varsa bunları yazarlara bildirmekle yükümlüdür. Hakemler, alanda atıfta bulunulmayan eserlere ya da benzer eserlerle çakışan alıntılara özellikle dikkat etmelidir. Hakemler, daha önce yayınlanmış herhangi bir çalışma ya da bilgiyle benzerliği olan yayınların farkedilmesi durumunda editörleri bilgilendirmelidir.

G. Bilgilendirme ve Çıkar Çatışması

Hakemler, çalışmasını değerlendirmekle görevlendirildikleri herhangi bir yazar, şirket ya da kurumla işbirliğine dayalı herhangi bir bağlantıları olması durumunda değerlendirme yapmayı kabul etmemeli ve durumdan editörü haberdar etmelidir.

Hakemler, değerlendirme için gönderilmiş, yayınlanmamış eserleri ya da eserlerin bölümlerini yazar(lar)ının yazılı onayı olmadan kendi çalışmalarında kullanamaz. Değerlendirme sırasında elde edilen bilgi ve fikirler hakemler tarafından gizli tutulmalı ve kendi çıkarları için kullanılmamalıdır. Bu kurallar, hakemlik görevini kabul etmeyen kişileri de kapsamaktadır.

YAZI GERİ ÇEKME TÜM YAZARLARIN ONAYI İLE OLMALIDIR.

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Faks: +90.264.295 6629

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Journal of Biotechnology and Strategic Health Research

HEALTH RESEARCH

INSTRUCTIONS FOR AUTHORS

Scope of the Journal

The JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH is published electronically 3 times a year by the Experimental, Biotechnological, Clinical and Strategic Health Research Association and accepts English or Turkish-language manuscripts in all fields of medicine(Experimental, Biotechnological, Clinical and Strategic Health Research) and other related health sciences. Contribution is open to researchers of all nationalities. The following types of papers are welcome: original articles (for the presentation of clinical and laboratory studies), case reports, review articles, and letters to the editor.

Submission Procedures

All manuscripts must be submitted electronically via the internet to the JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH through the online system for ULAKBIM dergipark http://dergipark.gov.tr/bshr You will be guided stepwise through the creation and uploading of the various files.

There are no page charges.

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All experimental or clinical researches done in humans or animals should follow the ethical rules. The ethical approval form must be sent and the number of approval must be given in the manuscript. The ethical problems belong only to the author(s).

All copyright of the published papers belong to Experimental, Biotechnological, Clinical and Strategic Health Research Association.

The copyright fee is not paid to all authors.

In manuscripts based on scanning of archieve records, a consent form is needed that shows the permission for retrospective work and signed by Head of the Department, hospital manager or clinic manager.

Preparation of Manuscript Style and format:

Manuscripts should be submitted to http://dergipark.gov.tr/bshr as Microsoft word file in Times New Roman font. All manuscripts including references should be typed in 12 font size,one and a half (1.5) line space and justified. Upon submission, the copyright release form should be filled and downloaded. The manuscript submissions without a copyright release form will not be evaluated.

Each page of main text of the manuscript should be numbered on the right hand side. Manuscripts should be written in Turkish or English. Contributors who are not native English speakers are strongly advised to ensure that a colleague fluent in the English language or a professional language editor has reviewed their manuscript. Repetitive use of long sentences and passive voice should be avoided. It is strongly recommended that the text be run through computer spelling and grammar programs.

Symbols, Units, And Abbreviations:

In general, the journal follows the conventions of Scientific Style and Format, The CSE Manual for Authors, Editors, and Publishers, Council of Science Editors, Reston, VA, USA (7th ed.). Spaces must be inserted between numbers and units (e.g., 3 kg), but not between numbers and mathematical symbols (+, –, ±, ×, =, <, >) and between numbers and percent symbols (e.g., 45%). Please use International System (SI) units. All abbreviations and acronyms should be defined at first mention. Thereafter, generic names should be abbreviated as appropriate without altering the species name.

Typs of Manuscripts Original Article

It should consists of "Introduction", "Methods", "Results" and "Discussion". Conclusion may be written as a last paragraph of discussion, there is no need to add a separate section for conclusion. The whole length of text should be maximum 5 000 words (except abstract, acknowledgements and references). The numbers of references should be maximum 50. Also, scientific names should be spelled italics throughout the text.

Review

It should be maximum 6 000 words (except abstract and references). The author(s) should have at least one published paper in a journal indexed in SCI/SCI-expanded related to the topics of the review. The abstract should be as one paragraph and should be written without a section. The numbers of references should be maximum 100.

Case Report

It should be maximum 1 500 words (except abstract, acknowledgement and references). Case reports should consist of abstract, keywords, introduction, case report and discussion sections. The numbers of references should be maximum 10. Figures or Tables should follow the main text in a separate pages.

Letter to Editor

It should be maximum 1 000 words (except abstract and references). No Tables or Figures are included. If it was written refering to another article, the number and the date should also be added. The name, affiliation(s) and address of author(s) should be written at the end of the text. The numbers of references should be maximum 5.

Manuscript Arrangement

Manuscripts should be arranged as follows: "Title page", "Abstract", "Keywords", "Main text", "Acknowledgements", "References", "Tables",and "Figures".

Title page

All submissions must include a title page, which is to be uploaded as a separate document. The title page should contain the full title in sentence case (e.g., Urothelial cancers: clinical and imaging evaluation). The title should be limited to 25 words or less and should not containabbreviations.The title should be a brief phrase describing the contents of the paper.Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible. It should be written in capital letters both in Turkish and in English. Title in English should be written using italic letters for Turkish manuscripts and vice versa. The first and the family names of the authors should be written in small letters as the first letter being the capital.

The full names and affiliations of all authors should be given clearly and briefly with theirinstitutions, address with zip code and name of country, and the contact details of corresponding author (E-mail address and telephone). In addition, ORCID (Open Researcher and Contributor ID) numbers of all authors should be included into the title page.

Abstract

The abstract should be brief, indicating the purpose/significance of the research, methodology, major findings and the most significant conclusion (s). The abstract shouldnot contain literature citations that refer to the main list of reference attached to the complete article. The abstract should be written as a single paragraph and should be in reported speech format (past tense); complete sentences, active verbs and the third person should be used.

The abstract should be structured to include the study's "Objective", "Methods", "Results", and "Conclusion" under 4 separate headings. Abstracts of review articles should be a brief overview of the main points from the review. In reviews and case reports, abstract should be written without any sections. The abstract (English and Turkish) should not be more than 300 words.

Keywords

The authors must provide 3-6 keywords for indexing purposes and to facilitate the retrieval of articles by search engines. Keywords should be different from the words that make up the title of the article. Keywords should be written below the abstracts both inTurkish andEnglish. Acronyms should be avoided. For English keywords, always try to use terms from the Medical Subjects Headings list from Index Medicus (www.nlm.nih.gov/mesh/MBrowser.html). For Turkish keywords, terms from Turkish Scientific Terms (www.bilimterimleri.com) should be used.

Main text

Introduction

The introduction should be clear and concise, with relevant references on the study subject and the proposed approach or solution. There should be no subheadings. Excessive citation of literature should be avoided. Only necessary and the latest citations of literature that are required to indicate the reason forthe research undertaken and the essential background should be given.

Methods

Explain clearly but concisely your clinical, technical, or experimental procedures. A precise description of the selection of your observational or experimental subjects (for example patients or laboratory animals including controls) must be presented. Experimental research involving human or animals should be approved by ethical committiee.All chemicals and drugs used must be identified correctly, including the generic names, the name of the manufacturer, city and country in parenthesis. The techniques or methodology adopted should be supported with standard references. Briefly describe methods that have been published but are not well known as well as new or substantially modified methods. Description of established procedures are unnecessary. Apparatus should be described only is it is non-standard; commercially available apparatus used should be stated (including manufacturers' name, address in parenthesis). Only SI units should be used for each measurements.

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Results

The result section should provide complete details of the experiment that are required to support the conclusion of the study. The results should be written in the past tense when describing findings in authors experiments. Previously published findings should be written in the present tense. Speculation and the detailed interpretation of the data should not be included in the results but should be put into the discussion section.

Discussion

Statements from the "Introduction" and "Results" sections should not be repeated here. The final paragraph shouldhighlight the main conclusions of the study.

Tables and Figures

The visual presentations like photographs, graphics, picturesetc. must be labelled "Figures". Whereas, the "Tables" shows the classifieddata.Tables should be added after the "References" section. Figure legends should be placed into the end of the main text. Figures should be uploaded as a separate file following the Dergipark System.

All tables and figures must have a caption and/or legend and be numbered (e.g., Table 1., Figure 2.), unless there is only one table or figure, in which case it should be labelled "Table" or "Figure" with no numbering. Captions mustbe written in sentence case (e.g., Figure 1. Macroscopic appearance of the samples.). The font used in the figures should beTimes New Roman. If symbols such as ×, μ, η, or ν are used, they should be added using the Symbols menu of Word.

All tables and figures must be numbered consecutively as they are referred in the text. Please refer to tablesand figures with capitalisation and unabbreviated (e.g., "As shown in Figure 2. …", and not "Fig. 2" or "figure 2").
The resolution of images should not be less than 118 pixels/cm when width is set to 16 cm. Images must bescanned at 300 dpi resolution and submitted in .jpeg, .png or .tif format.

Graphics and diagrams must be drawn with a line weight between 0.5 and 1 point. Scanned or photocopied graphs anddiagrams are not accepted.

Charts must be prepared in 2 dimensions unless required by the data used. Charts unnecessarily prepared in3 dimensions are not accepted.

Figures that are charts, diagrams, or drawings must be submitted in a modifiable format, i.e. our graphicspersonnel should be able to modify them. Therefore, if the program with which the figure is drawn has a "Save as"option, it must be saved as .pdf. If the "Save as" option does not include .pdf extension, the figure must becopied and pasted into a blank Microsoft Word document as an editable object. It must not be pasted as an imagefile (.tiff or.jpeg) unless it is a photograph.

Tables and figures, including caption, title, column heads, and footnotes, must not exceed 16 × 20 cm andshould be no smaller than 8 cm in width. For all tables, please use Word's "Create Table" feature, with no tabbedtext or tables created with spaces and drawn lines. Please do not duplicate information that is already presented inthe figures.
Tables must be clearly typed, each on a separate sheet, and single-spaced. Tables may be continued on anothersheet if necessary, but the dimensions stated above still apply.

Tables should be arranged as a horizontal borderline as well as below the last line. Moreover, there sould be vertical line on the right of first column on the left hand site. Abbreviations used in the tables such as (*) should be explained below the table in 10 font size.

In Tables written in Turkish, decimal numbers should be written with comma, however in English text, decimal numbers should be written with dots. Percentages (%) should be placed in front of the numbers without space and behind the numbers in Turkish and English text, respectively.

Example for a Table:

Table1. The reasons of not applying to general practioner for the first application.

The reasons	*n**	*%*
Only Psychiatrist can do it		
No information about general practioner Parents decision		
Not preferred	*47*	*53.4*
17	*19.3*	
12	*13.6*	
12	*13.6*	

**Total number of patients.*

Acknowledgement

All acknowledgements, poster/oral presentations, financial supports, grants, technical supports and the conflict of interest should be mentioned at the end of the text.

Funding

The type of Project or the financial support such as scientific projects of University, TUBITAK projects etc. should be added at the end of the text including the numbers and the year of the projects.

References

While talking about the source in the text, the first author's surname ın Er and his firends' study12"…… or ın Er et al.12. Both authors should be given the surnames of both authors (similar results were found in the study conducted by Öncü and Ilke13).

Citations in the text should be identified by numbers assuperscript, for example, "The results were as follows: 4
If there are more than one references, separate the numbers with comma, for example, "Several interventions have been successful at increasing compliance.11,14"

In following journals, first and the last numbers should be seperated by "-" , for example: Diabetes mellitus is associated with a high risk of foot ulcers1-3 or "As reported previously,1,3-6"

Do not include personal communications, unpublished data, or other unpublished materials as references, although such material may be inserted (in parentheses) in the text. In the case of publications in languages other than English, the published English title should be provided if one exists, with an annotation such as "(article inTurkish with an abstract in English)". If the publication was not published with an English title, provide the original title only; do not provide a self-translation. A short title for use as a running head (not to exceed 30 characters in length, including spaces between words) is needed. References should be formatted as follows (please note the punctuationand capitalisation):
The list of references at the end of the paper should be given in order of their first appearance in the text. All authors should be included in reference lists unless there are more than 6, in which case only the first 3 should be given, followed by "et al." in English and "ve ark." in Turkish references.

The number of references should not be more than 60 in original articles, not more than 100 in review articles, not more than 20 in case reports and not more than 5 in letter to editor. The journal requires DOI numbers, when available, to be included in all references. Personal experiences and researches without a DOI number should not be used.

In order to arrange the reference list easly, our journal suggest the use of reference arrangement programmes such as EndNote or Mendeley etc.).

For a reference in the reference list, the surname of author, the first letter of author's name, the title of the reference, the name of the journal, the year of the journal, the numbers of its volume, issue and pages should be written. The name of the journal should be abbreviated as in AMA (American Medical Association) ((http://library.nymc.edu/informatics/amastyle.cfm). If the abbreviation is not avalible, whole name of the journal should be written.

Published papers

Yoldas O, Bulut A, Altindis M. Current Approach to Hepatitis A Infections. Viral Hepatit J 2012; 18: 81-86..
Debes-Marun CS, Dewald GW, Bryant S, et al. Chromosome abnormalities clustering and its implications for pathogenesis and prognosis in myeloma. Leukemia. 2003;17:427–436.
Ozcelik F, Oztosun M, Gülsün M, ve ark. Pseudothrombocytopenia due to EDTA in a case with idiopathic thrombocytopenic purpura. Turk J Biochem. 2012;37(3):336–339.

Gage BF, Fihn SD, White RH. Management and dosing of warfarin therapy. Am J Med. 2000;109(6):481- 488. doi:10.1016/S0002-9343(00)00545-3.

If a supplement of a journal is referred, (suppl.) in English and (ES) in Turkish manuscripts should be used.

Electronic journal articles

If a journal from a website is used, the date of publishing is used. Usually, there is no numbers of volume, issue or pages. The web adress and date of download should be given.

Example:

Acetaminophen poisoning. In: DynaMed [database online]. EBSCO Information Services. http://0-search.ebscohost.com.topcat.switchinc.org/login.aspx?direct=true&site=DynaMed&id=113862.

Updated

March 09, 2010. Accessed March 23, 2010.

Book

Harmening D. Modern Blood Banking & Transfusion Practices. 6th ed. Philadelphia, PA: F.A. Davis Company; 2012.
Strunk W Jr., White EB. The Elements of Style. 4th ed. New York, NY: Longman; 2000.
Chapter in a book
Solensky R. Drug allergy: desensitization and treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. Allergens and Allergen Immunotherapy. 3rd ed. New York, NY: Marcel Dekker; 2004:585-606.
McCall RE, Tankersley CM. Phlebotomy and specimen considerations. In: Bishop ML, Fody EP, Schoeff LE, editors. Clinical Chemistry: Techniques, Principles, Correlations. Philadelphia, PA, USA: Lippincott Williams & Williams; 2010:33-73.

Conference proceedings

Weber KJ, Lee J, Decresce R, Subjasis M, Prinz R. Intraoperative PTH monitoring in parathyroid hyperplasia requires stricter criteria for success. Paper presented at: 25th Annual American Association of Endocrine Surgeons Meeting; April 6, 2004; Charlottesville, VA.

Chu H, Rosenthal M. Search engines for the World Wide Web: a comparative study and evaluation met-

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hodology. Paper presented at: American Society for Information Science Annual Conference; October 19-24, 1996; Baltimore, MD. http://www.asis.org/annual-96/electronicproceedings/chu.html. Accessed February 26, 2004.

Theses

Fenster SD. Cloning and Characterization of Piccolo, a Novel Component of the Presynaptic Cytoskeletal Matrix [master's thesis]. Birmingham: University of Alabama; 2000.

Publication Policy and Manuscript Evaluation Process

A. Double-blinded peer-reviewed method

Biotechnology and Strategic Health Research (J BSHRS) is published 3 times a year (April, August, December) and it is double-blinded peer-reviewed system national journal.

Editorial and publication processes of the BSHRS Derg. are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE). The journal is in conformity with Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice). Processing and publication is free of charge with the Biyoteknolojik ve Stratejik Sağlık Araştırmaları Dergisi. Authors are not charged a fee at any point during the publication process. All manuscripts should be submitted through the journal's web page at http://dergipark.gov.tr/bshr.

For the evaluation of papers, at least two referees are determined considering the content of the manuscript or the professional scientific area of the referees. In this step, referee assessment form is sent via internet without names. The personal data of the referee is not shown since the double-blind peer-reviewed method is used. Upon request, a written document given to referee as the referee for that contribute to the journal. The authors cannot directly contact with the referees. The referee's evaluation report is sent by the journal management system. The evaluation forms and the referees' reports are sent to the corresponding author(s) by the editor.

B. Decision process

After the referees' evaluation process, the editor decides whether the manuscript will be accepted or not considering the accuracy and the importance of the work, referee's reports, copyright infringement and ethical problems such as plagiarism.

As the editor decides about the manuscript, he or she may require the suggestions of the other member of editorial board or referees.

C. Instancy

A referee invited to the journal for the evaluation of a manuscript should inform the editor about the acceptance in 7 days. The referee should complete the evaluation in 15 days and the corresponding author(s) should download the revised manuscript in 15 days. The requested reading time for the last version of the manuscript by the corresponding author is only 3 days.

D. Confidentiality (Privacy Statement)

Personal information such as names and electronic mail addresses are only used for the scientific purposes of the journal. Other than these purposes this information will not be used and will not be shared with the third parties. The manuscripts sent to referees for assessment are kept as confidential documents. The manuscripts are not shown to other people and the contents of them should not be discussed. If it is necessary, reviewers may need suggestions from their colleagues after editorial permission. The editor may give that permission only in the presence of exceptional condition. The confidentiality rules are also valid for the referees not accepting the assessment of the manuscript.

E. Objectivity principles

In the evaluation process, no personal criticism of the authors should be done. The evaluations should contribute to the development of works and be objective.

F. Citation to reference

The referees should inform the authors if there are any citations that are not referred in the manuscript. The referees should pay particular attention to the citations that do not refer to the subject or to the citations that coincide with similar works. The referees should inform the editors if any publications that have similarity to any previously published work or information are recognized.

G. Information and Conflict of Interest

The referees should not agree to make any evaluation if they have any relation with any author, company or institution in which they are tasked to evaluate their work and inform the editor. The referees may not use the unpublished works or sections of the works submitted for evaluation in their own work without the written consent of the author(s). The information and ideas obtained during the assessment should be kept secret by the referees and should not be used for their own interests. These rules include those who refuse the manuscript assessment.

H. Prevention of Plagiarism

J of Biotechnology and Strategic Health Research(J of BSHR) reports the similarity rates of the articles through the iThenticate and Turnitin programs and shows the care and sensitivity required to prevent plagiarism.

THE WITHDRAW OF THE ARTICLE MUST BE WITH THE APPROVAL OF ALL AUTHORS.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLES*

OLGU SUNUSU / *CASE REPORTS*

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DOI:10.34084/bshr.989891 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Review / Derleme

http://dergipark.org.tr/tr/pub/bshr

SARS-CoV-2 Infection and Liver Involvement

SARS-CoV-2 Enfeksiyonu ve Karaciğer Tutulumu

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Öz

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, single-stranded RNA virus that can also be transmitted from person to person via the droplet (secretions shed when speaking, sneezing, or coughing) route, suspended droplet nuclei, and the mucous membranes of the eyes, nose, and mouth after touching a contaminated surface. It enters the cells through the angiotensin converting enzyme 2 (ACE- 2) receptor. Although non-specific respiratory symptoms such as fever, loss of smell/taste, runny nose, and cough are most common, SARS-CoV-2 can lead to a systemic and multiorgan involvement, including the gastrointestinal tract. The liver is the second most frequently involved organ after the lung. Gastrointestinal symptoms such as diarrhea, anorexia, nausea, vomiting, loss of appetite and abdominal pain are also common. Abnormal liver function enzyme levels may also be observed. The liver is affected by direct infection of hepatocytes, medical therapy of the management, or by indirect means if there is an underlying co-morbid disease. However, there are significant differences between studies in the reporting of gastrointestinal and liver symptoms. The most frequently reported gastrointestinal symptom in COVID-19 disease is diarrhea, reported in 1-36% of patients. In this review, it is aimed to review the current data on the effects of COVID-19 on the liver.

Anahtar Kelimeler COVID-19, hepatitis, AST, ALT, childhood.

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) insandan insana damlacık yolu (konuşurken, hapşırırken veya öksürürken saçılan sekresyonlar vb.), asılı damlacık çekirdekleri ve kontamine yüzeylere dokunma sonrası gözler, burun ve ağız mukozası ile temas sonrası bulaşabilen zarflı, tek zincirli bir RNA virüsüdür. Hücrelere anjiotensin converting enzim 2 (ACE- 2) reseptör aracılığı ile girmektedir. En sık ateş, koku/tat kaybı, burun akıntısı ve öksürük gibi non-spesifik solunum yolu semptomları görülse de SARS-CoV-2 enfeksiyonu gastrointestinal sistemi de içeren sistemik ve çoklu organ tutulumu ile giden bir tabloya yol açabilir. Karaciğer, akciğerden sonra ikinci sık tutulan organdır. İshal, anoreksi, mide bulantısı, kusma, iştah kaybı ve karın ağrısı gibi gastrointestinal semptomlar da sık görülmektedir. Anormal karaciğer fonksiyon enzim düzeyleri de gözlenebilir. Karaciğer hepatositlerin direk enfekte olmasıyla, tedavide kullanılan ilaçlar üzerinden ya da altta yatan bir ko-morbid hastalık varsa indirekt yollar ile etkilenir. Bununla beraber, gastrointestinal ve karaciğer semptomlarının bildirilmesinde, çalışmalar arasında ciddi farklılıklar söz konusudur. COVID-19 hastalığında da en sık bildirilen gastrointestinal semptom ishal olup, hastaların %1-36'sında bildirilmiştir. Bu derlemede COVID-19 hastalığının karaciğer üzerindeki etkilerine ilişkin güncel verilerin gözden geçirilmesi amaçlanmıştır.

Keywords *COVID-19, hepatit, AST, ALT, çocukluk çağı*

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen of 2019 novel coronavirus disease (COVID-19), has posed a serious threat to public health all over the world. The World Health Organization (WHO) has declared the outbreak of SARS-CoV-2 infection an international public health emergency. Respiratory system has been considered as the major damage caused by SARS-CoV-2 infection. However, gastrointestinal system has also been reported to occur during the course of the disease in severe cases.[1] It is not clear if the reason lay with the virus or the medications used in treatment of it. Also unclear is if COVID-19 makes existing liver disease worse.

SARS-CoV-2, the causative agent of the new coronavirus disease (COVID-19), which started in Wuhan, China in December 2019, has so far infected approximately 239.5 million people and caused a pandemic that resulted in the death of 4.89 million people.[1] SARS-CoV-2 infection is an RNA virus transmitted by droplet route. It enters cells via angiotensin converting enzyme 2 (ACE-2) receptor.[2,3]

The symptoms and severity of COVID-19 varies widely, but the majority of patients present with flu-like symptoms such as fever, cough, malaise, dyspnea, anosmia, and loss of taste.[4,5] Although mild symptoms are seen in most of the cases, it causes the development of acute respiratory distress syndrome (ARDS) in some patients. The course of the disease varies according to the patient's age, immune status and co-morbid diseases (hypertension, diabetes, chronic obstructive pulmonary disease, etc.). The incidence of severe disease has increased, especially in patients with co-morbidities. The incubation period is 2-11 days for other SARS viruses, while it is 4-5 days for SARS-CoV-2 disease. Symptoms may appear within 1-14 days of contact with the virus, but they're most common on the 4th and 5th days.[4-6] There are studies showing that asymptomatic patients are also contagious.[7]

Nucleic acid amplification methods (real-time reverse-transcriptase polymerase chain reaction, rRT-PCR), serological tests and computed tomography (CT) findings of SARS-CoV-2 RNA in nasopharyngeal and oropharyngeal swab samples are the most commonly used methods in the diagnosis of COVID-19.[8,9] In the identification and confirmation of COVID-19 cases; the rRT-PCR test is accepted as the gold standard test and is frequently used method in line with the protocol prepared by the World Health Organization (WHO).[10]

Since antibody tests cannot be used at an early stage in acute infection, their use in clinical diagnosis is limited. Tests which show antibody responses can be used for retrospective diagnosis by detecting the elevation of antibody levels in blood samples that are taken from patients in acute and convalescent periods in patients with negative SARS-CoV-2 RT-PCR results but with strong suspicion of COVID-19 disease.[7-11]

Other Coronaviruses, SARS-CoV-2 and Gastrointestinal System

In previous studies about SARS and Middle East Respiratory Syndrome (MERS) patients; it was determined that corona viruses invaded the gastrointestinal tract. In a study conducted in 2004, it was shown that SARS-CoV RNA was also detected in stool samples.[8] SARS- COV-2 shares the same genome structure 82% with SARS-CoV and 50% with Middle East Respiratory Syndrome Coronavirus (MERS-CoV).[12]

A study in 2003, electron microscopic examination of autopsy and biopsy materials of the SARS virus showed that the virus was actively replicating in the small and large intestines.[13] Similarly, in a study conducted in 2017, MERS-CoV virus was shown to cause enteric infection and show high affinity to intestinal epithelium.[14] It has been shown that SARS-CoV-2 can colonize the gastrointestinal tract like other coronaviruses as a result of the detection of the first coronavirus case in the United States (USA) from sto-

ol and respiratory tract materials by rRT-PCR in 2020.[15]

In a meta-analysis, higher Ferritin values were found in patients with severe disease and deceased patients when patients with severe disease and mild disease were compared. It has been observed that there is a relationship between severe acute liver injury and high Ferritin value.[16] Similar to cytokine release, immune activation and inflammation caused by some systemic viral infections, high laboratory values (pro-inflammatory values and cytokine values) of COVID-19 patients have been detected.[17,18] Albumin is a negative acute phase reactant which is synthesized by the liver, has a down-regulation effect on ACE-2 receptors. It suggests that hypoalbuminemia may be associated with increased mortality. The reason for the increase in AST, ALT, bilirubin, GGT and ALP is not known exactly, but it should be kept in mind that liver damage due to the use of multiple drugs such as anti-virals, antibiotics, antipyretics and analgesics used in the treatment with cytokine storm may also have a possible effect on the deterioration in laboratory tests.[19]

It has been shown in many studies that COVID-19 disease affects different systems such as the cardiovascular system, nervous system and gastrointestinal system. It has been determined that SARS-CoV-2 has a very high affinity for the ACE-2 receptor.[7, 11-14, 20-23] SARS-CoV-2 also enters the cells of the gastrointestinal tract via ACE receptors. The abundance of ACE-2 receptors in the gastrointestinal tract (hepatocytes and cholangiocytes) makes it a potential target for SARS-CoV-2 disease. Kuppfer cells, on the other hand, do not have ACE-2 receptors. Biopsy results of patients infected with SARS-CoV-2 and undergoing liver biopsy showed an increase in the number of mitosis and ballooning degeneration in hepatocytes. This suggests that COVID-19 disease may induce apoptosis of hepatocytes. On the other hand, Kuppfer cells do not have ACE-2 receptors. Biopsy results of patients infected with SARS-CoV-2 and undergoing liver biopsy showed an increase in the number of mitosis and ballooning degeneration in hepatocytes. This suggests that COVID-19 disease may induce apoptosis of hepatocytes.

In a study conducted with children infected with SARS-CoV-2, liver transaminases were found to be higher in children less than 3 years of age than in children over 3 years of age.[24] This suggests that it may be related to the immature immune system. Data are limited because SARS-CoV-2 infection in children is mostly asymptomatic. The effect of cytokine storm (IL-6 and IL-10) is great in liver damage seen in adults. IL-6 and IL-10 values of children infected with SARS-CoV-2 were found to be similar in those with normal and high transaminase values.[24] While fatigue, fever and joint pain were detected in addition to respiratory system complaints in COVID-19 patients, gastrointestinal system symptoms such as anorexia, diarrhea, vomiting and abdominal pain were reported in many patients (figure 1). According to the data obtained from the analysis of published case series and studies related to the COVID-19 pandemic, 3% -79% of patients have gastrointestinal symptoms.[25] While the most common gastrointestinal symptom in adults was anorexia, diarrhea was the most common gastrointestinal symptom in both adults and children.

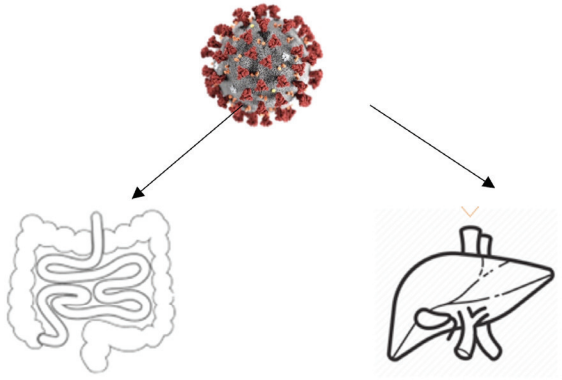

Figure 1: *Gastrointestinal system involvement and findings*

COVID-19 and Reflection of Liver Involvement in the Clinical Practice

Development of liver damage in COVID-19 patients is reflected in the laboratory as an increase in liver function enzymes (AST, ALT, bilirubin, etc.) and a decrease in serum albumin value. This has brought to mind the question of whether markers can be used to determine the severity and prognosis of COVID-19 disease, and many retrospective studies have been conducted on this subject. Various studies have reported that 14% -53% of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values may increase during the course of the disease, accompanied by a mild increase in bilirubin.[14]

The Mechanism of Liver Injury

The mechanism of liver damage hasn't clearly known, it is thought that it may cause direct invasion of hepatocytes by viruses, immune-mediated damage, toxicity of drugs used in the treatment, hypoxia, ischemia, systemic inflammatory syndrome (SIRS), sepsis, or exacerbation of underlying liver disease.[26] It has been determined that ACE-2 receptors, which are the target receptors for SARS-CoV-2, are highly expressed in epithelial cells of the gastrointestinal tract (gastric, duodenal and rectal).[4,5] ACE-2 receptors can be expressed in hepatic cholangiocytes and hepatocytes.[6] These receptors make gastrointestinal tract as a target for SARS-CoV-2 infection, which can actively infect and replicate. The intense affinity of the SARS-CoV-2 virus, especially to cholangiocytes, it's high binding rate to the ACE-2 receptor and it suggest that it's associated with impaired liver function.[12] In a meta-analysis of 3.772 patients obtained from 326 studies examining, SARS-CoV-2 and liver damage, it was concluded that there is a relationship between liver dysfunction and mortality.[27]

Medications such as hydroxychloroquine, immune modulators (tocilizumab, steroids, anakinra), anti-retroviral medications (remdesivir, favipravir, lopinavir), antibiotics (azithromycin, ceftriaxone) and antipyretics (paracetamol, ibuprofen), which are used in the treatment of COVID-19 disease, also have hepatotoxic effects. Patients are recommended to have close follow-up who have treatment with single and/or combined use of these potential hepatotoxic medications for possible liver damage.[26,28]

Histo-Pathology of Liver Injury

Moderate microvascular hepatosteatosis, mild portal and lobular activity were detected in liver biopsy material taken from a patient who died as a result of COVID-19 infection.[29] In another study, autopsy of four patients who died due to COVID-19 revealed mild sinusoidal dilatation in the middle zone of the liver, patchy hepatic necrosis and a slight increase in sinusoidal lymphocytes in the liver biopsy taken from the other two cases, direct SARS-CoV-2 RNA was detected.[30]

Clinical and Laboratory Findings of Liver Damage (Hepatitis) Due to COVID-19

In a study by Tian SF et al. with 148 COVID-19 patients; elevated liver function enzymes were found in 4 patients (37.2%).[12] Another study by Zhang et al. with 56 COVID-19 patients; showed an increase gamma-glutamyl transferase (GGT) value in 54% of the cases.[26] Liver function enzymes were elevated in 45 of 93 patients whose liver function enzymes were normal at the time of admission. The rate of use of lopinavir / ritonavir was higher and the length of hospital stay was longer in patients with elevated liver function enzymes.

In a study involving patients with COVID-19 in China, elevation in liver tests (AST, ALT, total bilirubin, GGT, etc.) was found in 76.3% of the patients, and this elevation was found in 21.5% of the patients while they were hospitalized. It has been reported to occur in the first two weeks. In another study, it was found that patients with biochemical findings suggestive of hepatocellular or mixed-type liver injury upon admission to hospital had a higher risk of progression to serious disease during their hospitalization.[31] In another study, liver function enzymes were found

to be elevated in 29% of deaths related to COVID-19.[32]

In a multicenter study of 1.099 patients, high AST levels were found in 112 (18%) patients without severe disease and 56 patients (39.4%) with severe disease. In addition, the rate of high ALT (28%) in patients with severe disease was found to be higher than those with mild disease (20%).[33] In another study, approximately half of the patients were found to have elevated GGT levels.[34]

Especially in studies from China, nearly half of the patients had gastrointestinal symptoms such as diarrhea, nausea, vomiting and abdominal pain, 20%-50% of COVID-19 patients had positive PCR testing in their stools, and SARS-CoV-2 was detected in some of the cases. It has been reported that it can be detected in feces for a long time (up to 30 days). This indicates that the coronavirus is excreted in the feces. Updated data have determined that SARS-CoV-2 RNA can be isolated from anal/rectal swabs and stool.[35,36]

Follow-up of Liver Damage (Hepatitis) due to SARS-CoV-2 in the Clinic

In most of the studies, it has been reported that liver dysfunction is mild, self-limiting, spontaneously regressed with supportive treatment, and has no effect on the course of COVID-19 disease.[37] Elevated levels of serum transaminase enzymes have also been explained by hepatotoxicity of drugs used in the treatment, cytokine storm and/or hypoxia associated with pneumonia.[37,38] The rate of liver dysfunction is not known exactly because there is not enough study with pediatric patients yet. It is known that children infected with SARS-CoV-2 infection have a milder disease and have a better prognosis than adults.

In a study conducted with 10 children born to mothers with COVID-19 pneumonia, elevated liver enzymes were found in only two children.[39] Rarely, mild increases in ALT and AST levels have been found in children infected with COVID-19. Because they are found to be normal in the vast majority of cases, the American Association for Liver Diseases Research recommends that all children with elevated liver enzymes must be evaluated for underlying liver diseases.[40] In addition; COVID-19 infection is more risky in chronic liver disease because of the immunosuppression in these patients. The effect of SARS-CoV-2 infection on the liver was more common in patients with non-alcoholic fatty liver disease and those with chronic liver disease.

Liver dysfunction has also been found in pediatric patients with COVID-19 infection.[37] In a study conducted with asymptomatic COVID-19 positive pediatric patients, isolated liver function enzymes were found to be elevated, and no other pathology was detected during their follow-up. The liver function test values of these patients regressed with supportive treatment, and they did not need further treatment.[1-5]

In COVID-19 disease patient who progresses with mild hepatic transaminase elevation; should be treated and liver enzymes must be closely monitored.

CONCLUSION

It has been determined that SARS-CoV-2 infection may be associated with different degrees of abnormal liver function tests, especially with transient and mildly elevated serum transaminase levels. It should be kept in mind that SARS-CoV-2 infection can also be seen in children as non-icteric hepatitis accompanying by mild upper respiratory tract infection. However, there are many studies that suggest that patients with chronic hepatitis, autoimmune liver diseases, or liver transplants patients more likely to progress severe COVID-19 disease. Therefore, close follow-up of liver function tests is recommended after the diagnosis of COVID-19 disease, especially in patients infected with SARS-CoV-2, who are in the risk group. Patients who do not have a known disease before, the causes of another underlying disease that may cause abnormal liver function enzymes should be considered, and further examination should be performed for differential diagnosis.

Declaration of Conflicting Interests

The authors declare that they have no conflict of interest.

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Author Contributions

MÇ and DÇ designed, wrote the article and reviewed the literature. ÖÖ contributed to writing and supervised/revised the article.

Kaynaklar

1. WHO Coronavirus (COVID-19) Dashboard, Situation by Region, Country, Territory & Area https://covid19.who.int/table
2. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271-280.e8. doi:10.1016/j.cell.2020.02.052
3. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020; 12(1):8. doi: 10.1038/s41368-020-0074-x.
4. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 382(18):1708-1720. doi: 10.1056/NEJMoa2002032.
5. Centers for Disease Control and Prevention (2020). People who are at higher risk for severe illness https://www.cdc.gov/coronavirus/2019-ncov/need-extraprecautions/people-at-higherrisk.html (Accessed on April 01, 2020).
6. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis. 2020; 20(6):689-696. doi: 10.1016/S1473-3099(20)30198-5.
7. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020;382(10);970-1. https://doi.org/10.1056/nejmc2001468.
8. Li D, Wang D, Dong J, et al. False-negative results of real-time reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome coronavirus 2: Role of deep-learning-based ct diagnosis and insights from two cases. Korean J Radiol. 2020;21(4):505-8. doi: 10.3348/kjr.2020.0146.
9. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020; 20(5):453-4. https://doi.org/10.1080/14737159.2020.1757437
10. WHO. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. Interim guidance 1-7, World Health Organization. [https://apps.who.int/iris/handle/10665/331501] (Accessed on 19/01/2021).
11. Hung IF, Cheng VC, Wu AK, et al. Viral loads in clinical specimens and SARS manifestations. Emerg. Infect. Dis. 2004; 10(9):1550-7. doi: 10.3201/eid1009.040058.
12. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol. Hepatol. 20205(5):428-430. doi: 10.1016/S2468-1253(20)30057-1.
13. Leung WK, To KF, Chan PK, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology 2003; 125(4):1011-7. doi: 10.1016/s0016-5085(03)01215-0.
14. Zhou J, Li C, Zhao G, et al. Human intestinal tract serves as an alternative infection route for Middle East respiratory syndrome coronavirus. Sci. Adv. 2017; 3(11):eaao4966. doi: 10.1126/sciadv.aao4966.
15. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med. 2020;382(10):929-936. doi: 10.1056/NEJMoa2001191.
16. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020 28; 395(10229): 1054–1062. doi: 10.1016/S0140-6736(20)30566-3.
17. García de Guadiana-Romualdo L, Morell-García D, Morales-Indiano C, et al. Characteristics and laboratory findings on admission to the emergency department among 2873 hospitalized patients with COVID-19: the impact of adjusted laboratory tests in multicenter studies. A multicenter study in Spain (BIOCOVID-Spain study). Scand J Clin Lab Invest. 2021; 81(3):187-193. doi: 10.1080/00365513.2021.1881997.
18. Pourbagheri-Sigaroodi A, Bashash D, Fateh F, et al. Laboratory findings in COVID-19 diagnosis and prognosis. Clin Chim Acta. 2020;510:475–82. doi: 10.1016/j.cca.2020.08.019.
19. Doğan Ö, Devrim E. Tanı ve İzlemde Laboratuvar Testleri. COVID-19 içinde Ed: Memikoğlu O, Genç V. E-Kitap Ankara Üniversitesi Basımevi, 2020; 35-40
20. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. New Engl J Med. 2020;382(8):727-733. doi: 10.1056/NEJMoa2001017.
21. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020; 181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052.
22. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020; 395(10224):565-574. doi: 10.1016/S0140-6736(20)30251-8.
23. Walls AC, Park YJ, Tortorici MA, et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell 2020; 181(2):281-292.e6. doi: 10.1016/j.cell.2020.02.058
24. Zhou YH, Zheng KI, Targher G, et al. Abnormal liver enzymes in children and infants with COVID-19: A narrative review of case-series studies. Pediatr Obes. 2020; 15(12): e12723. doi: 10.1111/ijpo.12723.
25. Tian Y, Rong L, Nian W, et al. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther. 2020; 51(9): 843-851. doi: 10.1111/apt.15731.
26. Xu L, Liu J, Lu M, et al. Liver injury during highly pathogenic human coronavirus infections. Liver Int. 2020;40(5):998-1004. doi: 10.1111/liv.14435.
27. Zeng-hong W. Dong liang Y. A meta-analysis of the impact of COVID-19 on liver dysfunction. Eur J Med Res. 2020;25(1):54. doi: 10.1186/s40001-020-00454-x.
28. Olry A, Meunier L, Délire B, et al. Drug Induced Liver Injury and COVID 19 Infection: The Rules Remain the Same. Drug Saf. 2020; 43(7):615-617. doi: 10.1007/s40264-020-00954-z.
29. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet Respir Med. 2020;8(4)420-422. doi: 10.1016/S2213-2600(20)30076-X.
30. Tian SF, Xiong Y, Liu H, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through post-mortem core biopsies. Modern Pathology. 2020; 33(6):1007-1014. doi: 10.1038/s41379-020-0536-x.
31. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395(10223): 507-513. doi: 10.1016/S0140-6736(20)30211-7.
32. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N. Engl. J. Med. 2020. 382(18):1708-1720. doi: 10.1056/NEJMoa2002032 .
33. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir. Med. 2020; 8(5):475-481. doi: 10.1016/S2213-2600(20)30079-5.
34. Schaefer EAK, Arvind A, Chung RT, et al. Interrelationship Between Coronavirus Infection and Liver Disease. Clinical Liver Disease 2020; 15(5):175-180. doi: 10.1002/cld.967.
35. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg. Microbes. Infect. 2020; 9: 386- 389. doi: 10.1080/22221751.2020.1729071.
36. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. Nat. Med. 2020. 26(4):502-505. doi: 10.1038/s41591-020-0817-4.
37. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. Lancet Gastroenterol Hepatol 2020; 5: 529-530. doi: 10.1016/S2468-1253(20)30084-4.
38. Wu J, Song S, Cao HC, Li LJ. Liver diseases in COVID-19: Etiology, treatment and prognosis. World J Gastroenterol 2020; 26: 2286-2293. doi: 10.3748/wjg.v26.i19.2286.
39. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr. 2020;9:51-60. doi: 10.21037/tp.2020.02.06.
40. American Association for the Study of Liver Diseases . Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic. https://www.aasld.org/about-aasld/covid19-resources. Accessed April 14, 2020.

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Investigation of COVID-19 Vaccine Hesitation In Turkey with Youtube Analysis Method

Türkiye'de COVID-19 Aşı Tereddüdünün Youtube Analiz Yöntemi Ile Araştırılması

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Abstract

Aim Nowadays many people search the internet to gain health information including Coronavirus disease 2019 (COVID-19) vaccines. YouTube™ is one of the most widely used websites. However, the quality and accuracy of health-related YouTube™ videos are still controversial. In this study we aimed to research the COVID-19 vaccine hesitation in Turkey by using YouTube analyses method.

Material and Method In this study, "COVID 19" OR "coronavirus" OR "SARSCOV 2" 'and "vaccine" OR "vaccination" and "vaccine hesitancy" OR "vaccine hesitation" keywords were used to search videos on YouTube™. Firstly, non-Turkish videos and duplicate videos were excluded. Some details about videos such as duration (seconds), view count, number of comments, total likes/ dislikes were recorded. DISCERN (Quality Criteria for Consumer Health Information), JAMA (Journal of the American Medical Association) scores, and Video Power Index (VPI) values of the videos were calculated.

Results Most of the videos were uploaded by news agencies (48%). DISCERN scores of the videos were ranged between very poor and good. The mean JAMA score was found 2.9 that is accepted as a high score. There was a statistically significant difference in the VPI and JAMA scores among videos' sources ($p < 0,05$).

Conclusion Vaccine hesitation can be reduced by increasing the quality of the video content prepared by academic and governmental organizations. The correct use of YouTube videos in community vaccination behaviours can play an important role in the spread of COVID 19 among the community and help control the pandemic.

Keywords YouTube analysis, COVID-19, vaccine, anti-vaccination, community behaviours, Turkey.

Özet

Amaç *Günümüzde pek çok kişi, Coronavirüs hastalığı 2019 (COVID-19) aşıları da dahil olmak üzere sağlık bilgilerine ulaşmak için internette arama yapmaktadır. YouTube en yaygın kullanılan web sitelerinden biridir. Bununla birlikte, sağlıkla ilgili YouTube videolarının kalitesi ve doğruluğu hala tartışmalıdır. Bu çalışmada, YouTube analiz yöntemini kullanarak Türkiye'deki COVID-19 aşı tereddütünü araştırmayı amaçladık.*

Gereç ve Yöntem *Bu çalışmada "COVID 19" VEYA "koronavirüs" VEYA "SARSCOV 2"" ve "aşı" VEYA "aşılama" ve "aşı tereddütü" VEYA "aşı kararsızlığı" anahtar kelimeleri kullanıldı. YouTube'da video aramak için ilk olarak, Türkçe dilinde olmayan videolar ve yinelenen videolar hariç tutuldu. Videolarla ilgili süre (saniye), izlenme sayısı, yorum sayısı, toplam beğeni/beğenmeme gibi bazı detaylar kaydedildi. Videoların DISCERN (Quality Criteria for Consumer Health Information), JAMA (Journal of the American Medical Association) puanları ve Video Güç İndeksi (VPI) değerleri hesaplandı.*

Sonuçlar *Videoların çoğu haber ajansları tarafından yüklendi (%48). Videoların DISCERN puanları çok kötü ile iyi arasında değişiyordu. Ortalama JAMA puanı 2.9 olarak bulundu ve yüksek puan olarak kabul edildi. Videoların kaynakları arasında VPI ve JAMA puanlarında istatistiksel olarak anlamlı bir fark vardı ($p < 0,05$).*

Sonuç *Akademik ve resmi kuruluşlar tarafından hazırlanan video içeriklerinin kalitesi artırılarak aşı tereddütü azaltılabilir. Topluluk aşılama davranışlarında YouTube videolarının doğru kullanımı, COVID 19'un topluluk arasında yayılmasında önemli bir rol oynayabilir ve pandeminin kontrol altına alınmasına yardımcı olabilir.*

Anahtar Kelimeler *YouTube analizi, COVID-19, aşı, aşı karşıtlığı, toplum davranışları, Türkiye.*

INTRODUCTION

Since December 2019, when the first case was detected, coronavirus disease 2019 (COVID-19) has affected 188 countries, causing 111,821,203 confirmed cases and 2,475,140 deaths.[1] The COVID 19 pandemic has caused behavioral changes in individuals in the social field as well as in the health field. As in every period, vaccines are re-inscribed into our social memory that every disease is evaluated with a bias at the beginning. A safe and effective COVID 19 vaccine was needed globally in a short time. For this, many countries worked in cooperation with many organizations.[2-6] Vaccination applications have started around the world. Positive and negative vaccine propaganda has also come to the fore with the vaccine. Hesitations about the vaccine prevent epidemic management like an iceberg. This iceberg includes public concerns about the safety and necessity of vaccines.[7]

Numerous YouTube content is viewed by people every day. YouTube, which is a website created in the year 2005 to provide free video sharing, is currently the most frequented internet site with 5.03 daily page views per visitor. Most of these views are for entertainment, although some are for educational purposes. This causes an increase in the number of videos added.[8] Today, health researchers and producers search the internet to gain health information about many vaccines, especially, including COVID-19 vaccines. However, with these videos such as the COVID-19 vaccine, panic behaviors may increase in society or misinformation can spread rapidly, as YouTube content is not always created by healthcare professionals, public institutions, or traditional media.[8] YouTube™ is one of the most widely used websites on the internet by Turkish people, too. However, the quality and accuracy of health-related YouTube™ videos are still controversial. Given the potential impact of this media on the transmission of health information, the primary purpose of this research was to identify the expressions of vaccine hesitation content on YouTube and to determine the effects of YouTube videos broadcast from Turkey on viewers, especially by comparing the expression of pro-vaccine and anti-vaccine sentiments. We also aimed to research the quality and accuracy of COVID-19 vaccine-related videos on YouTube™ as a secondary purpose.

MATERIALS and METHODS

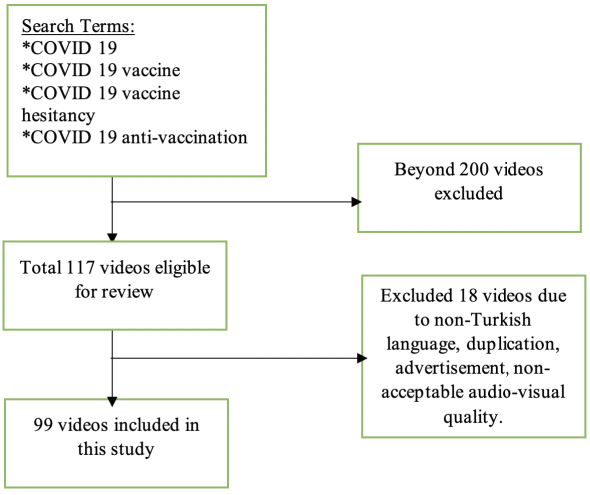
Data collection

In the present study, YouTube (https://www.YouTube.com) was searched using the keywords "COVID 19" OR "coronavirus" OR "SARS COV 2" and "vaccine" OR "vaccination" and "vaccine hesitancy" OR "vaccine hesitation" on March 15, 2021. The keywords of the research submitted to the YouTube™ search bar. The videos were analyzed by three researchers.

Firstly, non-Turkish videos and duplicate videos were excluded. Videos duplicated, shorter than 60 seconds, irrelevance, and nonrelated to research subjects were excluded and eliminated. In this study, the sample size was calculated at a 95% confidence level using the G*Power 3.1.9.2 program.[9] For the analysis, the minimum sample volume was calculated to be 60 seconds using a 0.80 power and 0.50 effect size. To reach the predetermined sample size (168), 200 videos had examined.

The inclusion criteria for the videos were as follows: Turkish language, primary content related to study, and acceptable audio-visual quality.

The following types of videos were excluded from the study: non-Turkish language, duplicate, advertisement, poor audio-visual quality. Search methodology was summarized in the Flow chart.



Flow chart. Search methodology for YouTube videos.

The data consisted of the video's duration, total views, comments, likes and dislikes, source of videos (society/non-profit organization, physician, patient/independent user, and news agency) were noted for each video in Excel form created by researchers.

The reliability, educational features, and quality of video contents were assessed using the modified DISCERN score (mDISCERN) (Quality Criteria for Consumer Health Content) and the modified Journal of the American Medical Association (mJAMA) benchmark criteria as previous similar studies. [8,10-12]

The DISCERN tool was originally developed and validated in 1998 at the University of Oxford, United Kingdom. The aim was to analyze written medical information with 15 questions in terms of reliability and details on treatment (score of 1–5 for each question).[8,10] The DISCERN scoring system is ranged from 15 to 75 points and is classified into five categories as below.[8,10-12]

- Excellent (63–75 points),
- Good (51–62 points),
- Fair (39–50 points),
- Poor (27–38 points),
- Very poor (15–26 points).

Similarly, Journal of the American Medical Association (JAMA)[8,10,11,12] and video power index (VPI) ratings are all widely used for evaluating health information on the internet. Therefore, in our study additionally, the video power index (VPI) method was used to analyze the videos' power on YouTube [VPI: (VPI =number of likes / (number of likes + number of dislikes) × 100)].[1]

Authorship (authors, editors, affiliations, and credentials), attribution (references and sources used for the content and copyright material), disclosures (sponsorship, ads, commercial support, and possible conflicts of interests), and currency (dates of posted and amended information) are the four metrics used by JAMA benchmark to assess the accuracy of online information.[14] The scale's ranking ranges from 0 to 4, with 0 being the lowest and 4 being the highest. Higher scores indicate that the information being analyzed is of higher quality.[14]

All these scores were preferred because they were used in a similar study previously conducted. [8,10-14]

YouTube contents, and view numbers, like and dislike numbers, region of uploading, qualification of uploaders, and presence of animation were recorded for YouTube videos.

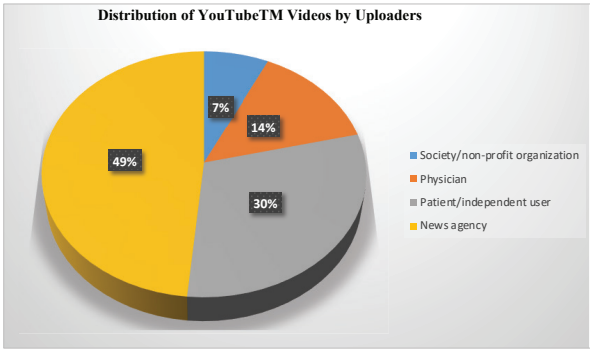
Statistical analyses

Statistical analysis of the data obtained in this study was performed using SPSS Statistics for Windows, Version 26.0 (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM.). Continuous variables are given with descriptive minimum, maximum, mean, and standard deviation values. Categorical variables are given as frequency (n) and percentage (%). Data normality test was analyzed using the Kolmogorov-Smirnov test. Since the data had normal distribution, evaluation of two independent variables was performed by parametric analysis methods such as Spearman correlation and ANOVA to examine the link between Variables. Interobserver agreement of JAMA and DISCERN scores was evaluated by using the Cronbach alpha

coefficient. $p < 0.05$ values were considered statistically significant. Moreover, in the present study, Cronbach's alpha coefficient value suggests a good internal consistency and exceeded the 0,70 value recommended.[9]

RESULTS

Of the 99 YouTube videos evaluated according to their source, 7,1% was uploaded by society/non-profit organization, 14,1% by physicians, 30,3% by patients, and independent users, and 48% was uploaded by the news agency. In addition, it was determined that the videos produced by the news agency were mostly watched and disliked (Graphic 1).



Graphic 1. Distribution and categorization of the reviewed videos according to uploaders.

Of the 99 YouTube videos, the mean number of views was 22087,141 ± 43,46 and were viewed 2,186,627 times. The maximum number of views was 222,195 and the minimum number of views was 875. Other video characteristics of videos are: The mean of video length is 427,78 (67-1397), the mean number of comments was 134,939 (0-1602), the mean number of likes was 630,263 (0-9332), the mean number of dislikes was 26,707 (0-319). 72 of the videos had positive and 7 negative content. The videos produced by the Society / non-profit organization received the highest rate of likes. Vaccine hesitation was present in 20 of the videos. Some videos had multiple contents (Table 1). The mean of total DISCERN of COVID-19 related YouTube was found 40.5 (min.-max.11-64). Accordingly, there was an agreement between the reviewers who assessed YouTube videos, in terms of total DISCERN score.

The mean JAMA score of the reviewed YouTube videos was found as 2.9 (min-max: 1–4). It showed that there was an agreement between the reviewers in terms of the JAMA scores of YouTube videos. And of the 99 YouTube videos, the mean VPI value was found 90,7(min-max:0-105,3) (Table 2).

From the first 117 videos identified, some were excluded because of duplication or irrelevance (22). The total DISCERN score of the 99 videos included was poor (average score 25.20). According to The DISCERN scoring system ranges and classifications the videos of this research are scored as very poor, poor, fair, or good. Excellent score ranges were not found in the sample (Table 3).[10]

The Journal of the American Medical Association (JAMA) ranking system contains four criteria for one possible point each and a cumulative possible score of four points (authorship, attribution, disclosure, and currency). A four-point score shows the best standard and highest quality.[9] As seen in Table 3 JAMA score is 2.9 that is the highest score (Table 3).

One-way ANOVA tests were used to compare the parameters between the groups according to the source of videos. As seen in Table 4 there was a statistically significant difference in the VPI and JAMA scores among videos' sources ($p < 0,05$). No statistically significant difference was found between YouTube videos in terms of the other DISCERN subscales and JAMA scores (for all videos' sources, $p > 0.05$). DISCERN, VPI and JAMA are analyzed as groups with ANOVA tests (Table 4).

VPI scores were found significant between groups ($p < 0,05$) and JAMA scores were found significant between groups ($p < 0,05$) but DISCERN scores was not found significant between groups($p>0,05$).

We analyzed and correlated DISCERN, VPI, and JAMA scores to examine the relationship between these variables. DISCERN, VPI, and JAMA scores of the videos were examined by the Pearson correlation analysis. Interestingly, a strong correlation was found between DISCERN and JAMA (p< 0,05;). However, the correlation between DISCERN and VPI; the correlation between JAMA and VPI was not found statistically significant (p>0,05) (Table 5). Moreover, Cronbach's alpha coefficient value was 0,84 that exceeding the 0.70 value recommended in the literature.

Table 1. Distribution of the videos' duration, view count, numbers of comments, likes, and dislikes.

Source of Videos	n	Duration (seconds)	Views	Comments	Likes	Dislikes
Society/non-profit organization	7	3443	500608	2922	18513	694
Physician	14	6107	330764	2162	14296	280
Patient/independent user	30	9737	491294	4030	17475	758
News agency	48	23063	863961	4245	12112	912

Table 2. Descriptive Statistics

	n	Minimum	Maximum	Mean	Std. Deviation
VPI score	99	0,00	105,33	90,70	13,37
JAMA Score	99	1	4	2,94	0,753
DISCERN score	99	12	51	25,20	11,61
Views	99	875	222195	22087,14	43464,63
Duration (seconds)	99	67	1397	427,78	291,89
Total likes	99	0	9332	630,26	1678,01
Total dislikes	99	0	319	26,71	56,74
Number of comments	99	0	1602	134,94	278,57
Opinion	99	1	3	1,57	0,812
Valid n (listwise)	99				

Table 3. DISCERN and JAMA scores

Total DISCERN Score (16-80)	
16-26 (very poor)	67
27-38 (poor)	12
39-50 (fair)	17
51-62 (good)	3
63-80 (excellent)	0
Average DISCERN score	25.2
Average number of JAMA benchmarks satisfied (0-4)	2.9

Table 4. VPI score, DISCERN score and JAMA scores according to sources.

		Sum of Squares	df	Mean Square	F	Sig.
VPI	Between Groups	2599,758	3	866,586	5,510	,002
	Within Groups	14940,355	95	157,267		
	Total	17540,113	98			
DISCERN	Between Groups	546,157	3	182,052	1,365	,258
	Within Groups	12673,803	95	133,408		
	Total	13219,960	98			
JAMA	Between Groups	14,314	3	4,771	10,970	,000
	Within Groups	41,322	95	,435		
	Total	55,636	98			
Valid n (listwise)		99				

Table 5. Correlation analysis of DISCERN, VPI and JAMA scores

		DISCERN	VPI	JAMA
DISCERN	Pearson Correlation	1	,178	,211*
	Sig. (2-tailed)		,078	,036
	N	99	99	99
VPI	Pearson Correlation	,178	1	,149
	Sig. (2-tailed)	,078		,142
	N	99	99	99
JAMA	Pearson Correlation	,211*	,149	1
	Sig. (2-tailed)	,036	,142	
	N	99	99	99

* Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

As a result of the high prevalence of COVID-19, an increasing number of patients/cases are expected to receive information about the vaccine and treatment of this disease. The internet and news agency are some of the most leading sources of information used for this purpose. This was the first study in the literature about evaluation of YouTube videos on Covid-19 vaccine hesitation by independent reviewers. According to the results of our study, approximately 50 % of COVID 19 vaccine related videos were uploaded by News agency, and overall quality of the contents was "very poor". The mean DISCERN score was calculated as>90. These findings were consistent with studies reporting low-quality videos about various COVID-19 vaccine. According to our study, there is a strong correlation was found between DISCERN and JAMA (p <0,05). Similarly in a study by Gokcen & Gumussuyu[13] evaluating YouTube videos pertaining to disc herniation, significant positive correlations have been reported for DISCERN and JAMA scores between the reviewers[9] and Aydin, & Aydin[15] evaluating the quality and reliability of information available on YouTube and Google pertaining to gastroesophageal reflux disease.

We analyzed and correlated DISCERN, VPI, and JAMA scores in order to examine the relationship between these variables by the Pearson correlation analysis. There was only was found a strong correlation between DISCERN and JAMA (p <0,05).

Moreover, Cronbach's alpha coefficient value was found 0,84 in our study. This value reflects high consistency

between the two raters/reviewers.

Due to the increasing number of people using YouTube to search for health-related information, public health policymakers should consider this method by which the public impact of these uses can be assessed. Therefore, analysis of social network data via web search can be effective in evaluating health concerns such as vaccines. Social platforms such as YouTube are known to be had the potential to influence people's health behaviors.[16,17]

YouTube analysis is one of the best methods to determine the attitude of society on a subject, and this analysis has been used for various medical and non-medical topics in previous years.[16,18] However, few studies have been done to understand how people use this social network for health purposes.[16,17] Limited similar studies on vaccine anti-vaccination, knowledge attitude about vaccination is encountered in the literature.[19,20] A YouTube analysis study was conducted on the vaccines made by Aquino et al.[21] from Italy. This study is one of the studies showing how web search trends and analysis of social network data represent vaccine hesitancy at the population level.[21] But no similar studies have been found on the topic of the COVID-19 vaccine, which has been applied globally due to the pandemic, although it is in the Phase 3 study. In addition, there is no similar YouTube analysis study conducted in our country about any vaccine. Our study is valuable in this area, especially because it reflects the data of our country, Turkey.

A study by Hernández-Garcia et al.[20] from Spain on the knowledge of influenza vaccination has been published very recently. A total of 100 videos were evaluated in this study, and it was determined that 74.0% were produced by mass media or health professionals. Of these videos containing 65.0% positive messages; the main issues were the benefits (59.0%) and side effects (39.0%) of the vaccine.[19] videos detected fraud. It has been determined that videos with user-generated content show a higher probability of fraud than healthcare professionals (Odds ratio (OR) = 15.56). This study included influenza videos between 2015-2020.[20] Our study included videos from the last months of 2020 and the first 2 months of 2021. The reason for this was that the effect of the pandemic was seen in our country on March 11, 2020, and the vaccine was just started to be applied. In our study, most of the videos were produced by news agencies (48%).
In a similar study conducted in Canada on vaccines, 56% of the video content was published by independent individuals.[22] In our study, when the uploaders of the videos are viewed, it was determined that 7,1% were uploaded by Society/non-profit organization, 14,1% by physicians, 30,3% by patients, and independent users, and 48% was uploaded by the news agency. It was found that the number of videos produced by experts on vaccines was very low.

In a study conducted in Vietnam, media data about vaccine side effects were evaluated. In this study, it was reported that there was a high rate of vaccine hesitation and rejection among subjects living in an urban environment.[23] It was found that; the most emphasized topics were autism causation (47,1%), undisclosed or poorly understood risks (42,5%), adverse reactions (40,2%), and thimerosal or mercury content in vaccines (36,8%) were detected as frequently mentioned side effects. In this study, it was stated that most of the videos (65,5%) deter the use of vaccines.[23] No data were found in our study about all of these effects, which were reported as standard vaccine side effects. The most frequently expressed reason for hesitation in our study was the uncertainty about vaccination. The rapid approval of vaccines by the World Health Organization (WHO) due to the pandemic was thought to be related to this situation.

Overall, anti-vaccination videos were reported to be three times more numerous than pro-vaccination videos.[24] In our study, the number of videos containing positive content about vaccination was higher. Since the beginning of our research, we've observed a growing number of positive

and hesitant videos about vaccines. Negative content was present in only 7 videos. The VPI and DISCERN scores of the videos with negative content were also below the average. This may be due to the public's urgent need for COVID 19 vaccine due to the pandemic. In terms of vaccine side effects, although the hesitation was in 72 of the contents, the videos had positive content in general.

Finally, it was observed that videos on COVID-19 vaccine side effects reached millions of viewers. Anti-vaccination behaviors and vaccine hesitation can be reduced by increasing the quality of the video content prepared by academic and governmental organizations. The correct use of YouTube videos in community vaccination behaviors can play an important role in the spread of COVID-19 among the community and help control the pandemic.

Ethics approval

This study did not require approval from the local research ethics committee as it contained only public data.

Conflict of interest

The authors declare no personal or financial conflict of interest

Disclosure

No financial support was received.

Author Contributions

Main idea/Planning: SA,BA,HOA
Analysis/Comment: BA
Data provision: All authors
Spelling: BA, HOA
Review and Correction: SA,BA
Confirmation: All authors

References

1. https://www.worldometers.info/coronavirus/ [Access date: 22.02.2021]
2. Evolution of the COVID-19 vaccine development landscape. (n.d.). Retrieved September 8, 2020, from https://www.nature.com/articles/d41573-020-00151- 8?S=03
3. Yıldırım, S. Salgınların Sosyal-Psikolojik Görünümü: Covid-19 (Koronavirüs) Pandemi Örneği. Electronic Turkish Studies 2020; 15(4):1331-1351.
4. Rzymski P, Borkowski L, Drąg M, et al. The strategies to support the COVID-19 vaccination with evidence-based communication and tackling misinformation. Vaccines 2021; 9(2):109.
5. Yenal S. COVID-19 Salgınının Uluslararası Güvenlik Açısından Değerlendirilmesi. Electronic Turkish Studies.2020; 15(4): 1315-1329.
6. Dindar Demiray E, Alkan Çeviker S. Aşı ve Toplumsal Korunma. J Biotechinol & Strategic Health Res 2020; 4: 37-44.
7. Kutlu HH, Altındiş M. Anti-Vaccination. Flora 2018;23(2):47-58.
8. Bozkurt AP, Aras I. Cleft Lip and Palate YouTube Videos: Content Usefulness and Sentiment Analysis. Cleft Palate Craniofac J 2021;58(3):362-368.
9. Faul F, Erdfelder E, Lang AG, et al. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39(2):175-191.
10. Abul-Fottouh D, Song MY, Gruzd A. Examining algorithmic biases in YouTube's recommendations of vaccine videos. Int J Med Inform 2020; 140:104175. doi: 10.1016/j.ijmedinf.2020.104175.
11. Charnock D, Shepperd S, Needham G, et al. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. J Epidemiol Community Health 1999;53(2):105-111.
12. Wu V, Lee DJ, Vescan A, et al. Evaluating YouTube as a Source of Patient Information for Functional Endoscopic Sinus Surgery. Ear Nose Throat J 2020:145561320962867. doi: 10.1177/0145561320962867.
13. Gokcen HB, Gumussuyu G. A Quality Analysis of Disc Herniation Videos on YouTube. World Neurosurg 2019: S1878-8750(19)30246-3. doi: 10.1016/j.wneu.2019.01.146.
14. Silberg WM, Lundberg GD, Musacchio RA. Assessing, controlling, and assuring the quality of medical information on the internet: Caveant lector et viewor--let the reader and viewer beware. JAMA 1997;277(15):1244–1245.
15. Aydin MF, Aydin MA. Quality and reliability of information available on YouTube and Google pertaining gastroesophageal reflux disease. Int J Med Inform 2020; 137:104107. doi: 10.1016/j.ijmedinf.2020.104107.
16. Yilmaz H, Aydin MN. YouTube™ video content analysis on space maintainers. J Indian Soc Pedod Prev Dent 2020;38(1):34-40.
17. Covolo L, Ceretti E, Passeri C, et al. What arguments on vaccinations run through YouTube videos in Italy? A content analysis. Hum Vaccin Immunother 2017;13(7):1693–1699.
18. Teng S, Khong KW, Pahlevan Sharif S, et al. YouTube Video Comments on Healthy Eating: Descriptive and Predictive Analysis. JMIR Public Health Surveill 2020;6(4): e19618. doi: 10.2196/19618.
19. St Lawrence S, Hallman J, Sherony R. Video from user-generated content as a source of pre-crash scenario naturalistic driving data. Traffic Inj Prev 2020:1-3.
20. Hernández-García I, Giménez-Júlvez T. YouTube as a Source of Influenza Vaccine Information in Spanish. Int J Environ Res Public Health 2021;18(2):727. doi: 10.3390/ijerph18020727.
21. Aquino F, Donzelli G, De Franco E, et al. The web and public confidence in MMR vaccination in Italy. Vaccine 2017; 35:4494–44948.
22. Yiannakoulias N, Slavik CE, Chase M. Expressions of pro- and anti-vaccine sentiment on YouTube. Vaccine 2019;37(15):2057-2064.
23. Tran BX, Boggiano VL, Nguyen LH, et al. Media representation of vaccine side effects and its impact on utilization of vaccination services in Vietnam. Patient Prefer Adherence 2018; 12:1717-1728.
24. Donzelli G, Palomba G, Federigi I, et al. Misinformation on vaccination: A quantitative analysis of YouTube videos. Hum Vaccin Immunother 2018;14(7):1654-1659.

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Seroprevalence of Hepatitis B and Hepatitis C in Inpatients for Alcohol and Drug Addiction Treatment in the Psychiatry Clinic of a Private Hospital

Bir Özel Hastane Psikiyatri Kliniği'nde Alkol ve Madde Bağımlılığı Tedavisi Almak İçin Yatarak Tedavi Gören Hastalarda Hepatit B ve Hepatit C Seroprevalansı

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Abstract

Aim Hepatitis B (HBV) and hepatitis C virus (HCV) infections pose a serious health problem in our country as well as all over the world. The main transmission routes of these agents include parenteral contact with infected blood or body fluids (percutaneous injury), sexual transmission, and contact with blood and body fluids of infected people. Accordingly, people with drug abuse are an important risk group for these infections. The number of studies in this field in Turkish context is limited. In this study, we aimed to evaluate the seroprevalence of HBV and HCV in inpatients for alcohol and substance addiction treatment in a private hospital psychiatry clinic.

Material and Method This retrospective study relied on the files of the patients who were hospitalized in the Alcohol and Substance Treatment Clinic in the sense that the results of HBsAg, anti-HBs, and anti-HCV parameters were evaluated retrospectively from the hospital automation system.

Results Of the 568 patient included in the study, 154 (27.1%) were female, 414 (72.9%) were male, and the mean age was 35 (18-88). Findings revealed that 7 (1.23%) of the patients were positive for HBsAg, 229 (40.4%) for anti-HBs, and 41 (7.21%) for anti-HCV. There was no significant difference between HBsAg and Anti-HCV positivity rates by gender.

Conclusion In our study, anti-HCV positivity was detected at a very high rate (7.21%). It can be concluded that the evaluation of these people in terms of test accuracy with HCV RNA as well as treating the infections detected in this group with effective new generation antivirals will also be beneficial with respect to reducing the number of people who can transmit the infection.

Keywords Drug abuse, Hepatitis B, Hepatitis C, seroprevalence.

Özet

Amaç *Hepatit B (HBV) ve hepatit C virüsü (HCV) enfeksiyonları, tüm dünyada olduğu gibi ülkemizde de oldukça önemli bir sağlık sorunudur. Bu etkenlerin başlıca bulaşma yolları, enfekte kan veya vücut sıvılarıyla parenteral temas (perkütan yaralanma), cinsel yolla bulaş ve enfekte kişilerin kan ve vücut sıvılarıyla temastır olup, madde kullanımı olan kişiler bu enfeksiyonlar açısından önemli bir risk grubudur. Ülkemizden bu alanda yapılmış çalışma sayısı sınırlıdır. Bu çalışmada, özel bir hastanede psikiyatri kliniğinde alkol ve madde bağımlılığı tedavisi almak için yatarak tedavi gören hastalarda HBV ve HCV seroprevalansını değerlendirmeyi amaçladık.*

Gereç ve Yöntem *Retrospektif olan bu çalışmada, Alkol ve Madde Tedavi Kliniğinde yatarak tedavi gören hastaların dosyaları, HBsAg, anti-HBs ve anti-HCV parametrelerinin sonuçları hastane otomasyon sisteminden retrospektif olarak değerlendirildi.*

Sonuçlar *Çalışmaya alınan 568 hastanın 154 (%27,1)'ü kadın, 414 (%72,9)'ü erkek ve yaş ortalaması 35 (18-88) idi. Hastaların 7 (%1,23)'sinde HBsAg, 229 (%40,4)'unda anti-HBs, 41 (%7,21)'inde anti-HCV pozitifliği saptandı. Cinsiyetlere göre HBsAg ve Anti-HCV pozitifliği oranları arasında fark yoktu.*

Sonuç *Çalışmamızda anti-HCV pozitifliği oldukça yüksek bir oranda (%7,21) saptandı. Bu kişilerin HCV RNA ile test doğruluğu açısından değerlendirilmesi ve yine bu grupta saptanan enfeksiyonların etkin yeni nesil antiviraller ile tedavi edilmesi enfeksiyonu bulaştırabilecek insan sayısını azaltmak açısından da yararlı olacaktır.*

Anahtar Kelimeler *Madde bağımlılığı, Hepatit B, Hepatit C, seroprevelans.*

INTRODUCTION

Hepatitis B (HBV) and hepatitis C virus (HCV) infections are very important health problems in our country as well as all over the world. While acute infection might cause serious mortality and loss of workforce, chronicity can increase the development of carriage, cirrhosis, and hepatocellular carcinoma. The main transmission routes of these viral agents are parenteral contact with infected blood or body fluids (percutaneous injury), infected mother to newborn (perinatal transmission), and contact with blood and body fluids of infected persons (horizontal transmission). Substance use is an important risk factor for the transmission of some infectious diseases and contributes to the global burden of disease. The prevalence of blood-borne infectious agents is found to be higher than the general population, especially in those with intravenous drug use, and this population serves as a source for viral transmission.[1,2]

Substance use and concomitant infections are important causes of morbidity and mortality. The prevalence of viral infections such as Human Immunodeficiency Virus (HIV) and HCV is also high in areas with high substance abuse. Most of the infections seen in substance abusers are blood-borne viral infections due to unsafe injections during intravenous drug use. Most of the infections seen in substance abusers are blood-borne viral infections due to unsafe injections during intravenous drug use. Most of the newly developed HCV infections in the world are infections that develop as a result of substance use, mainly intravenously. 60% of newly developing HCV infections each year are detected in substance users, especially intravenously.[1,2] In many studies, it has been reported that the rates of HBV and HIV infection in this group are higher than in the normal population.[3]

This study aimed to evaluate the HBV and HCV seroprevalence of patients who were hospitalized in Private Lara Anadolu Hospital Alcohol and Substance Treatment Clinic during the period between January 2015 and January 2020.

METHOD

This is a retrospective, non-intervention study. Data were obtained retrospectively from hospital records. In the study, the files of patients who were hospitalized for alcohol and substance addiction treatment in a psychiatry clinic in a private hospital between January 2015 and January 2020, and the laboratory results requested for HBV and HCV screening were evaluated retrospectively from the hospital automation system. All examinations were performed with the ARCHITECT ci4100 (Abbott) device using the Enzyme Linked Immunosorbent Assay (ELISA) method.

Inclusion Criteria

1. Patients over 18 years old
2. Patients receiving inpatient treatment for alcohol and substance addiction treatment in the Psychiatry Clinic
3. Those whose serological tests were sent for HBV and HCV infection

Exclusion Criteria

1. Patients under the age of 18
2. Duplicate test results from same patient
3. Outpatients

Statistical analysis

To analyze the data in question, the statistical program SPSS (The Statistical Packet for The Social Sciences) v. 23.0 (IBM, Armonk, NY, USA) was used. In statistical analysis, (f) frequency, (%) percentage and (X) arithmetic mean were calculated from descriptive statistical methods. Chi-square test was utilized to calculate the difference between the genders.

Ethical Aprroval

Necessary permissions were obtained from the institution where the study was carried out in order to undertake the

study. Within the scope of the study, the identity information and private data of the individuals were kept confidential. In addition, ethical approval was obtained from the ethics committee of Antalya Training and Research Hospital with the approval dated 19/08/2021 and numbered 12/9.

RESULTS

Of the 568 patients included in the study, 154 (27.1%) were female and 414 (72.9%) were male. The mean age was 35 (18-88). 7 (1.23%) of the patients were positive for HBsAg, 229 (40.4%) anti-HBs, and 41 (7.21%) anti-HCV positivity (Table 1). Anti-HCV positivity was detected in 41 patients, and the HCV RNA test requested for further examination was positive in 17 (2.99%) patients. Vaccination status of the patients could not be questioned as it was a retrospective study.

Table 1. Summary of Patients' Serological Test Results.

Gender	Number of patients	HBsAg positivity number (%)	Anti-HBs positivity number (%)	Anti-HCV positivity number (%)
Male	414	5 (1,2)	171 (41,3)	30 (7,25)
Female	154	2 (1,29)	58 (37,6)	11 (7,14)
Total	568	7 (1,23)	229 (40,4)	41 (7,21)

There was no statistically significant difference between the genders in terms of HBsAg and Anti-HCV positivity ($p>0.05$) (Table 2).

Table 2. Evaluation of HBsAg and Anti-HCV positivity by gender.

	Female (n=154) n, %	Male (n=414) n, %	P value
HBsAg positivity number (%)	2 (1,29)	5 (1,2)	1
Anti-HCV positivity number (%)	11 (7,14)	30 (7,25)	1

HBsAg positivity was found in 1.29% of foreign nationals and Anti-HCV positivity was detected in 0.52% of them. HBsAg positivity was found in 1.2% and Anti-HCV positivity was marked in 6.69% of the citizens of the Republic of Turkey (Table 3).

Table 3. Summary of serology results by nationality.

Gender	Number of patients	HBsAg positivity number (%)	Anti-HBs positivity number (%)	Anti-HCV positivity number (%)
Citizen of the Republic of Turkey	488	5 (1,2)	212 (37,4)	38 (6,69)
Foreign national	80	2 (1,29)	17 (3)	3 (0,52)
Total	568	7 (1,23)	229 (40,4)	41 (7,21)

DISCUSSION

Both HBV and HCV infections are blood-borne diseases. In recent years, outbreaks of HCV have emerged, especially among young people with substance abuse, underlining the need for routine HCV testing for people who continue to engage in high-risk behaviors. These patients constitute risk groups in terms of HCV and HBV infection due to risky behaviors (injecting some recreational substances, using the same injector jointly by more than one or several people, factors such as self-harm with the effect of the substance used). It has been reported that the prevalence in these groups is higher than the population in terms of many infections transmitted by blood-body fluids, especially these infections in question.[5,6]

In this study, we aimed to evaluate the frequency of HCV and HBV infections in inpatients for alcohol and substance abuse treatment in a private hospital. The mean age of the participants in the study was 35, and a similar age population was examined with the existing studies. In addition, since the included sample size is 568, it is higher than other similar studies published in our country.[5,7] In a recent study by Demiralay et al.[5], 153 patients hospitalized in the same hospital were evaluated in 2018. The study revealed that 8.5% of the patients had positive anti-HCV test results, 16.3% had HBV immunity, and there was no

anti-HIV test result positivity. In our study, the sample size was enlarged in the sense that 568 patients hospitalized in the same clinic between 2015 and 2020 were evaluated. In addition, the study conducted by Demiralay et al.[5] was written from the perspective of psychiatry, and the sociodemographic characteristics of the patients and the relationship between substance use were evaluated in this study. In the current study, we evaluated patients in terms of infectious diseases. Again, in a similar recent study published in Turkey in 2020, HBsAg positivity rate was reported as 2.8%, anti-HCV positivity rate was 1.4%, and anti-HIV positivity rate was 0%.7. In our study, HBsAg positivity was detected in 7 (1.23%) of the patients, Anti-HBs positivity was found in 229 (40.4%) and anti-HCV positivity in 41 (7.21%) patients. Anti-HCV positivity was detected in 41 patients, and the HCV RNA test requested for further examination was positive in 17 (2.99%) patients. When it comes to HIV, no evaluation was made in our study. HBsAg positivity was lower than Dağlı's study[7], which included 434 patients living in Bursa, but anti-HCV positivity was found at a higher rate. This may be due to the vaccination status of the patients, the characteristics of the substance used (intravenous or oral substance), or regional differences. Since our study was retrospective, information about vaccination characteristics could not be accessed.

The result that the frequency of HCV infection in injecting drug users reaches 80%, reveals that protection from HCV infection and its complications should be a priority for these individuals.[8] In addition, the fact that reports stating that approximately fifty percent of those infected with HCV are not aware of this situation emphasize the importance of HCV screening once again.[9]

More specific tests, such as HCV RNA, should be confirmed in patients who are found to be positive for anti-HCV in screening tests.[8] HCV genotypes are also important in the treatment and follow-up of the disease. It has been determined that there are 6 different known genotypes and subtypes of the HCV virus. They show different geographical distributions.[10] Genotypes 1, 2, 3 are common all over the world, while genotype 4 is seen in the Middle East and Africa. In a meta-analysis study, HCV genotype 1 was found to be largely predominant in non-Arab Middle Eastern countries such as Turkey (82%), Israel (68%), Cyprus (68%), and Iran (55%). In this study, the dominant subtype in Turkey was identified as 1b subtype.[11]

It has also been reported that different HCV genotypes can be seen in this population from the genotypes showing a general distribution in the population. It has been reported that the prevalence of genotypes 1a and 3 is particularly high in injecting drug users.[12] In addition, while it is known that the dominant genotype is genotype 1 in Turkey, variable genotypes can be detected in other countries. In our study, Anti-HCV positivity rate was 6.69% for Turkish citizens, 0.52% for foreign nationals; that is, it was lower for foreign nationals. In addition, this information could not be reached because the genotype could not be studied in our study.

In Demiralay et al.' study[5], the relationship between addicted substances and HCV positivity was evaluated, and anti-HCV positivity was found to be statistically significantly higher in heroin/cocaine users. In a meta-analysis, 722 people were included and it was revealed that HCV seroprevalence in patients addicted to non-intravenous substances ranged from 2.3 to 35.3%.[13]

In a recent meta-analysis examining the HCV seroprevalence in intravenous drug users in the Eastern Mediterranean Region (EMRO) countries of the World Health Organization, this rate was found to be 48.3%. In the same study, HIV seroprevalence was found to be 9.1%.[14]

Another systematic review attempting to estimate the global prevalence of HCV infection in intravenous drug addicts revealed that HCV seroprevalence among these individuals ranged from 78-93% in Pakistan and 54.9-80.1% in Iran.[15]

In our study, the cases were not evaluated in terms of addiction type. Anti-HCV positivity was found in 7.21% of the cases presented, and the HCV RNA test was positive in 2.99% of the cases. Our study results show a lower seroprevalence rate.

CONCLUSION

People who use addictive substances whether intravenously and via other routes (oral, inhaler, etc.) are at risk of contracting viral infections such as HBV, HCV, HIV. At the same time, those who use substances also serve as a source for these infections. It is very important to monitor this group very carefully in order to establish national data by determining the rates in different regions, and to develop prevention programs. Furthermore, the treatment of these infections detected in this group with effective new generation antivirals will also be beneficial in terms of reducing the transmission of infection.

Limitations of the study

The limitaions of the study included the retrospective design of the study, the limited number of patients as well as the fact that HCV genotypes were not studied and no discrimination was made according to the addicted substance.

Conflict of interest

There is no conflict of interest among the authors.

Financial Support

No financial support was obtained from any institution for the study.

Place of study

Antalya Private Lara Hospital

Author contributions

Concept: SOM., FMG.; Design: all authors.; Supervision: SA.; Fundings: NONE.; Materials: SOM., FMG.; Data Collection and/or Processing: SOM., FMG.; Analysis and/or Interpretation: SA.; Literature Review: all authors.; Writer: SA, SOM, FMG.; Critical Reviews: SA.; Approval: all authors.

References

1. Alter MJ. Epidemiology of hepatitis C virus infection. World J Gastroenterol 2007; 13:2436–2441.
2. Amon JJ, Garfein RS, Ahdieh-Grant L, et al. Prevalence of hepatitis C virus infection among injection drug users in the United States, 1994–2004. Clin Infect Dis 2008; 46:1852–1858.
3. Ferreira RC, Rodrigues FP, Teles SA, et al. Prevalence of hepatitis B virüs and risk factors in Brazilian non-injecting drug users. J Med Virol 2009; 81:602–609.
4. https://www.cdc.gov/hepatitis/populations/idu.html [Access date: 15 October 2021].
5. Demiralay Ş, Keser İ, Güven M. Özel bir hastanenin psikiyatri servisinde bağımlılık tedavisi alan hastaların sosyodemografik ve klinik özelliklerinin retrospektif analizi. Klinik Psikiyatri 2021; 24:383-393.
6. Altuğlu İ, Tanyeri S, Zeytinoğlu A, et al. Madde kullanımı olan olgularda HBsAg, Anti-HCV ve Anti-HIV seroprevalansı: retrospektif bir değerlendirme. Arch Neuropsychiatry 2019; 56: 186-190.
7. Dağlı Ö. Screening of hepatitis and HIV infections in an alcohol and drug addiction treatment center. Pamukkale Tıp Dergisi 2020; 13(1):177-186.
8. Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet 2011; 378:571-583.
9. Holmberg SD, Spradling PR, Moorman AC, et al. Hepatitis C in the United States. N Engl J Med 2013; 368:1859- 1861.
10. Yıldırım D, Hasbek M, Alkan S, et al. Relationship Between HCV RNA and Serum Alanine Aminotransferase and HCV Genotype Distribution. J Clin Anal Med 2015;6(6):1-3.
11. Ghaderi-Zefrehi H, Gholami-Fesharaki M, Sharafi H, et al. The Distribution of Hepatitis C Virus Genotypes in Middle Eastern Countries: A Systematic Review and Meta-Analysis. Hepat Mon 2016;16(9): e40357.
12. Evren C, Bilici R, Ucbilek E, et al. A call for action for hepatitis C infection among people who inject drugs in Turkey. Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2017; 30:271-277.
13. Scheinmann R, Hagan H, Lelutiu-Weinberger C, et al. Non-injection drug use and Hepatitis C Virus: a systematic review. Drug Alcohol Depend 2007;89(1):1-12.
14. Shayan SJ, Nazari R, Kiwanuka F. Prevalence of HIV and HCV among injecting drug users in three selected WHO-EMRO countries: a meta-analysis. Harm Reduct J 2021;18(1):59.
15. Aceijas C, Rhodes T. Global estimates of prevalence of HCV infection among injecting drug users. Int J Drug Policy 2007;18(5):352–358

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The Relationship of Laboratory Parameters and Rates with Prognosis and Mortality in COVID-19 Infection

Laboratuvar Parametreleri ve Oranlarının COVID-19 Enfeksiyonunda Prognoz ve Mortalite İle İlşkisi

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Abstract

Aim In this study, to evaluate the clinical course and prognosis in COVID-19 patients, to evaluate the hematological and biochemical parameters at the time of admission to the hospital.

Material and Method This retrospective study was performed in a multicenter study in April and October 2020. Demographic characteristics, clinical features, age, gender and length of stay of patients who exitus (EX) and were discharged due to COVID-19 were examined.

Results Of the patients (n:180) included in the study, 89 were female and 91 were male. There was a significant difference between the patients who were discharged from the hospital and died gender and complaints at the time of admission ($p<0.05$). There was no significant difference between age distribution and comorbid factors ($p>0.05$). While the length of stay, platelet (PLT), mean corpuscular volume (MCV), serum C-reactive protein (CRP), albumin, lymphocyte, monocyte, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase (LDH), ferritin, international normalized ratio (INR), Plateletcrit (PCT), troponin, and white blood cell counts are all increased in EX. There is a statistically significant difference in red blood cell distribution width (RDW) between EX and discharge patients ($p<0.05$), as well as in monocyte/albumin ratios, procalcitonin/albumin ratios, CRP/albumin ratios, LDH/albumin ratios, and ürea/albumin ratios. There is not significant for lymphocyte/monocyte ratio ($p>0.05$). While the RDW, monocyte/albumin, PCT/albumin, CRP/albumin, LDH/albumin, and ürea/albumin ratios are increased in EX patients, the PCT/PLT and MPV/PLT ratios are increased in discharged patients.

Conclusion In this study, we demonstrated that hematological and biochemical markers may be utilized as an early prognostic indicator for patients identified with COVID-19.

Keywords COVID-19, Plateletcrit/Platelet, Platelet/Mean Platelet Volum, Lymphocyte/Monocyte monocytes, C-Reactive Protein/Albumin, Mortality.

Özet

Amaç *Bu çalışma amaç, COVID-19 hastalarında hastaneye başvuru anındaki hematolojik ve biyokimyasal parametreleri ile klinik seyir ve prognozu değerlendirmektir.*

Gereç ve Yöntem *Bu retrospektif çalışma, Nisan ve Ekim 2020'de çok merkezli çalışma olarak yapıldı. COVID-19 nedeniyle taburcu olan ve ölen (EX) hastaların demografik özellikleri, klinik özellikleri, yaşı, cinsiyeti ve kalış süreleri incelendi.*

Sonuçlar *Çalışmaya alınan hastaların (n:180) 89'u kadın, 91'i erkekti. Hastaneden taburcu olan ve ex olan hastalar arasında cinsiyet ve başvuru anındaki şikayetleri arasında anlamlı fark vardı ($p<0.05$). Yaş dağılımı ile komorbid faktörler arasında ise anlamlı fark yoktu ($p>0.05$). Kalış süresi, trombosit (PLT), ortalama korpüsküler hacim (MCV), serum C-reaktif protein (CRP), albümin, lenfosit, monosit, alanin aminotransferaz, aspartat aminotransferaz, laktat dehidrojenaz (LDH), ferritin, international normalized ratio (INR), Plateletcrit (PCT), troponin ve beyaz kan hücresi sayılarının tümünün ex olan hastalarda arttığı gözlendi. EX ve taburcu olan hastalar arasında kırmızı kan hücresi dağılım genişliği (RDW), monosit/albümin oranları, PCT/albümin oranları, CRP/albümin oranları, LDH/albümin oranları, ve üre/albümin oranları arasında anlamlı fark vardı ($p<0.05$). Lenfosit/monosit oranı açısından anlamlı fark yoktu ($p>0.05$). EX olan hastalarında RDW, monosit/albümin, prokalsitonin/albümin, CRP/albümin, LDH/albümin ve üre/albümin oranları artarken, taburcu olan hastalarda PCT/PLT ve MPV/PLT oranları artmaktaydı.*

Sonuç *Çalışmada, COVID-19 ile hastaları için hematolojik ve biyokimyasal belirteçlerin erken prognostik gösterge olarak kullanılabileceğini gösterilmiştir.*

Anahtar Kelimeler *COVID-19, Plateletkrit/Platelet, Platelet/Ortalama Trombosit Hacmi, Lenfosit/Monosit monositleri, C-Reaktif Protein/Albümin, Mortalite.*

INTRODUCTION

SARS-CoV-2, a new severe acute respiratory syndrome coronavirus, has spread around the world, posing a hazard to public health. The signs and symptoms of SARS-CoV-2 might vary from patient to patient. It might be asymptomatic or have a mild, moderate, or severe course. Even though some patients recover after being treated in an intensive care unit, others pass away there[1,2]. The infection with SARS-Cov2 should be regarded a systemic illness. The cardiovascular, pulmonary, gastrointestinal, neurological, hematopoietic, and immunological systems are all impacted[3,4].

Initial clinical manifestations of SARS-CoV-2 infection are not infection-specific, and further evidence is required to establish the diagnosis. Demonstrated that standard laboratory testing, particularly anomalies in hematological assays, has the ability to rapidly, practically, and economically establish the necessity for specialized laboratory testing for the diagnosis of SARS-CoV-2 infection[5-8]. Among the most often reported hematological abnormalities are lymphocytopenia, neutrophilia, and moderate thrombocytopenia[8,9].

The COVID-19 pandemic has seen a significant increase in the number of patients. Thus, a rapid and thorough knowledge of laboratory data related to the severity of the disease and mortality in the early period provides insight into the clinical course throughout this time frame. Although the indicators indicating the severity of the disease are unknown, it has been established that the clinical course is largely caused by host factors' immunological responses rather than viral genetic changes[10].

In this study, we aimed to investigate the early hematological and biochemical that may be associated with the severity of COVID-19 disease in the light of the available literatüre. We aimed to reveal that determining the parameters that predict the course of the disease will contribute to the literatüre in reducing morbidity and mortality by enabling the effective treatment of patients.

MATERIAL and METHODS

The study was carried out as a multicenter study in Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital and Sinop Ayancık State Hospital in April and October 2020. COVID-19 patients treated in 90 intensive care units and 90 clinics were included in the study. Demographic characteristics, clinical characteristics, age, gender and length of stay of patients discharged and died (EX) due to COVID-19 were retrospectively analyzed from the hospital information system. The blood tests of the patients who were hospitalized with the diagnosis of COVID-19 were taken at the time of admission to the clinic and laboratory tests were analyzed in the microbiology and biochemistry laboratory of our hospital. Complete blood count analyses were carried out in 2 ml tubes containing K3 ethylenediamine tetraacetic acid (EDTA) on a Sysmex XP-300 instrument (Sysmex Corp., Kobe Japan) within 2 hours. Serum lipid parameters (total cholesterol, HDLc, LDLc, and triglyceride), calcium and phosphorus levels and glucose keratin etc.was studied in biochemistry autoanalysis using standard methods on the ARCHITECTc8000 (Abbot, USA) device from the obtained serum. Daily quality control was carried out with commercial quality control materials to ensure the precision and accuracy of measurements in our laboratory. Plateletcrit is the percentage of platelets in peripheral blood and is measured with a hemocounter device.

The data were analyzed using the SPSS 26 software and a confidence level of 95% was used. For categorical (qualitative) variables, frequency and n (%) statistics are provided; for numerical (quantitative) variables, mean, standard deviation (meansd), minimum, maximum, and median (Max-Min(M)) statistics are provided. The prediction levels and probabilities of the cut-off values for the rate variables utilized in the calculated measurements were established using ROC analysis. We computed the sensitivity (rate of detecting ex status), specificity (rate of detecting

discharge status), positive predictive (rate of expiration of positive value of measurement), and negative predictive (rate of discharge of negative value of measurement) probabilities. The chi-square test is a statistical tool for determining the connection between two category variables. The Mann Whitney/independent groups t test is a statistical technique for comparing two independent groups on the basis of a quantitative variable.

To determine if the measurements followed the normal distribution, the Shaphiro Wilk normality test was used. While mean platelet volume (MPV) and hemoglobin (HGB) values indicate normal distribution ($p<0.05$), other data do not ($p>0.05$). Parametric or non-parametric approaches were used for analysis, depending on the normal distribution of the measurement.

RESULTS

Of the patients (n:180) included in the study, 89 were female and 91 were male. When the demographic data of the patients who were discharged from the hospital and died; there was a significant difference between the patients' gender and complaints at the time of admission (respectively, $p=0.005$; $p=0.000$); There was no significant difference between age distribution and comorbid factors (respectively, $p=0.175$; $p=0.119$; $P=0.286$) (Table 1). The majority of EX patients (61.1%) were male, 33.3% had a fever, and complained of dyspnea (36.7 %) (Figure 1).

While the length of stay, platelet (PLT), mean corpuscular volume (MCV), serum C-reactive protein (CRP), albumin, lymphocyte, monocyte, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), ferritin, international normalized ratio (INR), procalcitonin, troponin, and white blood cell (WBC) counts are all increased in EX (Table 2).

There is a statistically significant difference in red blood cell distribution width (RDW) between EX and released patients ($p<0.05$), as well as in monocyte/albumin ratios, procalcitonin/albumin ratios, CRP/albumin ratios, LDH/albumin ratios, and ürea/albumin ratios. The change was not significant for lymphocyte/monocyte ratio ($p>0.05$). While the RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, and ürea/albumin ratios are increased in EX patients, the PCT/PLT and MPV/PLT ratios are increased in discharged patients. There was a statistically significant difference in PLT, lymphocyte, creatinine, and INR levels between males and females released ($p<0.05$). The difference was not statistically significant in other metrics ($p >0.05$). While women's PLT and lymphocyte counts are higher, men's creatinine and INR levels are higher. PLT, lymphocyte, creatinine, HGB, and INR levels were significantly different between women and men with EX ($p <0.05$). The difference was not statistically significant in other metrics ($p >0.05$). Men had higher PLT, creatinine, HGB, and INR levels than women do (Table-3). There is a statistically significant difference in MCV, CRP, urea, albumin, creatinine, ALT, Ferritin, INR, procalcitonin, troponin, procalcitonin/albumin, CRP/albumin, and ürea/albumin measurements between discharged persons and those aged 65 years and above ($p=0.05$). The difference was not statistically significant ($p>0.05$) for other metrics. While MCV, CRP, urea, creatinine, ferritin, INR, procalcitonin, troponin, procalcitonin/albumin, CRP/albumin, and urea/albumin levels are higher in people 65 years of age and older, albumin and ALT levels are higher in persons under 65 years of age. There was a statistically significant difference in urea, ALT, ferritin, INR, RDW, and urea/albumin measurements between EX patients aged 65 years and older ($p=0.05$). The difference was not statistically significant ($p >0.05$) for other metrics. While urea, RDW, and urea/albumin concentrations are higher in patients 65 years and older, ALT, ferritin, and INR concentrations are higher in individuals younger than 65 years of age. There was a statistically significant difference in MCV and ferritin levels between patients discharged from the hospital and those who did not develop subsequent illness ($p <0.05$). The difference was not statistically significant ($p>0.05$) for other metrics. Ferritin levels are considerably higher in co-

morbid people, but MCV levels are much higher in those without comorbidity (Table 4).

There was a statistically significant difference between EX patients and those without extra illness in terms of urea, creatinine, INR, potassium, RDW, and urea/albumin values (p <0.05). In other measurements (p >0.05), the difference was not significant. While measures of urea, creatinine, potassium, RDW, and urea/albumin are greater in individuals with comorbidity, INR readings are higher in those without.

Lymphocyte/monocyte, RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, and ürea/albumin measures all vary statistically significantly in predicting patients' EX status (p <0.05). PCT/PLT values were not significant (p>0.05) for MPV/PLT. Procalcitonin/albumin, CRP/albumin, and LDH/albumin ratios, in particular, are quite useful for determining EX status (Table 5).

The table summarizes the estimation and detection probability for the ratios with a significant predictive level for the EX status based on the cut-off values. Monocytes/albumin, procalcitonin/albumin, and LDH/albumin are the best predictors of patients with EX. Procalcitonin/albumin, CRP/albumin, LDH/albumin, and ürea/albumin are the ratios that most accurately predict the EX status of patients who test positive at the specified cut-off value. The EX status of the patients had a statistically significant association with the lymphocyte/monocyte, RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, and ürea/albumin groups (p <0.05). The majority of individuals with positive lymphocyte/monocyte, RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, or ürea/albumin ratios (equal to or more than the cut-off value) are EX patients (Figure 2,3,4). There was a statistically significant difference in the lymphocyte/monocyte, RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, and ürea/albumin cut-off values (p<0.05). According to the cut-off values, patients with positive lymphocyte/monocyte, RDW, monocyte/albumin, procalcitonin/albumin, CRP/albumin, LDH/albumin, or ürea/albumin ratio readings had a longer hospital stay (Table 6).

Table 1: The Relationship between Demographic Characteristics and Exitus Status

		Discharge	Exitus	X^2	p
Senility	Under 65	19 (21,1)	28 (31,1)	1,843	**0,175**
	Upper 65	71 (78,9)	62 (68,9)		
Gender	Female	54 (60)	35 (38,9)	8,023	**0,005***
	Male	36 (40)	55 (61,1)		
Application complaint	Fever	21 (23,3)	30 (33,3)	45,550	**0,000***
	Cough	28 (31,1)	23 (25,6)		
	Dyspne	7 (7,8)	33 (36,7)		
	GCD	10 (11,1)	4 (4,4)		
	Diğer	24 (26,7)	0 (0)		
Comorbidity	None	17 (18,9)	27 (30)	2,436	**0,119**
	Positive	73 (81,1)	63 (70)		
Comorbidity	HT	38 (52,1)	44 (69,8)	1,138	**0,286**
	CAD	5 (6,8)	3 (4,8)		
	HL	1 (1,4)	0 (0)		
	DM	18 (24,7)	10 (15,9)		
	Other	11 (15,1)	6 (9,5)		

*p<0.05 significant relationship, p>0.05 no significant relationship; Chi-square,
GCD: General Condition Disorder, HT: Hypertension, CAD: Coronary Artery Disease HL: Hyperlipidemia, DM: Diabetes Mellitus

Tablo 2: Comparison of Measurements by EX Condition

	Discharge		EX		U/t	p
	Max-Min(M)	**Median±SD**	**Max-Min(M)**	**Median±SD**		
Age	94-38 (76)	72,91±12,26	92-29 (73)	70,13±13,45	3574,5	**0,173**
Duration of Hospitalization	14-4 (7)	7,18±2,24	30-5 (11)	12,93±6,5	1554,5	**0,000***
PLT	347-73 (167)	171,94±54,64	597-51 (189,5)	199,91±82,28	3277,0	**0,027***
MPV(t)	12,3-6,9 (10)	10,09±1,07	12,5-7,2 (10,1)	10,21±1,04	-0,767	**0,444**
PCT	0,5-0,08 (0,1845)	0,2±0,09	0,52-0,06 (0,19)	0,2±0,07	3793,5	**0,463**
MCV	106,6-70,8 (87,15)	86,96±5,36	109,2-66,2 (90,45)	89,54±7,29	2983,0	**0,002***
CRP	245,5-2 (14,5)	31,68±39,64	350-10,4 (123,5)	121,45±71,26	891,5	**0,000***
Urea	97,7-20,7 (38,7)	42,53±17,31	176-14 (44,5)	55,61±35,69	3494,0	**0,112**
Albumin	51-35 (42)	42,1±3,32	39-16 (29)	29,53±4,34	73,5	**0,000***
Lymphocyte	2,9-0,4 (1,1)	1,18±0,52	2,64-0,21 (0,83)	0,89±0,41	2566,5	**0,000***
Monocyte	0,8-0,07 (0,3)	0,33±0,18	1,19-0,1 (0,37)	0,4±0,2	3124,5	**0,008***
Creatinine	2,1-0,6 (0,9)	1,03±0,35	5,83-0,55 (1,08)	1,3±0,91	3381,0	**0,055**
HGB(t)	17,3-9,3 (13)	13,01±1,7	17,4-9,1 (13,05)	13,06±1,83	-0,182	**0,856**
AST	66-14 (25)	28,3±11,28	135-4 (40)	46,17±26,62	2091,0	**0,000***
ALT	88-6 (17)	21,17±13,17	95-6 (27)	31,46±19,81	2506,0	**0,000***
LDH	472-136 (233,5)	257,74±82,26	971-140 (417,5)	445,87±204,76	1615,5	**0,000***
Ferritin	742,9-15,8 (107,95)	167,44±172,68	2000-21 (588)	756,87±575,46	998,0	**0,000***
INR	1,65-0,78 (1,05)	1,08±0,18	1,64-0,91 (1,2)	1,21±0,15	2158,5	**0,000***
Calcium	9,7-7 (8,6)	8,58±0,55	11-4,84 (8,72)	8,74±0,7	3464,0	**0,093**
Potassium	5,5-3,1 (4,2)	4,27±0,53	6,21-2,77 (4,15)	4,32±0,7	4027,0	**0,948**
Sodium	142-121 (137)	136,19±3,26	151-121 (137)	136,38±5,18	3988,0	**0,859**
Procalcitonin	0,2-0,01 (0,05)	0,06±0,04	5,53-0,02 (0,19)	0,63±1,09	909,0	**0,000***
Troponin	0,33-0 (0,007)	0,02±0,04	0,6-0,1 (0,1)	0,13±0,09	309,0	**0,000***
WBC	9,6-2,6 (5)	5,12±1,56	30,8-3,48 (7,78)	9,04±4,77	1521,0	**0,000***

*p<0.05 significant difference, p>0.05 no significant difference; Mann Whitney/t
Platalet; PLT, Plateletcrit; PCT; Mean Palatelet Volüm; MPV, Mean Corpusclar Volum; MCV, C-Reactive Protein; CRP, Hemoglobin; HGB, aspartate aminotransferase; AST, alaninaminotransferase; ALT, lactate dehydrogenase; LDH, Internalization Ratio: INR, White Blood Cell; WBC

Table 3: Comparison of Proportion Measurements by EX Condition

	Discharge		EX		U/t	p
	Max-Min(M)	**Median±SD**	**Max-Min(M)**	**Median±SD**		
RDW	17,7-12,2 (13,4)	13,64±1,08	22-12,4 (13,95)	14,43±1,71	2748,0	**0,000***
PCT/PLT	0,0031-0,0006 (0,001)	0,0012±0,0005	0,0013-0,0007 (0,001)	0,001±0,0001	3361,0	**0,000***
MPV/PLT	0,16-0,03 (0,06)	0,07±0,02	0,22-0,01 (0,06)	0,06±0,03	3383,5	**0,049***
Lymphocyte/Monocyte	18,06-0,63 (3,67)	4,3±2,54	7,6-0,34 (2,26)	2,69±1,65	2100,5	**0,057**
Monocyte /Albumin	0,02-0,0016 (0,0068)	0,0079±0,0042	0,0519-0,0026 (0,0127)	0,014±0,0078	1806,0	**0,000***
Procalcitonin/Albumin	0,0057-0,0002 (0,0013)	0,0014±0,001	0,2096-0,0006 (0,0067)	0,0222±0,0392	570,0	**0,000***
CRP/Albumin	5,71-0,04 (0,33)	0,77±0,96	16,69-0,27 (3,97)	4,39±3,05	669,0	**0,000***
LDH/Albumin	10,83-3,04 (5,84)	6,17±2,07	41,83-4,24 (14,06)	15,76±8,32	746,5	**0,000***
Urea/Albumin	2,78-0,41 (0,95)	1,03±0,47	6,56-0,37 (1,48)	1,96±1,38	2132,0	**0,000***

*p<0.05 significant difference, p>0.05 no significant difference; Mann Whitney

Table 4: Comparison of Measurements by Age in the Discharged Group

Discharge	Under 65		Upper 65		U/t	p
	Max-Min(M)	Median±SD	Max-Min(M)	Median±SD		
Duration of hospitalization	14-5 (6)	6,63±2,03	14-4 (7)	7,32±2,29	522,0	**0,124**
PLT	310-122 (178)	187,53±62,86	347-73 (164)	167,77±51,92	587,0	**0,387**
PCT	0,31-0,1 (0,2)	0,18±0,06	0,5-0,08 (0,18)	0,2±0,09	657,0	**0,863**
MPV(t)	11,5-7,8 (10,1)	9,87±1,08	12,3-6,9 (10)	10,15±1,07	-1,001	**0,325**
MCV	92,1-75,2 (85,2)	84,66±4,24	106,6-70,8 (87,5)	87,57±5,49	432,0	**0,016***
CRP	44,5-2 (6,3)	12,79±13,49	245,5-2 (21,2)	36,73±42,76	426,0	**0,014***
Üre	57,8-20,7 (27,5)	29,92±8,84	97,7-21,6 (41,8)	45,91±17,5	230,5	**0,000***
Albumin	51-39 (44)	44,16±3,42	48-35 (41)	41,55±3,08	406,0	**0,008***
Lymphocyte	2,6-0,6 (1,2)	1,29±0,6	2,9-0,4 (1,1)	1,15±0,5	600,5	**0,463**
Monocyte	0,7-0,1 (0,3)	0,35±0,18	0,8-0,07 (0,3)	0,33±0,17	623,5	**0,609**
Creatinine	1,3-0,6 (0,8)	0,81±0,17	2,1-0,6 (1)	1,09±0,36	311,5	**0,000***
HGB(t)	16,7-9,4 (13)	13,04±1,64	17,3-9,3 (13)	13,01±1,72	0,068	**0,946**
AST	61-17 (24)	26,37±10,23	66-14 (25)	28,82±11,56	582,0	**0,360**
ALT	88-11 (22)	25,47±16,87	58-6 (16)	20,01±11,88	470,0	**0,043***
LDH	472-141 (231)	259,16±97,07	468-136 (234)	257,37±78,62	646,0	**0,778**
Ferritin	345,2-15,8 (54,8)	79,08±78,92	742,9-16 (140,2)	191,09±183,37	331,0	**0,001***
INR	1,21-0,87 (0,96)	1±0,11	1,65-0,78 (1,06)	1,11±0,18	434,5	**0,018***
Calcium	9,2-7,7 (8,7)	8,62±0,43	9,7-7 (8,6)	8,57±0,58	645,0	**0,770**
Potassium	4,9-3,1 (4,1)	4,06±0,41	5,5-3,3 (4,3)	4,32±0,55	500,5	**0,085**
Sodium	139-133 (136)	136,11±2,13	142-121 (137)	136,21±3,51	626,0	**0,629**
Procalcitonin	0,14-0,01 (0,04)	0,04±0,03	0,2-0,01 (0,05)	0,06±0,04	469,5	**0,041***
Troponin	0,06-0 (0)	0±0,01	0,33-0 (0,01)	0,02±0,04	282,5	**0,000***
WBC	8,9-2,7 (4,7)	5,08±1,82	9,6-2,6 (5,1)	5,13±1,5	646,5	**0,782**
RDW	17,2-12,2 (13)	13,48±1,25	17,7-12,2 (13,5)	13,69±1,03	514,5	**0,113**
PCT/PLT	0,0011-0,0008 (0,001)	0,001±0,0001	0,0031-0,0006 (0,001)	0,0012±0,0005	486,0	**0,062**
MPV/PLT	0,0839-0,0269 (0,0614)	0,0587±0,0202	0,1557-0,0265 (0,0616)	0,0674±0,0258	568,0	**0,292**
Lymphocyte / Monocyte	9-1,33 (3,8)	4,21±1,89	18,06-0,63 (3,67)	4,32±2,69	634,0	**0,689**
Monocyte /Albumin	0,0175-0,0023 (0,0067)	0,008±0,0041	0,02-0,0016 (0,007)	0,0079±0,0042	671,5	**0,976**
Procalcitonin /Albumin	0,0034-0,0002 (0,0008)	0,001±0,0008	0,0057-0,0002 (0,0013)	0,0016±0,0011	446,0	**0,024***
CRP/Albumin	1,14-0,04 (0,15)	0,3±0,34	5,71-0,04 (0,53)	0,9±1,04	405,5	**0,008***
LDH/Albumin	10,81-3,08 (5,63)	5,89±2,22	10,83-3,04 (5,84)	6,25±2,04	590,5	**0,406**
Urea/Albumin	1,2-0,41 (0,63)	0,68±0,21	2,78-0,48 (1,01)	1,12±0,48	219,0	**0,000***

*p<0.05 significant difference, p>0.05 no significant difference; Mann Whitney/t

Table 5: ROC Analysis of Measurements Determined for EX Condition

Measurements	Range	p	95% CI	
			lower	upper
PCT/PLT	0,575	**0,051**	0,502	0,678
MPV/PLT	0,582	**0,057**	0,499	0,666
Lymphocyte / Monocyte	0,740	**0,000***	0,667	0,813
RDW	0,661	**0,000***	0,582	0,740
Monocyte /Albumin	0,777	**0,000***	0,710	0,844
Procalcitonin /Albumin	0,930	**0,000***	0,891	0,968
CRP/Albumin	0,917	**0,000***	0,879	0,955
LDH/Albumin	0,908	**0,000***	0,865	0,951
Urea/Albumin	0,737	**0,000***	0,665	0,809

*p<0,05 significant difference, p>0,05 no significant difference; ROC

Table 6: Cutoffs and Estimation Probabilities of Measurements Determined for Case EX

Mesurements	Cut off	Sensitivity	Specificity	PP+	PP-
Lymphocyte / Monocyte	2,9848	0,711	0,700	0,703	0,708
RDW	13,85	0,556	0,710	0,658	0,615
Monocyte /Albumin	0,0077	0,833	0,622	0,682	0,786
Procalcitonin/Albumin	0,0025	0,878	0,889	0,888	0,879
CRP/Albumin	2,1189	0,767	0,900	0,885	0,880
LDH/Albumin	7,5874	0,878	0,800	0,859	0,867
Urea/Albumin	1,5638	0,489	0,911	0,846	0,641

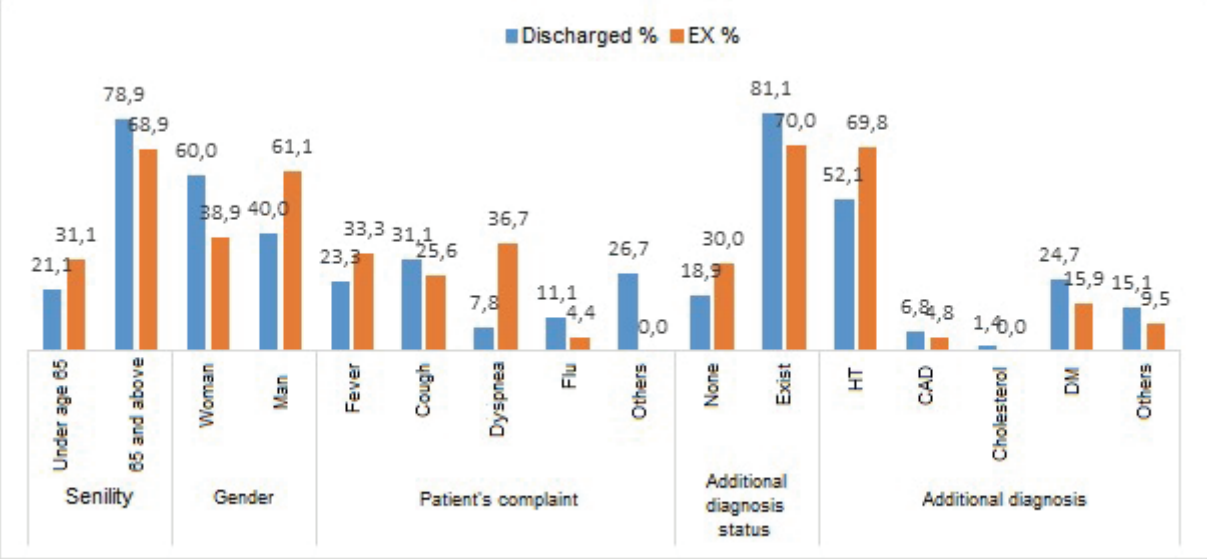

Figure 1: Complaints of COVID-19 patients discharged and exitus at the time of admission

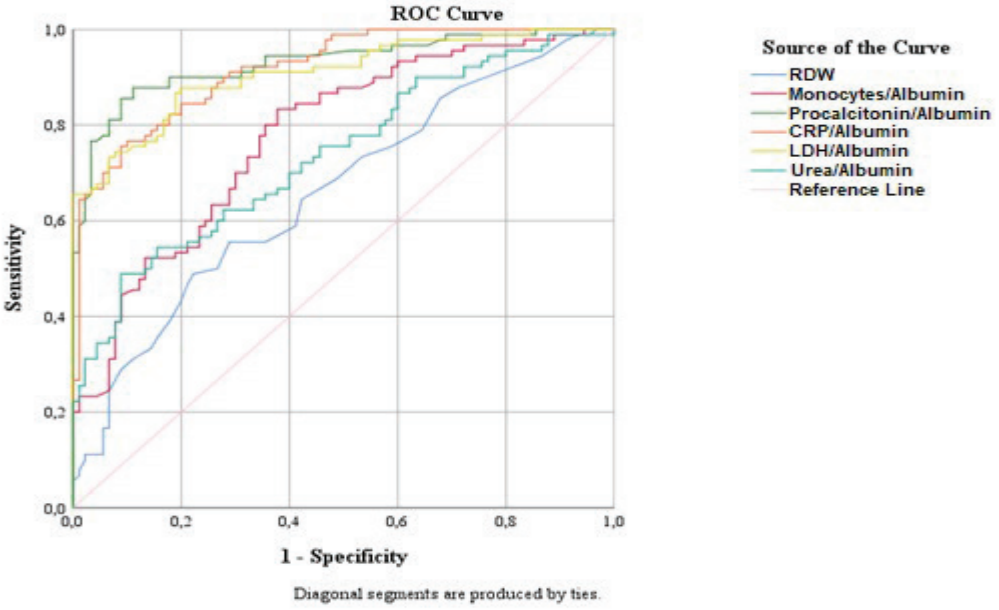

Figure 2: Hematological and biochemical blood parameters (equal to or more than the cut-off value) of COVID-19 patients who were discharged and died

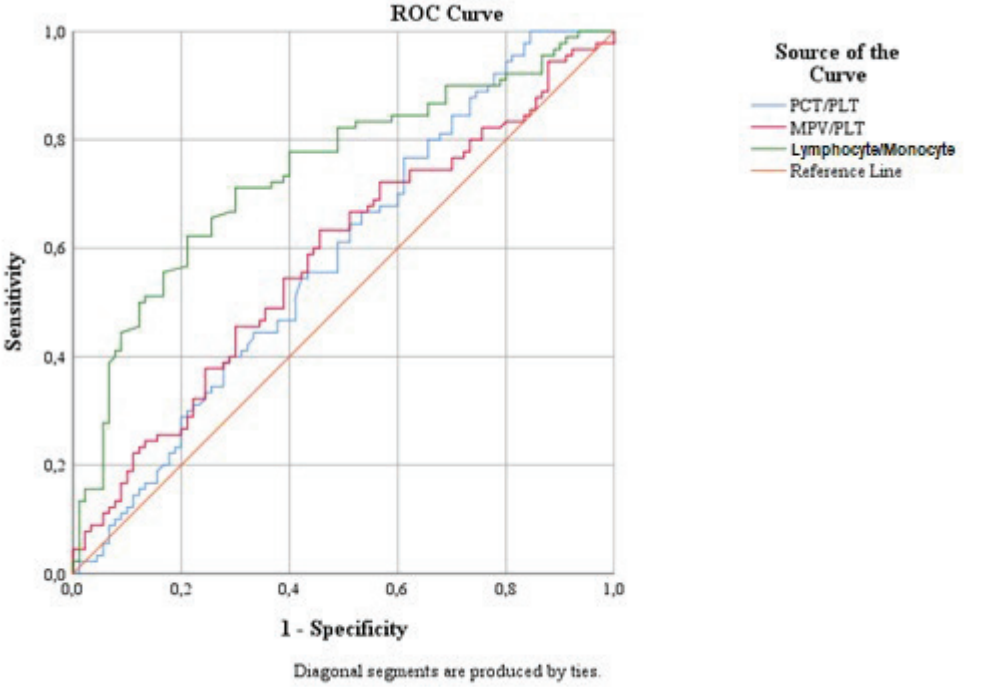

Figure 3: Hematological and biochemical blood parameters (equal to or more than the cut-off value) of COVID-19 patients who were discharged and died

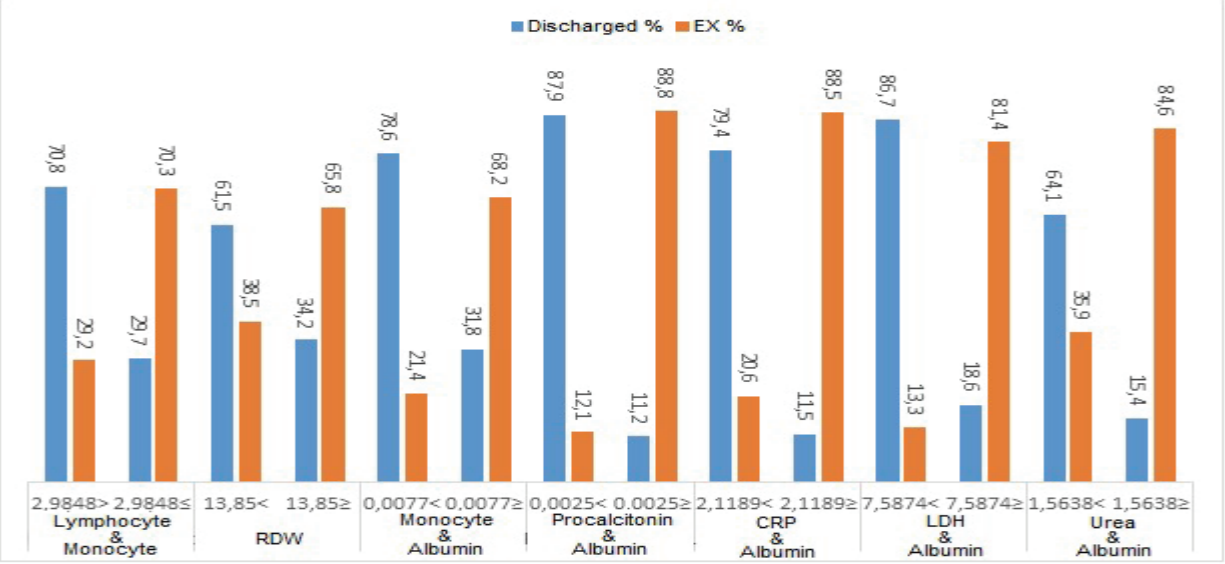

Figure 4: Hematological and biochemical blood parameters of COVID-19 patients who were discharged and died

DISCUSSION

The purpose of this study was to determine the efficacy of using hematological and biochemical markers as an early predictor of prognosis in individuals diagnosed with COVID-19. When our findings were compared to the existing literature, it was discovered that the majority of patients who died in a similar manner were male (61.1 %). Thus, we have proven that mortality may be reduced by predicting and changing treatment choices early in the disease's progression. Males and females have the same incidence of SARS-CoV-2 infection, while men with COVID-19 have a more severe disease course and a greater mortality rate, regardless of their age[11-13].

The infection's clinical course is quite varied, with fever, coughing, and malaise being the most prevalent symptoms[14]. Guan and et al. in a series of 1099 instances, it was revealed that the most often encountered symptoms were fever (88.7 %) and cough (67.8 %)[15]. Another clinical trial done in Spain discovered that the onset of dyspnea indicated a more severe clinical course for the illness[16]. According to the literature, the most common symptoms of patients released in excellent health were cough and fever. In a French observational research, it was shown that patients admitted to the critical care unit had much longer hospital stays than those admitted to the general service[17]. Our investigation yielded comparable findings to those seen in the literature. In our study, individuals who died of COVID-19 infection required a longer inpatient stay than those who recovered. PLT, MCV, CRP, monocytes, AST, ALT, LDH, ferritin, INR, procalcitonin, troponin, and WBC levels were found to be significantly higher in patients who died in line with the literature at the time of admission.

COVID-19; It can cause thrombosis in both venous and arterial systems with the effect of increased inflammation, platelet activation, endothelial dysfunction and stasis in blood flow. This condition, which has started to be named as COVID-19-associated coagulopathy, is thought to be related to the severity of the disease, the pathogenesis is not yet known, but it occurs as a result of the "thrombo-inflammation" picture. This picture becomes evident with coagulopathy, increased D-dimer and fibrinogen levels, minimal change in prothrombin time (PZ), activated partial thromboplastin time (aPTZ), and platelet count. High D-dimer level at admission is associated with increased mortality. The continuation of D-dimer increase after hospitalization is a harbinger of multiorgan failure and intra-

vascular coagulation. Bleeding findings are not common despite coagulopathy . In our study, it was determined that there was a statistically significant difference between the INR levels of ex and surviving COVID-19 patients.

As with inflammatory disorders, increased capillary permeability caused by systemic infection results in albumin leakage into the interstitial space, resulting in hypoalbuminemia[18]. The monocyte albumin ratio has been proven to be a reliable predictor of long-term mortality in patients receiving percutaneous coronary intervention[19]. This rate was substantially higher in patients than previously reported in the literature in our research. Hypoalbuminemia is implicated in the mortality of COVID-19 infected patients with cardiac complications.

Procalcitonin/albumin ratio is a marker for urosepsis in urinary tract infection. Simultaneously, there is evidence that a high procalcitonin/albumin ratio may be a predictor of the development of septic shock, particularly in severe septic shock patients after infection[20]. Our investigation found that patients with a high procalcitonin/albumin ratio had a higher death rate, which was consistent with previous research. These investigations shown that procalcitonin/albumin ratios may be a biomarker for early septic shock development in COVID-19 infection.

CRP concentrations more than 130 mg/l have been linked to an increased risk of death. Simultaneously, it was discovered that the CRP/albumin ratio was considerably greater in individuals with severe disease and those who died than in those with moderate disease in COVID-19 infections[21]. The CRP/albumin ratio was substantially greater in individuals who died according to the literature in our research. The study's limitations include the following: data were gathered from a single clinical research facility, not from many clinical research centers. The findings of this study may differ from those of other scientists in the United States and overseas and should be further explored in clinical situations.

CONCLUSION

According to our research, males are more likely to mortal from COVID-19 disease.

- The disease manifests initially as mild thrombocytopenia and lymphopenia.
- D-Dimer and INR levels are elevated in fatal cases, suggesting that coagulopathy is present.
- Ferritin, RDW, monocyte/albumin ratio, procalcitonin/albumin ratio, BUN/albumin ratio, CRP/albumin ratio, and LDH/albumin ratio all indicate that hypoalbuminemia is a prognostic factor for the disease.
- Comorbid conditions have a significant impact on disease prognosis.

Ethics Approval

The study protocol was approved by the Ethics Committee of Samsun Research and Treatment Hospital and was conducted in accordance with the principles of the Declaration of Helsinki (no:GOKA/2021/9/7)

Conflict of Interest

The authors have no conflicts of interest relevant to this article.

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Author contributions

HE: Contributed to the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. IH: Contributed to the collecting data of the work. ZE: Contributed to the collecting data of the work. SA: Contributed to the collecting data of the work. MU: Contributed to the collecting data of the work. CK: Contributed to the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. GK: Contributed to the collecting data of the work

References

1. Mackenzie JS, Smith DW. COVID-19: a novel zoonotic disease caused by a coronavirus from China: what we know and what we don't. Microbiol Aust. 2020 Mar 17:MA20013. doi: 10.1071/MA20013
2. Oladejo BO, Adeboboye CF, Adebolu TT. Understanding the genetic determinant of severity in viral diseases: a case of SARS-Cov-2 infection. Egypt J Med Hum Genet. 2020;21(1):77. doi: 10.1186/s43042-020-00122-z.
3. Driggin E, Madhavan MV, Bikdeli B. et al. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. J Am Coll Cardiol. 2020 May 12;75(18):2352-2371. doi: 10.1016/j.jacc.2020.03.031.
4. Mehta P, McAuley DF, Brown M. et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020 Mar 28;395(10229):1033-1034. doi: 10.1016/S0140-6736(20)30628-0.
5. Guan WJ, Ni ZY, Hu Y. et al; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720. doi: 10.1056/NEJMoa2002032.
6. Ruan Q, Yang K, Wang W. et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020 May;46(5):846-848. doi: 10.1007/s00134-020-05991-x.
7. Wang F, Nie J, Wang H et al. Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia. J Infect Dis. 2020 May 11;221(11):1762-1769. doi: 10.1093/infdis/jiaa150.
8. Sun S, Cai X, Wang H. et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clin Chim Acta. 2020 Aug;507:174-180. doi: 10.1016/j.cca.2020.04.024.
9. Chen N, Zhou M, Dong X. et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020 Feb 15;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7
10. World Health Organization. (2020). Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization. https://apps.who.int/iris/handle/10665/332196.
11. Zhang JJ, Dong X, Cao YY. et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020 Jul;75(7):1730-1741. doi: 10.1111/all.14238.
12. Li Q, Guan X, Wu P. et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. The New England journal of medicine. 2020;382(13):1199-207.
13. Jin JM, Bai P, He W. et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health. 2020 Apr 29;8:152. doi: 10.3389/fpubh.2020.00152.
14. Lovato A, de Filippis C. Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms. Ear Nose Throat J. 2020 Nov;99(9):569-576. doi: 10.1177/0145561320920762.
15. Guan WJ, Ni ZY, Hu Y. et al. China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720. doi: 10.1056/NEJMoa2002032.
16. Rodríguez-Molinero A, Gálvez-Barrón C, Miñarro A. et al; COVID-19 Research Group of CSAPG. Association between COVID-19 prognosis and disease presentation, comorbidities and chronic treatment of hospitalized patients. 2020 Oct 15;15(10):e0239571. doi: 10.1371/journal.pone.0239571.
17. Boëlle PY, Delory T, Maynadier X. et al. Trajectories of Hospitalization in COVID-19 Patients: An Observational Study in France. J Clin Med. 2020 Sep 29;9(10):3148. doi: 10.3390/jcm9103148.
18. Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. JPEN J Parenter Enteral Nutr. 2019 Feb;43(2):181-193. doi: 10.1002/jpen.1451.
19. Zhang ZL, Guo QQ, Tang JN. et al. Monocyte-to-albumin ratio as a novel predictor of long-term adverse outcomes in patients after percutaneous coronary intervention. Biosci Rep. 2021 Jul 30;41(7):BSR20210154. doi: 10.1042/BSR20210154.
20. Luo X, Yang X, Li J. et al. The procalcitonin/albumin ratio as an early diagnostic predictor in discriminating urosepsis from patients with febrile urinary tract infection. Medicine (Baltimore). 2018 Jul;97(28):e11078. doi: 10.1097/MD.0000000000011078.
21. Gemcioglu E, Davutoglu M, Catalbas R. et al. Predictive values of biochemical markers as early indicators for severe COVID-19 cases in admission. Future Virology. 2021;16(5):353-67. doi.org/10.2217/fvl-2020-0319

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The İmpact of COVID-19 Pandemic on The Diagnostic Distribution in Dermatology Outpatient Clinic

COVID-19 Pandemisinin Dermatoloji Polikliniğinde Tanı Dağılımına Etkisi

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Abstract

Aim After the COVID-19 epidemic, the admission frequency of dermatological diseases has changed. The aim of this study is to evaluate admission diagnoses in dermatology outpatient clinics during the COVID-19 pandemic.

Material and Method The International Codes of Diseases (ICD-10) categories and patient's diagnoses were evaluated before and after the pandemic. All patients, who applied to the dermatology outpatient clinic between June 1, 2020, and September 1, 2020, were included in our study. This information was compared with the same period of the previous year.

Results The hospital admissions were found reduced by 42.6%. The ratio of the patients with dermatophytosis, anogenital warts, scabies, seborrheic keratosis, urticaria, and xerosis cutis was significantly increased ($p < 0.05$), while the ratio of patients with actinic keratosis, callosities and corns, allergic contact dermatitis, lichen simplex, melasma, mycosis fungoides, nail disorders, nevi, prurigo nodularis, pruritus, psoriasis, and warts were significantly decreased after the COVID-19 pandemic ($p < 0.05$).

Conclusion The present study shows the frequency and most common types of outpatient dermatology visits, during the period of restriction reduction 3-6 months after the coronavirus pandemic. Many factors such as restrictions and hygiene practices, that affecting the quality of life, may cause changes in the diagnostic distribution of dermatology.

Keywords COVID-19; skin diseases; diagnose.

Özet

Amaç *COVID-19 salgını sonrası dermatolojik hastalıkların başvuru sıklığı değişmiştir. Bu çalışmanın amacı, COVID-19 pandemisi sırasında dermatoloji polikliniklerine başvuru tanılarını değerlendirmektir.*

Gereç ve Yöntem *Pandemiden önceki ve sonraki Uluslararası Hastalık Kodları (ICD-10) kategorileri ve hasta tanıları değerlendirildi. Çalışmamıza 1 Haziran 2020 ile 1 Eylül 2020 tarihleri arasında dermatoloji polikliniğine başvuran tüm hastalar dahil edildi. Bu bilgiler bir önceki yılın aynı dönemi ile karşılaştırıldı.*

Sonuçlar *Hastane başvurularının %42.6 azaldığı bulundu. COVID-19 pandemisinden sonra dermatofitozlar, anogenital siğil, uyuz, seboreik keratoz, ürtiker ve kserozis kutis hastalarının oranı önemli ölçüde artarken; aktinik keratoz, kallus ve boynuzlaşma, alerjik kontakt dermatit, liken simpleks, melazma, mikozis fungoides, tırnak bozuklukları, nevüs, prurigo nodularis, pruritus, psoriazis ve siğiller anlamlı olarak azalmıştır ($p < 0.05$).*

Sonuç *Bu çalışma, koronavirüs pandemisinden 3-6 ay sonraki kısıtlama azaltma döneminde, ayaktan hasta dermatoloji ziyaretlerinin sıklığı ve en yaygın türlerini göstermektedir. Yaşam kalitesini etkileyen kısıtlamalar ve hijyen uygulamaları gibi birçok faktör dermatolojinin tanısal dağılımında değişikliklere neden olabilir.*

Anahtar Kelimeler *COVID-19; cilt hastalıkları; tanı.*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an emerging respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first recognized in Wuhan, China, in December 2019[1]. It has spread rapidly all over the world and been declared as a pandemic by the World Health Organization (WHO). Healthcare services internationally have reduced or canceled the majority of elective activity to focus on emergency care during the pandemic.

The first case was seen on March 11 2020 in Turkey, the day WHO declared a pandemic[2]. The rapid increase of the infected count created the necessity to take precautions to reduce the spread of the infection. The government gradually took a series of strict measures, including curfews, to ensure social isolation due to arising new cases in all cities across the country within a short time. As of June, restrictions have been eased and some have been ended. Routine dermatology outpatient care was also started again in June. However, the number of patients who want to admit dermatology outpatient clinics, as well as the diagnostic spectrum of the dermatologic diseases, was significantly affected due to the psychological consequence or other type effects of the pandemic[3,4].

The aim of this study is to evaluate the changes in the frequency and profiles of dermatologic diseases, after restrictions were reduced, by comparing with the same period of the last year.

MATERIALS and METHODS

Study design and patients

The current study was an observational single-centre study and conducted retrospectively by examining the numbers and diagnoses of patients who applied to the dermatology outpatient clinic in Sakarya University Education and Research Hospital in Turkey. The total number of patient and their diagnoses, who applied to the outpatient clinic between June 1, 2020 and September 1, 2020 were included in the present study. The total number and diagnosis of patients, who applied to the hospital in the same period of the previous year, were also investigated in order to exclude seasonal effects by scanning the hospital registry system. The diagnoses were listed based on the primary and digit categories of ICD-10 (International Classification of Diseases-10th Revision) codes. Category codes with three characters including code letters and the following two numerical digits were used, and subcategories were collected under its category. However, subcategoric numerical digits were used to differentiate several diagnoses This study complied with the Declaration of Helsinki and was approved by the independent medical ethics committee of Sakarya University Education and Research Hospital, Sakarya, Turkey (20/10/2020: 71522473/050.01.04/559).

Statistical analysis

Analyses were performed using commercial software (MedCalc Statistical Software version 19.5.3, MedCalc Software bvba, Ostend, Belgium). The Chi-Square test was used to compare the prevalence of various dermatological diseases between 2019 and 2020 years. Odds ratios and 95% Confidence Intervals (CI) were calculated for dermatological diseases. Categorical variables were presented as a count and percentage. A p-value <0.05 was considered significant.

RESULTS

A total of 17494 patients were admitted to the dermatology outpatient clinic between 1 June 2019 and 1 September 2019, while 10054 patients were admitted between 1 June 2020 and 1 September 2020 with a 42.6% reduction in admissions to our dermatology outpatient clinic. The percentage of patients with scabies, anogenital warts, dermatophytosis, seborrheic keratosis, urticaria, and xerosis cutis were significantly increased after the pandemic (Table 1). However; the percentage of patients with actinic keratosis, callosities and corns, allergic contact dermatitis, lichen simplex chronicus, melasma, mycosis fungoides, nail disorders, melanocytic nevi, prurigo nodularis, pruritus,

psoriasis, and warts were significantly decreased after the COVID-19 pandemic (Table 2). The percentage of other dermatologic diseases were not significantly changed after the COVID-19 pandemic (Table 3). The odds ratio for diseases that increased or decreased after the COVID-19 pandemic is shown in Table 4.

Table 1. Dermatologic diseases which increased significantly 3-6 month after the occurrence of the COVID-19 pandemic.

Diseases	ICD-10 code	Before COVID-19	After COVID-19	P values
Scabies	B86	211 (%1,2)	277 (%2,75)	<0,001
Anogenital warts	A63.0	152 (%0,87)	112 (%1,11)	0,049
Dermatophytosis	B35	1493 (%8,53)	998 (%9,93)	<0,001
Seborrheic keratosis	L82	156 (%0,89)	122 (%1,21)	0,010
Urticaria	L50	799 (%4,57)	556 (%5,53)	<0,001
Xerosis cutis	L85.3	1035 (%5,91)	989 (%9,83)	<0,001

Data are n (%).
Abbreviation: ICD, International Classification of Diseases

Table 2. Dermatologic diseases which decreased significantly 3-6 month after the occurrence of the COVID-19 pandemic.

Diseases	ICD-10 code	Before COVID-19	After COVID-19	P values
Actinic keratosis	L57.0	152 (%0,86)	51 (%0,5)	<0,001
Allergic contact dermatitis	L23	159 (%0,9)	58 (%0,58)	0,004
Prurigo nodularis	L28.1	128 (%0,73)	47 (%0,47)	0,009
Pruritus	L29	636 (%3,63)	231 (%2,3)	<0,001
Lichen simplex	L28	235 (%1,34)	94 (%0,93)	0,003
Melasma	L81. 1	322 (%1,84)	129 (%1,28)	<0,001
Mycosis fungoi-des	C84	195 (%1,11)	44 (%0,44)	<0,001
Nail disorders	L60	132 (%0,75)	46 (%0,46)	0,004
Callosities and corns	L84	272 (%1,55)	99 (%0,98)	<0,001
Melanocytic nevi	D22.9	207 (%1,18)	70 (%0,7)	<0,001
Psoriasis	L40	1032 (%5,9)	466 (%4,63)	<0,001
Warts	B07	755 (%4,31)	314 (%3,12)	<0,001

Data are n (%).
Abbreviation: ICD, International Classification of Diseases.

Table 1. Dermatologic diseases which increased significantly 3-6 month after the occurrence of the COVID-19 pandemic.

Diseases	ICD-10 code	Before COVID-19	After COVID-19	P values
Acne	L70.0	2795 (%15,97)	1591 (%15,82)	0,743
Alopecia areata	L63	170 (%0,97)	83 (%0,82)	0,208
Atopic dermatitis	L20	250 (%1,43)	170 (%1,69)	0,090
Irritant contact der-matitis	L24	1779 (%10,17)	1003 (%9,98)	0,614
Erythema intertrigo	L30. 4	159 (%0,91)	98 (%0,97)	0,618
Herpes zoster	B02	135 (%0,77)	59 (%0,59)	0,086
Mollucum contagio-sum	B08.1	53 (%0,3)	24 (%0,24)	0,363
Neoplasms	D48.5	202 (%1,15)	119 (%1,18)	0,823
Pityriasis versicolor	B36.0	301 (%1,72)	154 (%1,53)	0,234
Rosacea	L71	172 (%0,98)	98 (%0,97)	0,935
Seborrheic dermati-tis	L21	564 (%3,22)	342 (%3,4)	0,420
Hypertrophic disor-ders of the skin	L91.8	255 (%1,46)	137 (%1,36)	0,500
Other follicular di-sorders	L73	278 (%1,59)	143 (%1,42)	0,268
Telogen effluvium	L65	274 (%1,57)	134 (%1,33)	0,113
Vitiligo	L80	222 (%1,26)	137 (%1,36)	0,480
Recurrent aphthous stomatitis	K12.0	39 (%0,22)	23 (%0,23)	0,866
Pemphigus vulgaris	L10.0	45 (%0,26)	36 (%0,36)	0,142
Androgenetic alope-cia	L64	84 (%0,48)	54 (%0,54)	0,498
Dyshidrosis	L30.1	101 (%0,58)	47 (%0,47)	0,230
Herpes simplex	B00	54 (%0,3)	31 (%0,31)	0,885

Data are n (%).
Abbreviation: ICD, International Classification of Diseases.

Table 4. The odds ratio for diseases which increased or decreased during the COVID-19 pandemic.

Diseases	Odds Ratio	95% Confidence Interval
Scabies	2,321	1,937 - 2,781
Anogenital warts	1,285	1,006 - 1,643
Dermatophytosis	1,181	1,086 - 1,285
Seborrheic keratosis	1,365	1,076 - 1,732
Urticaria	1,223	1,094 - 1,367
Xerosis cutis	1,735	1,584 - 1,9
Actinic keratosis	0,582	0,423 - 0,8
Allergic contact dermatitis	0,633	0,468 - 0,855
Prurigo nodularis	0,637	0,456 - 0,891
Pruritus	0,623	0,535 - 0,726
Licken simplex	0,693	0,545 - 0,882
Melasma	0,693	0,564 - 0,851
Mycosis fungoides	0,39	0,281 - 0,541
Nail disorders	0,605	0,432 - 0,846
Callosities and corns	0,63	0,5 - 0,794
Melanocytic nevi	0,586	0,446 - 0,769
Psoriasis	0,775	0,693 - 0,867
Warts	0,715	0,625 - 0,817

DISCUSSION

Hospital admissions decreased in countries affected by COVID-19 as a result of the restrictions taken against the pandemic. The COVID-19 pandemic has also a significant impact on dermatologic practice[5]. The distribution of dermatological disease in any country is affected by many factors. Therefore, the distribution of diagnoses after the pandemic needs to be investigated. As far as we know, there are several studies on the diagnostic profile of dermatologic diseases for those who applied to the outpatient clinic. The present study documented that, there was a 42.6% decrease in the number of applications to the dermatology outpatient clinic compared to the previous year after the restrictions were reduced in June. According to our results; acne, contact dermatitis, xerosis cutis, psoriasis, and urticaria were the most common diagnoses before the pandemic, respectively. Moreover, acne, contact dermatitis, callus, urticaria, and psoriasis were the most common diagnoses after the pandemic. The percentages of scabies, anogenital warts, dermatophytosis, seborrheic keratosis, urticaria, and xerosis cutis were found significantly increased after the onset of the COVID-19 pandemic. On the other hand, the percentages of diseases actinic keratosis, callosities and corns, allergic contact dermatitis, lichen simplex, melasma, mycosis fungoides, nail disorders, melanocytic nevi, prurigo nodularis, pruritus, psoriasis, and warts significantly decreased.

The previous studies have shown that psychological disorders such as depression and anxiety increase in the community with the COVID-19 pandemic[6,7]. An increasing percentage of psoriasis and urticaria is expected during the pandemic, which has profound effects on the quality of life8,9. Moreover, acute urticaria may be one of the presentations of COVID-19[10,11]. In the present study, both increase in social anxiety and stress and the negative impact of COVID-19 pandemic on the quality of life may explain the significant increase in urticaria. Psoriasis is a chronic disease in dermatology practice that has a well-known negative effect on the quality of life. Furthermore, psoriasis patients usually require regular follow-up. The percentage of psoriasis was found significantly decreased but remained one of the most common diagnoses after the pandemic. The admission to the hospital may have been reduced due to the convenience of receiving systemic therapy or biologic agents without going to the hospital with the issued regulation for these patients in Turkey. Furthermore, it is known that diseases such as pruritus, prurigo nodularis, telogen effluvium, vitiligo, alopecia areata, lichen simplex chronicus, and herpes zoster are associated with stress[12,13]. In the present study, it was found that these stress-triggered diseases decreased or did not change after the pandemic. In our country, the flexible working model has been started after the pandemic, therefore there may have been a decrease in stress levels.

Melasma, warts, nail disorders, melanocytic nevi, and actinic keratosis are among diseases that also significantly decreased during the COVID-19 pandemic as compared

with the corresponding period in the previous year. The significant decrease in the number of patients with these diseases may indicate that these diseases may be delayed under certain conditions. Moreover, people are also avoid going to the hospital due to fear of being exposed to the virüs. Therefore, the significant decrease in the number of certain diseases may be related to the fact that these diseases affect the quality of life less than other dermatological diseases that increased after the beginning of the pandemic.

In this study, we found that scabies cases increased 2.[32] times compared to the same period of the previous year. The increasing percentage of scabies during the pandemic have also been reported in other studies from Turkey[14-16]. The increased rate of scabies may be due to increased close contact as a result of home stay orders. Dermatophytosis and anogenital warts were also found significantly increased during the COVID-19 outbreak compared to the corresponding period in the last year. In previous studies, different results were obtained regarding the frequency of these diseases[15,17,18]. Since our study represents a high population and a long period, we think the consistency in the result may be more accurate. In the current study, xerosis cutis cases were found to be increased 1.73 times as compared with the corresponding period of the last year. Hygienic concerns led to the frequent use of soap, disinfectant, and cologne which might cause skin irritation[19,20]. So, the percentage of xerosis cutis may be increased due to the excessive use of protective hygiene measures.

According to our results, the admission to dermatology outpatient clinic with complaints of irritant contact dermatitis remained unchanged after the pandemic. Preventive hygienic measures have resulted in an increased in irritant contact dermatitis cases. However, patient education might have been playing an important role in decreasing these cases during the COVID-19 pandemic. In our study, we think that the unchanged in irritant contact dermatitis cases were caused by the balancing of these two factors. Atopic dermatitis also did not significantly change after the pandemic in our study. However, the ratio of allergic contact dermatitis was significantly decreased. This result may be due to restrictions on workplaces and encouragement to stay at home.

The present study has some limitations. First of all, our study was conducted in a single tertiary care center, and there was no demographic information of patients. Secondly, it was a retrospective design and there was no data such as detailed clinical examinations, anxiety levels, life quality, and their treatments. Tertiary, physicians may have made an error in ICD coding, especially in patients with multiple diagnoses.

In conclusion, the applications for dermatology outpatient clinics decreased significantly after COVID-19 arose in Turkey. This study shows the frequency and nature of outpatient dermatology visits and the most common types of diseases, seen 3-6 months after the coronavirus pandemic, reflecting the period when restrictions were reduced. Many factors caused the change in the diagnostic distribution of dermatology patients during the pandemic period. Understanding the effects of COVID-19 on health systems and patients will enable dermatologists to prepare faster for the diagnosis and etiology of diseases during the COVID-19 pandemic.

Confilict of Interest

None declared by the authors.

Financial Disclosure

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This study was approved by Sakarya University Education and Research Hospital Ethics Committee (20/10/2020: 71522473/050.01.04/559).

Authors contributions:

All authors have read and approved the final manuscript. N.C.C., M.Y. and B.S.D. performed the research. N.C.C.,

M.Y., B.S.D., and Ü.E. designed the research study. N.C.C, M.Y., B.S.D., and Ü.E. contributed essential reagents or tools. Ü.E. analysed the data. N.C.C. wrote the paper.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet; 2020; 395:497–506.
2. Sahin M, Haymana C, Demirci I, et al. The clinical outcomes of COVID-19 infection in patients with a history of thyroid cancer: A nationwide study. Clin Endocrinol (Oxf). 2021;95(4):628-637.
3. Gupta M, Abdelmaksuoud A, Jafferany M, et al. COVID-19 and economy. Dermatol Ther. 2020; 33(4): e13329.
4. Białynicki-Birula R, Siemasz I, Otlewska A, et al. Influence of COVID-19 pandemic on hospitalizations at the tertiary dermatology department in south-West Poland. Dermatol Ther. 2020;33(4): e13738.
5. Gisondi P, Piaserico S, Conti A, et al. Dermatologists and SARS-CoV-2: The impact of the pandemic on daily practice. J Eur Acad Dermatol Venereol. 2020; 34:1196-201.
6. 6. Ni MY, Yang L, Leung CM, et al. Mental health, risk factors, and social media use during the COVID-19 epidemic and cordon sanitaire among the community and health professionals in Wuhan, China: Cross-sectional survey. JMIR Ment Health. 2020;7(5): e19009.
7. Ozamiz-Etxebarria N, Dosil-Santamaria M, Picaza-Gorrochategui M, et al. Stress, anxiety, and depression levels in the initial stage of the COVID-19 outbreak in a population sample in the northern Spain. Cad Saude Publica. 2020;36: e00054020.
8. Kutlu Ö, Metin A. A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: will cases of psoriasis increase after COVID-19 pandemic? Dermatol Ther. 2020;33(4): e13383.
9. Kutlu Ö, Metin A. Dermatological diseases presented before COVID-19: are patients with psoriasis and superficial fungal infections more vulnerable to the COVID-19? Dermatol Ther. 2020;33(4): e13509.
10. Henry D, Ackerman M, Sancelme E, et al. Urticarial eruption in COVID-19 infection. J Eur Acad Dermatol Venereol. 2020;34: 244-245.
11. Aktas¸ H, Hamidi AA. Urticaria in a patient with COVID-19: therapeutic and diagnostic difficulties. Dermatol Ther. 2020; 33(4): e13610.
12. Livengood JM. The role of stress in the development of herpes zoster and postherpetic neuralgia. Curr Rev Pain. 2000; 4:7-11.
13. Osman OT, Mufaddel A, Almugaddam F, et al. The psychiatric aspects of skin disorders. Expet Rev Dermatol. 2011; 6:195-209.
14. Kutlu O, Güneş R, Coerdt K, et al. The effect of the "stay-at-home" policy on requests for dermatology outpatient clinic visits after the COVID-19 outbreak. Derm Ther. 2020; 33(4): e13581.
15. Turan C, Metin N, Utlu Z, et al. Change of the diagnostic distribution in applicants to dermatology after COVID-19 pandemic: What it whispers to us? Derm Ther. 2020; 33(4): e13804.
16. Ozden MG, Erturk K, Kartal SP, et al. An extraordinary outbreak of scabies in Turkey. J Eur Acad Dermatol Venereol. 2020;34(12): e818-e820.
17. Kutlu O, Metin A. Relative changes in the pattern of diseases presenting in dermatology outpatient clinic in the era of the COVID-19 pandemic. Dermatol Ther. 2020;33(6): e14096.
18. Kartal SP, Çelik G, Sendur N, et al. Multicenter study evaluating the impact of COVID-19 outbreak on dermatology outpatients in Turkey. Dermatol Ther. 2020; 33: e14485.
19. Singh M, Pawar M, Bothra A, et al. Overzealous hand hygiene during the COVID19 pandemic causing an increased incidence of hand eczema among general population. J Am Acad Dermatol. 2020;83(1):37-41.
20. Abtahi-Naeini B. Frequent handwashing amidst the COVID-19 outbreak: prevention of hand irritant contact dermatitis and other considerations. Health Sci Rep. 2020;3(2): e163.

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Dissociative Symptoms In Generalized Anxiety Disorder and Panic Disorder and Its Relationship with Temperament-Character Features

Yaygın Anksiyete Bozukluğu ve Panik Bozukluğunda Dissosiyatif Belirtiler ve Bunun Mizaç-Karakter Özellikleri ile İlişkisi

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Abstract

Aim The relationship between anxiety and dissociative symptoms is frequently mentioned, but dissociative symptoms are not seen in all patients with anxiety disorder. The aim of this study is to investigate the relationship between dissociative symptoms and temperament-character features in patients with anxiety disorders.

Material and Method The study sample consisted of 75 patients diagnosed with generalized anxiety disorder (GAD) and panic disorder (PD) according to DSM-5 and 75 healthy individuals for the control group (HC). The severity of their complaints were assessed using Hamilton Anxiety and Depression Rating Scales (HAM-A, HAM-D). Sociodemographic data form, Dissociative Experiences Scale (DES), Dissociation Scale (DIS-Q) and Temperament-Character Inventory (TCI) were filled for every participant.

Results There was a significant difference between the groups in terms of HAM-A, HAM-D, DES and DIS-Q scores (PD> GAD> HC). The factors affecting DES and DIS-Q scores were high HAM-A scores, diagnosis, low self-directedness(SD) and high self-transcendence(ST) scores, and when the diagnosis was checked, DES and DIS-Q scores continued to be affected by HAM-A, SD and ST scores.

Conclusion The high prevalence of dissociative symptoms was confirmed in patients with anxiety disorder. It was observed that character traits of low SD and high ST may be predisposing for the development of dissociative symptoms, while temperament traits were not influential on dissociative symptoms. These results may suggest that dissociation is not only related to trauma.

Keywords Anxiety, dissociation, temperament, character

Özet

Amaç *Anksiyete ve dissosiyatif semptomlar arasındaki ilişki sıklıkla belirtilir, ancak anksiyete bozukluğu olan tüm hastalarda dissosiyatif semptomlar görülmez. Bu çalışmanın amacı anksiyete bozukluğu olan hastalarda görülen dissosiyatif belirtilerin mizaç-karakter özellikleriyle ilişkisini araştırmaktır.*

Gereç ve Yöntem *Çalışmanın örneklemini DSM-5'e göre yaygın anksiyete bozukluğu (YAB) ve panik bozukluğu (PB) tanısı alan 75 hasta ve kontrol grubu (KG) için 75 sağlıklı birey oluşturmuştur. Şikayetlerinin şiddeti Hamilton Anksiyete ve Depresyon Derecelendirme Ölçekleri (HAM-A, HAM-D) kullanılarak değerlendirildi. Her katılımcı için sosyodemografik veri formu, Disosiyatif Yaşantılar Ölçeği (DES), Disosiyasyon Ölçeği (DIS-Q) ve Mizaç-Karakter Envanteri (TCI) dolduruldu.*

Sonuçlar *Gruplar arasında HAM-A, HAM-D, DES ve DIS-Q skorları (PB> YAB> KG) açısından anlamlı fark vardı. DES ve DIS-Q skorlarını etkileyen faktörler; yüksek HAM-A skorları, tanı, düşük kendini yönetme(KY) ve yüksek kendini aşma(KA) skorlarıdır ve tanı kontrol edildiğinde DES ve DIS-Q skorları HAM-A'dan, KY ve KA skorlarından etkilenmeye devam etmiştir.*

Sonuç *Anksiyete bozukluğu olan hastalarda dissosiyatif semptomların yüksek prevalansı doğrulandı. Düşük KY ve yüksek KA karakter özelliklerinin dissosiyatif semptomların gelişimine yatkınlık oluşturabileceği, mizaç özelliklerinin dissosiyatif semptomlar üzerinde etkili olmadığı gözlenmiştir. Bu sonuçlar, dissosiyasyonun sadece travma ile ilgili olmayabileceğini düşündürmektedir.*

Anahtar Kelimeler *Anksiyete, dissosiyasyon, mizaç, karakter*

INTRODUCTION

Dissociation is defined as"disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior". According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) dissociative symptoms can potentially disrupt all aspects of psychological functioning.[1] Dissociative experiences can occur during a wide spectrum of phenomena ranging from imagination, forgetfulness to dissociative identity disorder. Depersonalization and derealization might be experienced temporarily in case of fatigue and hypnosis.[2] Previous studies have shown that patients with anxiety disorder experience more dissociation than those without anxiety disorders.[3] Depersonalization and derealization in anxiety disorders are symptoms that can be easily observed, especially during panic attacks. It is reported that 7-69% of patients with a panic disorder experience depersonalization and derealization during panic attacks.[4,5] Segui et al. reported that 24,1% of patients with a panic disorder also suffer from depersonalization¸ frequency of dissociative symptoms vary according to culture. The rate of this frequency, however, is not less than 10%.[5]

There is a well established relationship between dissociative disorders and trauma. However, dissociative symptoms in individuals who have been exposed to similar trauma may vary. Only 25% of individuals suffering from developed post traumatic stress disorder (PTSD) and the proportion of those with dissociative disorder remained unknown. Therefore, a stress-diathesis model has been proposed for both PTSD and dissociative disorders. Although the risk factors for PTSD are well defined, there are few known risk factors that may predispose to dissociative symptoms except for high hypnotizability.[6] In a study examining the relationship between personality and dissociation in general psychiatric patients and healthy individuals, dissociation scores were found to be associated with low self-directedness (SD) and high self-transcendence (ST) character traits.[7] In a community study of psychological defense styles, mature defenses were associated with low dissociation scores.[8] Some reports have also found that dissociative experiences were observed more frequently in those with B cluster personality traits[9] and there is literature on low SD in character traits in cluster B personality disorders.[10] İt is important to understand whether the dissociative symptoms seen in anxiety patients are caused by the disease itself or by the temperament-character characteristics of the patient.

The aim of this study is to investigate the relationship between dissociative symptoms and temperament-character features in patients with anxiety disorders. According to the statistical (regression analysis) results of our study, anxiety could be a contributing factor to dissociation when SD is controlled from the characteristics of dissociative symptoms in patients with anxiety disorder.

METHODS

Study sample

Patients with anxiety disorder who were consecutively admitted to Xxxxxxxxx University Medical Faculty Hospital Psychiatry Outpatient Clinic between July 2018 and December 2018 and known to be in remission for six months were included in the study. 200 participants were included in the study together with the patient and healthy control group. Semi-structured psychiatric interview was held face to face with the participants. The diagnoses were made according to DSM-5. Hamilton Depression / Anxiety Scales were completed as a baseline assessment. The control group completed a standardized Symptom Checklist-90-R (SCL-90-R) questionnaire. Participants were also asked to complete their Sociodemographic Data, Dissociative Experiences Scale (DES), Dissociation Scale (DIS-Q), Temperament and Character Inventory (TCI).

44 participants who did not complete the scales were excluded from the study. In addition, since there were only 6 patients from the anxiety disorder group other than the generalized anxiety disorder and panic disorder, these pa-

tients were excluded from the study considering that their representation power would be weak. 75 patients with anxiety disorder(45 of them were General Anxiety Disorder-GAD, 30 of them were Panic Disorder-PD) aged 18-65 and 75 healthy volunteers were included in the study. Statistical analyzes were made by dividing the participants into three groups: generalized anxiety disorder (45 patients), panic disorder (30 patients) and healthy control group (75 healthy volunteers).

Those who did not have cognitive competence to fill the scales (delirium, dementia, mental retardation ..) were not included in the study. Except for major depressive disorder those with comorbid psychiatric diseases and those with a significant increase in any of the SCL-90-R subscales used in the healthy control group were excluded. The study was conducted following the approval of Xxxxxxxxx University Clinical Research Ethics Committee. All participants gave written informed consent.

MATERIALS

Sociodemographic Data Form

A sociodemographic data form was used to obtain information from each participant on age, sex, marital status, employment status, educational status, duration of illness, most recently used treatment items, economic situation according to the participant's own assessment, alcohol and substance abuse.

The Symptom Checklist-90-Revised (SCL-90-R)

It is a 90-item self-report symptom inventory developed by Leonard R. Derogatis in the mid-1970s to measure psychological symptoms and psychological distress.

Hamilton Anxiety Rating Scale (HAM-A)

The Hamilton Anxiety Rating Scale (HAM-A) is a semi-structured scale which was developed by Hamilton in 1959 to determine the severity of anxiety neuroses. It consists of 14 items to evaluate the physical and psychic symptoms of anxiety. Yazıcı et al. conducted the Turkish reliability and validity of the scale.[11]

Hamilton Depression Rating Scale (HAM-D)

The Hamilton Depression Rating Scale (HAM-D) is widely used to measure the degree of depression, was developed by Hamilton in 1960. It consists of 17 items for evaluating the symptoms of depression in the last week. Items question the difficulty of falling asleep, waking up at midnight, waking up early in the morning, somatic symptoms, genital symptoms, attenuation and insight. The validity and reliability of the scale's Turkish version was studied by Akdemir et al.[12]

Dissociative Experiences Scale-DES

Currently, the Dissociative Experiences Scale (DES) is the most widely used psychometric tool for evaluating dissociative experiences. DES is a self-assessment tool consisting of 28 items based on the assumption that dissociative continuity range from mild-normative to severe pathological dissociation. Amnesia, depersonalization, derealization and absorption scans of each item in the scale ranging between 0–100 are presented by 10-point increments. The overall DES score is the average score every item, it ranges from 0 to 100. Scoring 30 and above is an important pathological sign of dissociation[13]. Reliability and validity of this scala in Turkey was studied by Şar et al in 1995.[14]

Dissociation Scale (DIS-Q)

The Dissociation Scale(DIS-Q) is the first European dissociation scale[15,16]. DIS-Q is a questionnaire that is filled out by the participants themselves; it consists of 63 questions and each question is scored between 1-5. It scans more symptoms than DES and includes symptoms of eating disorders. Reliability and validity of the scale in Turkey was studied by Şar et al.[16]

Temperament and Character Inventory (TCI)

The inventory consists of 240 items in total. Each item is answered as either right or / wrong, it was developed by Cloninger et al(1994).[17] The TCI-R is designed to measure

4 temperaments, Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Persistence (PS), and three characters, Self-directedness (SD), Cooperativeness (CO), and Self-transcendence (ST). The items in the inventory are listed in random order and grouped into different facets. Approximately half of the items are reverse scored. Validity and reliability and standardization studies have been done in Turkish.[17,18]

Statistical analysis

The data obtained from the sample were analyzed with IBM SPSS 20 software. Chi-square test was used to compare categorical variables between groups. Whether numerical variables are normally distributed was determined by Shapiro-Wilk test. In comparison of the normally distributed numerical values, Student-t test was used between the two groups and the one-way analysis of variance (ANOVA) test was applied between the multiple groups. In all ANOVA tests, post hoc analysis was performed with Bonferroni correction. Mann Whitney-U test and Kruskal-Wallis one-way analysis of variance were applied for numerical values that did not show normal distribution.

Linear dependent regression analysis was used to understand the effect of diagnosis and temperament-character on dissociation symptom severity. DES and DIS-Q are dependent variables. All analyzes were bidirectional and the statistical significance level was accepted as $p < 0.05$.

RESULTS

150 participants in total, (75 patients and 75 healthy controls), were included in the study. 45 patients had a GAD and 30 patients had PD. There was no significant difference between the three groups in terms of gender, marital status, employment status, economic status, distribution of alcohol use and distribution of drug use or / non-use status of the patient group (Table 1) (all p values respectively; $p = 0.63$, $p = 0.452$, $p = 0.58$, $p = 0.271$, $p = 0.278$, $p = 0.154$). When the age and year of education of the groups were compared with one-way ANOVA, a significant difference was found in terms of both age and duration of education. Post-hoc Bonferroni correction presented a significant difference in terms of the length of education of the subjects. Hence, the length of education of the healthy control group was found to be higher than the patient group. There was no significant difference between the two patient groups (GAD and PD) in terms of education. Although there was a difference between the groups according to ANOVA in terms of age, the significance of age disappeared in post hoc Bonferroni correction. The comparison of the groups in terms of age and length education is given in Table 2.

In the comparison of patient groups according to Student t-test in terms of disease duration (in months); the mean duration for GAD groups was 19.16 months (SD: 23.14) and the mean duration for PD group was 22.47 months (SD: 28.11) and there was no significant difference ($p = 0.58$).

There was a significant difference between the three groups in terms of clinical assessment scales (HAM-A, HAM-D, DES, DIS-Q) in one-way ANOVA. The comparison of the groups in terms of clinical assessment scale scores is shown in Table 3. This significant difference was due to the PD group having higher scores in all clinical assessment scales than the GAD group, and the HC group had lower scores in all scales than the two patient groups.

One-way ANOVA was used to compare the 3 groups (HC, GAD and PD) in terms of TCI sub-scale scores. Significant differences were obtained in temperament sub-scales concerning HA score and in character sub-scales concerning, SD and ST scores. The comparison of the participants in terms of TCI sub-scale scores is presented in Table 4. The significant difference observed in HA scores was due to HA scores being significantly lower in HC group than the other two patient groups; no significant difference was found between the patient groups. It was observed that the significant difference in SD scores was due to the higher SD scores in the control group compared to the two pa-

tient groups, no significant difference was found between the patient groups. It was seen that the significant difference in ST scores was caused by the difference between the PD group and the HC group. There was no significant difference between the HC and GAD groups.

Age, education, HAM-A, HAM-D were found to be different between the groups. In the one-way ANOVA, the difference between the groups was determined as HA, SD, ST as the covariate. Linear regression analysis was also performed (DES scores dependent variable, HA, SD, ST, HAM-A, HAM-D, education, age and diagnosis independent variable). The factors determining DES scores were found to be SD, ST and HAM-A. Similar results were observed when DIS-q was taken as the dependent variable instead of DES (Table 5). The results showed that dissociation was associated with diagnosis, HAM-A, and character subscales (self-directedness and self-transcendence). The effect of anxiety on dissociation continued even when the diagnosis was controlled.

Table 1: The comparison of the groups in terms of gender, marital status, working status, economic status, alcohol-substance use and treatment use / non-use distributions

	HC	GAD	PD	p
Sex				
Female	45	25	20	0.63
Male	30	20	10	
Marital Status				
Married	30	21	10	0.452
Single	43	22	17	
Widow	2	2	3	
Employment Status				
Working	31	14	5	0.58
Unemployed	15	16	13	
Student	29	15	12	
Economical Status				
Bad	0	2	2	0.271
Middle	57	35	23	
Good	18	8	5	
Alcohol Use				
No	64	39	29	0.278
Social Drinker	11	6	1	
Drugs				
No		22	15	0.154
SSRI		18	15	
SNRI		5	0	

HC: Healthy Control; **GAD:** General Anxiety Disorder; **PD:** Panic Disorder; **SSRI:** Selective Serotonin Reuptake Inhibitor; **SNRI:** Serotonin–Norepinephrine Reuptake Inhibitor

Table 2: Comparison of the groups in terms of age and length of education

		N	Mean	Std. Deviation	Std.Error	95% Confidence Interval for Mean		Min.	Max.	F	P
						Lower Bound	Upper Bound				
Education (year)	HC*	75	15.40	4.08	0.47	14.46	16.34	5.00	22.00	12.66	0.01
	GAD	45	12.82	3.98	0.59	11.63	14.02	5.00	20.00		
	PD	30	11.40	3.91	0.71	9.94	12.86	4.00	17.00		
Age	HC	75	32.63	11.71	1.35	29.93	35.32	19.00	63.00	3.67	0.028
	GAD	45	28.69	8.89	1.32	26.02	31.36	19.00	48.00		
	PD	30	27.33	8.53	1.56	24.15	30.52	18.00	45.00		

*: The group that makes a significant difference compared to post hoc Bonferroni
HC: Healthy Control; GAD: General Anxiety Disorder; PD: Panic Disorder.

Table 3: The comparison of the groups in terms of clinical scale scores

		N	Mean	Std. Deviation	Std.Error	95% Confidence Interval for Mean		Min.	Max.	F	P
						Lower Bound	Upper Bound				
HAM-A	HC*	75	4.39	2.24	0.26	3.87	4.90	0.00	9.00	329.19	0.000
	GAD	45	19.06	5.25	0.78	17.49	20.65	9.00	33.00		
	PD	30	25.80	6.22	1.14	23.48	28.12	6.00	39.00		
HAM-D	HC *	75	3.54	2.17	0.25	3.05	4.05	0.00	9.00	89.45	0.000
	GAD	45	10.02	4.37	0.65	8.70	11.34	3.00	20.00		
	PD	30	12.67	4.78	0.87	10.89	14.46	4.00	25.00		
DES**	HC	75	6.08	4.78	0.55	4.98	7.18	0.00	27.80	57.87	0.000
	GAD	45	13.30	11.20	1.67	9.94	16.67	0.00	52.50		
	PD	30	28.96	15.60	2.85	23.14	34.79	0.00	58.90		
DIS-Q**	HC	75	1.51	0.30	.034	1.44	1.58	1.03	2.25	39.36	0.000
	GAD	45	1.89	0.57	0.09	1.72	2.06	1.03	3.31		
	PD	30	2.41	0.65	0.12	2.16	2.65	1.12	3.73		

*: This is a group that differs from Post hoc Bonferroni. **: Significant differences in post hoc Bonferroni between the three groups. HC: Healthy Control; GAD: General Anxiety Disorder; PD: Panic Disorder; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; DES: Dissociative Experiences Scale; DIS-Q: Dissociation Scale.

Table 4: Comparison of the TCI sub-scale scores of the groups

		N	Mean	Std. Deviation	Std.Error	95% Confidence Interval for Mean		Min.	Max.	F	P
						Lower Bound	Upper Bound				
Novelty Seeking	HC	75	18.39	5.08	0.59	17.21	19.56	9.00	33.00	0.02	0.97
	GAD	45	18.40	4.66	0.70	16.00	19.80	11.00	30.00		
	PD	30	18.17	6.02	1.09	15.91	20.42	5.00	30.00		
Harm Avoid-an-ce(HA)	HC *	75	18.25	5.59	0.65	16.97	19.54	5.00	33.00	26.34	**0.000**
	GAD	45	24.42	5.62	0.84	22.73	26.11	6.00	33.00		
	PD	30	25.10	4.77	0.87	23.31	26.88	14.00	34.00		
Reward Dep-en-dence	HC	75	13.64	3.48	0.40	12.83	14.44	7.00	22.00	0.33	0.72
	GAD	45	14.13	3.39	0.50	13.11	15.15	8.00	21.00		
	PD	30	14.00	3.04	0.56	12.87	15.14	8.00	20.00		
Persistence	HC	75	4.88	1.74	0.20	4.48	5.28	1.00	8.00	1.44	0.24
	GAD	45	4.33	1.80	0.27	3.80	4.87	0.00	7.00		
	PD	30	4.57	1.63	0.30	3.96	5.17	1.00	7.00		
Self-directed-ness(SD)	HC *	75	31.36	6.40	0.74	29.89	32.83	17.00	44.00	22.79	**0.000**
	GAD	45	24.96	7.21	1.07	22.79	27.12	8.00	38.00		
	PD	30	22.50	7.48	1.37	19.71	25.29	11.00	38.00		
Cooperative-ness	HC	75	29.44	6.09	0.70	28.04	30.84	18.00	40.00	3.04	0.051
	GAD	45	26.67	5.83	0.87	24.91	28.41	12.00	37.00		
	PD	30	27.87	6.28	1.14	25.52	30.21	12.00	39.00		
Self-tran-scend-ence**(ST)	HC	75	14.32	5.64	0.65	13.02	15.62	2.00	30.00	5.75	**0.004**
	GAD	45	15.64	5.01	0.74	14.14	17.15	5.00	24.00		
	PD	30	18.43	6.38	1.16	16.05	20.81	7.00	30.00		

*: Post hoc Bonferroni' significant difference is due to the HC group. **: Post hoc Bonferroni showed a significant difference between the HC and PD group. HC: Healthy Control; GAD: General Anxiety Disorder; PD: Panic Disorder; TCI :Temperament and Character Inventory.

Table 5: Linear regression analysis where DES / DIS-q scores are dependent variables

Novelty Seeking	DES						DIS-q				
	B	Std. Error	Beta	t	P		B	Std. Error	Beta	t	p
Diagnosis	2.634	2.170	0.158	1.214	0.227		-0.063	0.093	-0.084	-0.671	0.504
Age	0.036	0.077	0.029	0.460	0.646		-0.001	0.003	-0.024	-0.396	0.693
Education	0.024	0.202	0.008	0.121	0.904		0.002	0.009	0.016	0.249	0.804
Harm Avoid-an-ce(HA)	-0.143	0.139	-0.069	-1.025	0.307		0.001	0.006	0.008	0.117	0.907
Self-Directed-ness(SD)	-0.368	0.121	-0.220	-3.034	**0.003**		-0.022	0.005	-0.290	-4.145	**0.000**
Self –Transcend-ence(ST)	0.401	0.141	0.177	2.842	**0.005**		0.025	0.006	0.247	4.100	**0.000**
HAM-A	0.662	0.213	0.505	3.112	**0.002**		0.039	0.009	0.676	4.310	**0.000**
HAM-D	-0.229	0.264	-0.092	-0.869	0.386		-0.020	0.011	-0.183	-1.785	0.076

HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; DES: Dissociative Experiences Scale; DIS-Q: Dissociation Scale.

DISCUSSION

150 participants in total, (75 patients and 75 healthy controls), were included in the study. 45 patients had a GAD and 30 patients had PD. There was no significant difference between the three groups in terms of gender, marital status, employment status, economic status, distribution of alcohol use and distribution of drug use or / non-use status of the patient group. The length of education of the healthy control group was found to be higher than the patient group. The most common anxiety disorder in patients applying to primary healthcare is the generalized anxiety disorder. In women, both GAD and PD are twice as much as men.19 Although it was not statistically significant in our study, both the number of GAD patients were higher than the number of PD and the number of female patients compared to the number of male patients.

In the literature, it is reported that patients with anxiety disorder experience more dissociation than healthy individuals.[3] Our study as also produced similar results (see Table 3). There are other studies in the literature reporting that 7-69% of patients with panic disorder experience depersonalization and derealization during panic attacks.[4,5] The relationship between depersonalization and anxiety is reported to have a higher rate in patients with a panic disorder compared to patients with other anxiety disorders or psychiatric disorders documented in the literatüre.[20] According to our knowledge, a study in the literature examining the relationship between GAD and dissociative experiences, suggests that there is a relationship between GAD and dissociative symptoms.[21]

HA scores are reported to be high in major depressive disorder, GAD and PD, whereas SD, ST, and CO scores are reported to be low in the literatüre.[22] It was reported that the relationship between depression and anxiety symptoms and high HA scores and low SD scores persisted when variables such as age, gender and education were controlled. High HA and low SD profile has been repeatedly shown in clinical groups with various anxiety disorders and in many non-clinical samples.[23] In our study, we also obtained consistent result with the literature (see Table 4). Considering high HA and low SD scores; it can be said that these are the most common temperament-character traits in anxiety disorders.

In a study conducted with 53 patients with depersonalization disorder and 22 healthy controls and examining the relationship between dissociation and personality factors, various personality factors were associated with pathological dissociation; specifically, harm avoidance and immature defenses were found to be quantitatively associated with dissociation and the severity of dissociation.[24] However, in this study, Cloninger's 3-dimensional personality questionnaire was used the investigation; temperament and character dimensions were taken into consideration. In a study examining the relationship between personality and dissociation in both psychiatric patients and healthy individuals, it was observed that dissociation scores were associated with low SD and high ST characteristics and were not affected by temperament characteristics.[7] In our study, ST scores were found to be higher in PD than in GAD and HC groups, but no significant difference was found between the HC and GAD groups. In a study of depersonalization and personality in PD, both subgroups of patients with depersonalization (during panic attacks and depersonalization disorder) also had a significantly lower score on SD and a higher score on ST. Depersonalization symptom or depersonalization disorder was not associated with temperament dimensions.[4]

SD is generally a dimension that is highly associated with personality disorders[10] and is also associated with panic disorder.[25] In a study investigating the relationship between PD subtypes and temperament and character dimensions, Somato-dissociative subtype was found to show negative correlation with SD.[26] Low SD explains the typical difficulties of people with personality disorders in accepting responsibility, having persistent low self-esteem, and disagreement with one's self. Usually, these people are also

less likely to cooperate. SD correlates with schizotypal symptoms (explaining the magical thinking and rich imagination in patients with personality disorders), narcissistic, and borderline (describing dissociative tendencies in patients with personality disorders) personalities. ST is a high TCI dimension over time test-retest correlation[27], but recent research has shown that modification of neural activity in temporoparietal areas can lead to rapid modulation of this personality trait. Urgisi et al. showed that temporoparietal region gliomas increased significantly after the operation.[28] These brain regions have been associated with depersonalization in both seizure-related disorders[29] and personality disorders.[30] Those who score high in ST may experience extra-sensorial perceptions and thoughts similar to those induced by certain drugs such as cannabinoids, hallucinogens, and ecstasy or ketamine.[31,32] These findings in addition to our own suggest that there is a high tendency of dissociation in GAD, although not at the same severity as panic disorders, that self-transcendent character and dissociative experience of anxiety may originate more from common neuroanatomic centers rather than similar clinical courses. It can also be interpreted that a feature that should be consistent over time as a dimension of personality (- when it comes to self-transcendence) may be associated with the fact that the tendency for dissociative symptoms increases as anxiety increases.

This study is important, because it is the first study according to our knowledge that examines dissociative symptoms in anxiety disorders and their relationship with temperament-character traits. Aligned with the literature, our findings showed that dissociation was associated with diagnosis, HAM-A, SD, and ST from the character subscales. We observed that HA subscale did not affect dissociative symptoms when anxiety was controlled. This finding shows us that HA sub-scale is a factor that affects dissociation via affecting anxiety rather than a direct affecting dissociation.

The study does have some limitations. Including more participants in the study may increase the power of the study. Another limitation of our study is that the control group and the patient group could not be matched in terms of age and duration of education.

CONCLUSION

Even if it is not possible to define a category of patients with a higher risk of developing dissociative symptoms, early identification of potentially susceptible personality traits might be clinically useful. Additionally, the presence of personality traits that are potentially prone to develop dissociative symptoms may contribute to discussions claiming that dissociation is mainly due to traumatic experiences. Further prospective studies are necessary to establish.

The research was started after getting approval from the local ethics committee.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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Author Contributions

Concept - MS, OMK; Design - MS, OMK; Supervision - OMK, ŞBN; Resource - MS; Materials - MS; Data Collection and/ or Processing - MS, OMK; Analysis and/or Interpretation - MS, OMK; Literature Search - MS, ŞBN; Writing - MS; Critical Reviews – ŞBN, OMK.

References

1. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub, 2013.
2. Spiegel D. Trauma, dissociation, and memory. Annals of the New York Academy of Sciences 1997, 821:225-237. doi: 10.1111/j.1749-6632.1997.tb48282.x
3. Wolfradt U, Meyer T. Interrogative suggestibility, anxiety and dissociation among anxious patients and normal controls. Personality and Individual Differences 1998, 25:425-432. doi.org/10.1016/S0191-8869(98)00023-3
4. Mendoza L, Navines R, Crippa JA, et al. Depersonalization and personality in panic disorder. Compr Psychiatry 2011, 52:413-419. doi: 10.1016/j.comppsych.2010.09.002.
5. Segui J, Marquez M, Garcia L, et al. Depersonalization in panic disorder: a clinical study. Comprehensive Psychiatry 2000, 41:172-178. doi: 10.1016/s0010-440x(00)90044-0.
6. Butler LD, Duran RE, Jasiukaitis P, et al. Hypnotizability and traumatic experience. The American journal of psychiatry 1996, 153:42-63. doi: 10.1176/ajp.153.8.A42.
7. Grabe H-J, Spitzer C, Freyberger HJ. Relationship of dissociation to temperament and character in men and women. American Journal of Psychiatry 1999, 156:1811-1813. doi: 10.1176/ajp.156.11.1811.
8. Romans SE, Martin JL, Morris E, et al. Psychological defense styles in women who report childhood sexual abuse: A controlled community study. American Journal of Psychiatry 1999, 156:1080-1085. doi:10.1176/ajp.156.7.1080.
9. Korzekwa MI, Dell PF, Links PS, et al. Dissociation in borderline personality disorder: a detailed look. Journal of Trauma & Dissociation 2009, 10:346-367.doi: 10.1080/15299730902956838.
10. Marchesi C, Cantoni A, Fonto S,et al. The effect of temperament and character on response to selective serotonin reuptake inhibitors in panic disorder. Acta Psychiatrica Scandinavica 2006, 114:203-210. doi: 10.1111/j.1600-0447.2006.00772.x.
11. Yazıcı MK DB, Tanrıverdi N, Karaağaoğlu E, ve ark. Hamilton Anksiyete Değerlendirme Ölçeği, derecelendiriciler arası güvenilirlik ve geçerlilik çalışması. Türkiye Psikiyatri Dergisi 1998, 9:114-117
12. Akdemir A, Örsel S, Dağ İ, ve ark. Hamilton Depresyon Derecelendirme Ölçeği (HD-DÖ)'nin geçerliği, güvenirliği ve klinikte kullanımı. Psikiyatri Psikoloji Psikofarmakoloji Dergisi 1996, 4:251-259.
13. Bernstein EM, Putnam FW. Development, reliability, and validity of a dissociation scale. Journal of nervous and mental disease 1986, 174(12):727-735. doi: 10.1097/00005053-198612000-00004.
14. Yargic LI, Tutkun H, Sar V. Reliability and validity of the Turkish version of the Dissociative Experiences Scale. Dissociation: Progress in the Dissociative Disorders 1995, 8(1):10-13.
15. Vanderlinden J, Van Dyck R, Vandereycken W, et al. The dissociation questionnaire (DIS-Q): Development and characteristics of a new self-report questionnaire. Clinical Psychology & Psychotherapy 1993, 1:21-27. doi:10.1002/cpp.5640010105
16. Şar V. Dissosiyasyon Ölçeği(DIS-Q)-Türkçe Versiyon (Uyarlama). İstanbul Tıp Fakültesi Psikiyatri Anabilim Dalı Klinik Psikoterapi Birimi, İstanbul 1996.
17. Cloninger CR, Przybeck TR, Svrakic DM, et al. The Temperament and Character Inventory (TCI): A guide to its development and use. 1994.
18. Arkar H, Sorias O, Tunca Z, ver ark. Mizaç ve karakter envanteri'nin Türkçe formunun faktör yapısı, geçerlik ve güvenilirliği. Türk Psikiyatri Dergisi 2005, 16:190-204.
19. Horwath E, Gould F, Weissman MM. Epidemiology of anxiety disorders. Textbook in psychiatric epidemiology 2011:311-328.
20. Hunter EC, Sierra M, David AS. The epidemiology of depersonalisation and derealisation. Social psychiatry and psychiatric epidemiology 2004, 39:9-18.doi: 10.1007/s00127-004-0701-4.
21. Carlson EB, Putnam FW. An update on the dissociative experiences scale. Dissociation: progress in the dissociative disorders 1993, 6(1):16-27.
22. Svrakic DM, Przybeck TR, Cloninger CR. Mood states and personality traits. Journal of affective disorders 1992, 24:217-226. doi.org/10.1016/0165-0327(92)90106-G
23. Samochowiec J, Kucharska-Mazur J, Hajduk A, et al. Personality profile of patients with anxiety disorder, as studied with the 16PF Cattell's questionnaire and Cloninger's TCI. Psychiatria polska 2005, 39:527-536.
24. Simeon D, Guralnik O, Knutelska M, et al. Personality factors associated with dissociation: temperament, defenses, and cognitive schemata. American Journal of Psychiatry 2002, 159:489-491. doi: 10.1176/appi.ajp.159.3.489.
25. Praško J, Houbová P, Novák T, et al. Influence of personality disorder on the treatment of panic disorder-comparison study. Neuro Endocrinol Lett 2005, 26:667-674.
26. Bruno A, Muscatello MRA, Pandolfo G, et al. Does personality matter? Temperament and character dimensions in panic subtypes. Archives of Neuropsychiatry 2018, 55:325-329. doi: 10.5152/npa.2017.20576
27. Brändström S, Schlette P, Przybeck TR, et al. Swedish normative data on personality using the Temperament and Character Inventory. Comprehensive psychiatry 1998, 39:122-128. doi: 10.1016/s0010-440x(98)90070-0.
28. Urgesi C, Aglioti SM, Skrap M, et al. The spiritual brain: selective cortical lesions modulate human self-transcendence. Neuron 2010, 65:309-319. doi: 10.1016/j.neuron.2010.01.026.
29. Blanke O, Mohr C, Michel CM, et al. Linking out-of-body experience and self processing to mental own-body imagery at the temporoparietal junction. Journal of Neuroscience 2005, 25:550-557. doi.org/10.1523/JNEUROSCI.2612-04.2005.
30. Irle E, Lange C, Weniger G, et al. Size abnormalities of the superior parietal cortices are related to dissociation in borderline personality disorder. Psychiatry Research: Neuroimaging 2007, 156:139-149. doi: 10.1016/j.pscychresns.2007.01.007.
31. Borg J, Andrée B, Soderstrom H, et al. The serotonin system and spiritual experiences. American Journal of Psychiatry 2003, 160:1965-1969. doi: 10.1176/appi.ajp.160.11.1965.
32. Freese TE, Miotto K, Reback CJ. The effects and consequences of selected club drugs. Journal of substance abuse treatment 2002, 23:151-156. doi.org/10.1016/S0740-5472(02)00267-2.

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Is Youtube Effective On Covid-19 Vaccination During Pregnancy?

Youtube Gebelik Döneminde Covid 19 Aşılaması Üzerine Etkili mi?

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Abstract

Aim YouTube® is one of the most frequently used social media platforms worldwide. The quality of the videos is of utmost significance in terms of the accurate information for pregnant women and in the diagnosis, treatment, and prevention of life-threatening diseases such as COVID-19. This study aimed to evaluate the content and quality of YouTube videos that pregnant women make use of as a source of information for covid-19 vaccines.

Material and Method A search was made on YouTube with the keywords and phrases such as "pregnancy and covid vaccination", "is the covid vaccine risky in pregnancy?". A total of 54 videos in English were analyzed. Video sources were divided into 5 groups hospitals, professional medical chambers, pregnant women, physicians and news channels. The quality of the contents was evaluated with DISCERN, GQS and the pregnancy covid vaccine index (CVI) we have developed for this purpose.

Results Of these videos, we have detected that 20 (37%) were shared by hospitals, 5 (9%) were shared by physicians, 5 (9%) were shared by pregnant women, 22 (41%) were shared by news programs or news program hosts, and 2 (4%) were shared by medical chambers. The mean DISCERN score was 33.2±17. The pregnant group was significantly different from the other groups in terms of GQS (p=0.048). There was no significant difference between the groups in terms of covid vaccination index during pregnancy (p= 0.501).

Conclusion This study revealed that there is an urgent need to regulate the content of videos according to the medical guideline.

Keywords COVİD-19, pregnancy, vaccination, YouTube

Özet

Amaç *YouTube® dünya çapında en sık kullanılan sosyal medya platformlarından biridir. Videoların kalitesi, hamile kadınlara doğru bilgi verilmesi ve COVID-19 gibi hayatı tehdit eden hastalıkların teşhisi, tedavisi ve önlenmesi açısından son derece önemlidir. Bu çalışma, hamile kadınların covid-19 aşıları için bilgi kaynağı olarak kullandığı YouTube videolarının içerik ve kalitesini değerlendirmeyi amaçlamıştır.*

Gereç ve Yöntem *YouTube'da "hamilelik ve covid aşısı", "covid aşısı gebelikte riskli midir?" gibi anahtar kelime ve ifadelerle arama yapıldı. Toplam 54 İngilizce video analiz edildi. Video kaynakları hastaneler, meslek odaları, hamileler, doktorlar ve haber kanalları olarak 5 gruba ayrıldı. İçeriklerin kalitesi DISCERN, GQS ve bu amaçla geliştirdiğimiz gebelik covid aşı indeksi (CAI) ile değerlendirilmiştir*

Sonuçlar *Bu videolardan 20'sinin (%37) hastaneler tarafından, 5'inin (% 9) doktorlar tarafından, 5'i (%9) hamile kadınlar tarafından, 22'si (%41) haber programları veya haber programı sunucuları tarafından ve 2'si (%4) tabip odaları tarafından paylaşılmıştır. Ortalama DISCERN skoru 33.2±17 idi. Gebe grup GQS açısından diğer gruplardan anlamlı olarak farklıydı (p=0.048). Gruplar arasında gebelikte covid aşı indeksi açısından anlamlı fark bulunmadı (p= 0,501).*

Sonuç *Bu çalışma, videoların içeriklerinin takip eden kişiler için acilen tıbbi kılavuza göre düzenlenmesi gerektiğini ortaya koydu*

Anahtar Kelimeler *COVİD-19, gebelik, aşı, YouTube*

INTRODUCTION

Today, many people make use of online systems to obtain health information. In this regard, YouTube is the second most used source of information throughout the world. Although its reliability has been tested and verified concerning many health-related issues, no evaluation has been made concerning the videos of COVİD-19 vaccination during pregnancy[1,2]. Covid -19 was declared a pandemic on March 11, 2020, and had caused significant morbidity and mortality worldwide[3].

During the current covid 19 infection, the impacts on pregnant women, fetuses, and infants were uncertain and undetermined at the beginning[4]. Although there are small-scaled studies which had been conducted demonstrating that it causes an increase in preterm birth, cesarean section delivery rates and intensive care unit admissions, its impacts within the scope of miscarriage, stillbirth, intrauterine growth retardation, long-term effects and neurodevelopmental side effects remained unanswered. A systematic multi-national review of 60 studies on SARS-CoV-2 in pregnancy reported that severe illness occurred in up to 18% of pregnant patients and critical disease complicated up to 5% of cases, comparable to rates in the general population[5]. While vaccine studies were initiated for the Covid 19 pandemic, pregnant women were excluded from the clinical study according to the traditional approach due to the fear of fetal side effects. There is negligible data available on the safety and efficacy of the vaccine in pregnancy, as vaccine companies exclude pregnant women from their phase studies. Considering the heavy burden and severity of the disease all pregnant women should be recommended to be vaccinated. It is not quite a correct approach to expect a different side effect from the non-pregnant population with respect to mRNA vaccines which have never been experienced before.[6-8]

In this study, we aimed to evaluate the quality and reliability of the informative role of social media with respect to these concerns while evaluating the anxious concerns we have while giving information about vaccination during the COVID 19 pandemic period to pregnant women who applied to our outpatient clinic.

METHODS

In September 2021, "pregnancy and covid vaccination" and "does covid vaccine bear risks in pregnancy" were scanned on YouTube (http://www.youtube.com). Duplicate videos, non-English videos, non-related content, videos that were included because only the keywords namely covid and pregnancy were excluded by using the YouTube filtering system. As a result of this scanning, 77 videos were reduced to 54 videos in total and an evaluation was made. A total of 54 videos were evaluated by two independent obstetricians and gynecologists (Ş.D. and F.A.). For each video, first of all the uploading users or institutions were taken into consideration and then they were divided into 5 groups as hospitals (A), professional medical chambers (B), pregnant women (C), physicians (D) and news channels (E). The date of publication of all videos, the number of views, the duration of the video, the number of likes and dislikes, and the number of comments were recorded. The proficiency and quality of the videos were evaluated using DISCERN and the Global Quality Scale (GQS). DISCERN is a scoring method consisting of a total of sixteen questions, scored from 1 to 5, and evaluated with a minimum of 16 and a maximum of 80 points (high quality). According to this method of scoring, 64-80 points are deemed excellent, 52-63 points are deemed good, 41-51 points are deemed poor, 30-40 points are deemed bad, 16-29 points are deemed very bad. The GQS uses a 5-point scale (1 to 5) to rate the overall quality of the video, based on the value of the information and how useful the reviewer thought the particular video would be to a patient . One point was scored to represent low quality (most of the information is missing, not useful for viewers at all) and 5 points to high quality (beneficial for viewers)[9]. There is no reliable video scoring system available which is specific to covid vaccination during pregnancy. In this study, we scored all videos by creating an index of covid vaccination in pregnancy

(CVI). Within the scope of this scoring, provided that the vaccine side effects, safety, non-teratogenicity, formation of fetal and maternal antibodies, the risks of covid disease in pregnancy, vaccination in pregnant women who previously had covid, the number of doses to be made, the authorized vaccine brand recommendation and the suitable trimester during which vaccination may be administered is mentioned, the videos were rated as 1 corresponding to each question whereas the videos in which such questions were not made mention of were rated as 0. For the video that answered all questions, 9 points had been given whereas for the video that did not answer the mentioned questions at all had been given 0 points (Table 1). We did not apply to any medical ethics committee for approval of this study, according to the Declaration of Helsinki of the World Medical Association, because no patient data or material was used and all videos used for the study were available on a public social media website (YouTube).

Table 1. Index of covid vaccination in pregnancy (CVI)	
Parameters	Value
sıde effect	1
safety	1
teratogenıcıty	1
formatıon of fetal maternal antıbodıes	1
rısks of covıd dısease	1
vaccınatıon of pregnant women who previously had covıd	1
number of vaccıne doses	1
suıtable trımester durıng whıch vaccınatıon may be admınıstered	1
vaccıne brand	1

Statıstıcs Statistical calculations were performed using SPSS version 25 (IBM Corp. Armonk, NY, USA). Categorical values were denoted as frequency, and continuous data were denoted as mean, median, and standard deviation. Shapiro-Wilk test was used to evaluate the normal distribution and the Levene test was used for variance homogeneity. Spearman correlation test was utilized. Kruskal-Wallis and Dunn Bonferroni's post-hoc tests were used for analysis between groups. Inter-rater reliability was determined by Cohen's kappa score (≤0 indicating no agreement, 0.01-0.20 indicating none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 substantial, 0.81–1.00 as almost perfect agreement). The correlation was determined as poor (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), or excellent (0.81-1.00) respectively. The significance threshold was acknowledged as $p<0.05$.

RESULTS

A total of 77 videos were encountered regarding pregnancy and covid 19 vaccination. Of these, 54 videos were found suitable for the criteria. All calculations were evaluated over these determined 54 videos. Of these 54 videos, we have detected that 20 (37%) were uploaded by hospitals, 5 (9%) were uploaded by physicians, 5 (9%) were uploaded by pregnant women, 22 (41%) were uploaded by news programs or news program hosts, and 2 (4%) were uploaded by medical chambers. The mean DISCERN score was 33.2±17. Accordingly, five (10%) videos were evaluated as excellent, six(11%) videos were evaluated as good, seven (13%) videos were evaluated as moderate, eight (15%) videos were evaluated as bad, and twenty-eight (51%) videos were evaluated as very bad.

The oldest dated video was added in December 2020, and the latest dated video was added in September 2021. The number of views per video was 19,154,15±31.092 and the total number of views of the videos was 2,068,648. The average number of likes and dislikes per video was 178.46 and 98.22, respectively. The average total video duration in terms of seconds was 331.11 secs. A detailed descriptive analysis of 54 videos is given in Table 2.

According to the analyze between groups (A, B, C, D, E), DISCERN scores were determined as 35.25, 35.40, 20.20, 34.00, 31.50, respectively. Looking at these values, it was seen that the videos were generally weak and of poor quality. There was no significant difference between the groups

Table 2. Video evaluation				
	Mean	Std. Deviation	Minimum	Maximum
Video Seconds	331,11	223,413	25	962
Video Streamıng	98,50	78,277	6	270
Like	178,46	638,325	0	4600
Unlike	,22	308,631	0	1800
Comment	67,31	213,354	0	1385
Number Of Vıews	19154,15	31092,640	13	155900
GQS	2,63	1,138	1	5
DISCERN	33,22	17,475	16	76
CVI	4,33	2,119	1	9
GQS: Global Qalıty Score; CVI: Covid Vaccination Index				

in terms of DISCERN scores, (p= 0.391). Through the instrumentality of the Global Quality Scale, the average score was 2.63 over 5. If we were to analyze between groups (A, B, C, D, E), GQS scores were 3.00, 2.20, 1.40, 2.68, and 2.50, respectively. Group C was significantly different from other groups in terms of GQS (p=0.048). A significant difference was found between the hospital (A) and pregnant women (C) groups in terms of GQS scores (p=0.003). If we were to analyze between groups (A, B, C, D, E), CVI during pregnancy were 4.80, 4.00, 3.00, 4.27, 4.50, respectively. No significant difference was observed between the groups in terms of CVI during pregnancy (p= 0.501) (Table 3 and 4). According to our scoring system, 48.1% of the video contents did not make mention of vaccines' side effects, 48.1% of them did not mention antibody response, 59.3% of them did not mention teratogenicity, 68.5% of them did not mention the number of vaccine doses, 68.5% did not mention the pregnancy trimesters, 88.9% failed to refer to vaccination in those who have previously had covid-19, 55.6% did not mention vaccine types, 55.6% did not mention brand recommendation for vaccination.

According to the reliability analysis (kappa score) for the inter-rater assessment agreement, it was seen that the kappa score for the GQS was 0.926 (p=0.0001), the kappa score for DISCERN was 0.919 (p=0.001), and the kappa score for CVI was 0.915 (p=0.001). It was determined that there was a perfect fit for the CVI scoring system.

Table 3. Comparison of scoring systems with respect to video sources						
Scoring type	Hospital(A) n=20(min-max)	Organization(B) n=2(min-max)	Pregnant(C) n=5(min-max)	Physician(D) n=5(min-max)	News(E) n=22(min-max)	p value
DISCERN	30(16-75)	31.5(16-47)	16(16-27)	38(16-57)	26.5(16-76)	.391
GQS	3 (2-5)	2.5(2-3)	1(1-2)	2(1-4)	3 (1- 5)	.048
CVI	5(1-8)	4.5(2-7)	4(1-5)	3(2-8)	4.5(1-9)	.501
Kruskal-wallis test, median (minimum-maximum) values, GQS: Global Quality Score; CVI: Covid Vaccination Index, GQS and DISCERN scoring systems were in positive correlation with each other (p=0.00).						

Table 4. Correlation Scoring Systems			
	CVI	GQS	DISCERN
CVI	-	,723 (p=.00)	,637(p=.00)
GQS	,723 (p=.00)	-	,792 (p=.00)
DISCERN	,637(p=.00)	,792 (p=.00)	-
GQS: Global Quality Score; CVI: Covid Vaccination Index, GQS and DISCERN scoring systems			

DISCUSSION

The purpose of this research was to evaluate the acquisition of information with the YouTube database, which became more important during the COVID-19 pandemic period. Although there is a YouTube study evaluating 48 videos about the COVID-19 vaccine in the literature, no research has been detected on the COVID-19 vaccine in pregnancy[10].

Within the scope of the COVID-19 vaccine initiative, approximately 150 vaccines have been preclinically studied, but fewer than 50 vaccines have reached and succeeded phase II-III trials.[11] BNT162b2 (Pfizer-BioNTech COVID-19 vaccine) was indicated for individuals at 12 years of age and older. But from October 2021 this vaccination was indicated for children between 5 to 11 years old according to FDA. mRNA-1273 (Moderna COVID-19 vaccine) is indicated for individuals 18 years of age and older. Ad26. COV2.S (Janssen COVID-19 vaccine) is indicated for individuals 18 years of age and older. Sinovac's CoronaVac vaccine, on the other hand, has been approved for a wide audience, but there have been concerns about its effectiveness. The choice between COVID-19 vaccines is based on availability and patient preference. Data concerning the safety of COVID-19 vaccines on pregnant women are limited, but in the light of new data, it has been demonstrated that mRNA vaccines are safe with respect to pregnancy[12] The anti-vaccination movement and the opposition to vaccination that we have heard about frequently in recent years, unfortunately, poses a great risk in terms of health all over the world.

This study aims to compare the educational content in YoutTube videos about the administration of COVID-19 vaccines during pregnancy, which is an extremely sensitive subject[13]. The videos about the COVID-19 vaccination during pregnancy on YouTube were evaluated according to the scoring systems that are well known in the literature and that we have adapted for this particular matter[14], 15. The high correlation between DISCERN, GQS and the CVI scoring systems we developed indicates the safe usability of the CVİ scoring system. As new scoring systems developed for YouTube are improved, choosing high-quality content and videos that provide accurate information will become an important part of education for the sake of the health system in the future according to the study conducted by Yüksel et al. YouTube videos are easily accessible COVID-19 information resources for pregnant women. This study demonstrated that videos about pregnancy and COVID-19 have high viewing rates, but they are generally poor in terms of quality and reliability[16] In our study, videos were uploaded mainly by news sources and hospitals. The videos with the lowest quality and insufficient content were those uploaded by pregnant women.

Each passing day, health literacy is increasing through social media.[17] No anti-vaccine video was detected in our study due to the measures taken by youtube in October 2020, "COVID-19 medical information policy". Yet another important feature of YouTube is that it allows even illiterate communities to learn and to get acquainted with new developments[18]. According to statistics, 74% of the global world watches YouTube and as of 2021, YouTube's world user base is approximately 2,240.03 billion users. In the course of the internet age when we are aware that YouTube is such effective, we think that the contents of health-related videos should be informative, scientifically proven and should not allow for misunderstandings. Brendi Drozd et al. have also shown in their study that there is no substantial scoring system developed for the assessment of YouTube videos[19]. The fact that a video is watched by umpteen users or received a large number of comments does not show that it is sufficient in terms of content. No correlation was determined between the length of the videos we evaluated, the number of views, likes and dislikes. There was only a moderate correlation between likes and comments. We did not examine whether the comments were in favor or adverse.

In our study, we found that videos with a high number

of views did not receive higher scores than other videos. When all videos were evaluated with three separate scoring systems, the group with the lowest score consisted of videos uploaded by pregnant women. The greatest difference was seen in the GQS. Since the videos uploaded by pregnant women were few in our study, there may not have been a statistical discrepancy. In the videos evaluated by two physicians (Ş.D. and F.A.), the kappa score was found to be low in terms of DISCERN and GQS systems, while a high agreement level was observed in the CVİ scoring system. Thus we have speculated that the reason for this high agreement level was that the score we developed necessitated quantal responses.

There are certain limitations to our study. Our review of videos uploaded and watched in a short period is one of them. The fact that the subject is on the agenda and the data regarding the COVID-19 vaccine and its use during pregnancy are insufficient at the time of the study may be the reason for the low number of relevant videos. Watching only English videos is also one of the limited aspects of the study. Furthermore, the lack of explicit data about some of the parameters (teratogenicity, etc.) examined in the CVİ scoring system shows that there is a need for new evaluation systems.

In conclusion, incomplete or incorrect information may lead patients to non-scientific treatments and the physician-patient relationship may be seriously damaged. For this reason, it is necessary to critically analyze the quality of health-related videos on YouTube which are very popular and frequently watched. All videos must be audited by experts before they are published.

Disclosure of interest

The authors report no conflict of interest

Author contributions

The authors declare their following contribution to the manuscript: Dr. Şükran Doğru: conception and design, analysis and interpretation of data, article drafting, and accountability for all aspects of the work. Dr. Aslı Altınordu Atcı: acquisition of data, article drafting. Dr. Fatih Akkuş: analysis and interpretation of data, article drafting.

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Ethics committee

We did not apply to any medical ethics committee for approval of this study, according to the Declaration of Helsinki of the World Medical Association, because no patient data or material were used and all videos used for the study were available on a public social media website (YouTube).

References

1. Szmuda T, Rosvall P, Hetzger TV, Ali S, Słoniewski P. YouTube as a source of patient information for hydrocephalus: a content-quality and optimization analysis. World neurosurgery. 2020;138:e469-e77.
2. Szmuda T, Ali S, Słoniewski P. Letter to the Editor Regarding" A Quality Analysis of Disk Herniation Videos on YouTube". World neurosurgery. 2019;130:570-2.
3. Chang W-H. A review of vaccine effects on women in light of the COVID-19 pandemic. Taiwanese Journal of Obstetrics and Gynecology. 2020.
4. Heath PT, Le Doare K, Khalil A. Inclusion of pregnant women in COVID-19 vaccine development. The Lancet Infectious Diseases. 2020;20(9):1007-8.
5. Pettirosso E, Giles M, Cole S, Rees M. COVID-19 and pregnancy: a review of clinical characteristics, obstetric outcomes and vertical transmission. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2020;60(5):640-59.
6. Masarwa R, Levine H, Gorelik E, Reif S, Perlman A, Matok I. Prenatal exposure to acetaminophen and risk for attention deficit hyperactivity disorder and autistic spectrum disorder: a systematic review, meta-analysis, and meta-regression analysis of cohort studies. American journal of epidemiology. 2018;187(8):1817-27.
7. Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus disease 2019 (COVID-19) vaccines and pregnancy: what obstetricians need to know. Obstetrics and gynecology. 2021;137(3):408.
8. Graham Jr JM. Update on the gestational effects of maternal hyperthermia. Birth defects research. 2020;112(12):943-52.
9. Charnock D, Shepperd S, Needham G, Gann RJJoE, Health C. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. 1999;53(2):105-11.
10. Chan C, Sounderajah V, Daniels E, Acharya A, Clarke J, Yalamanchili S, et al. The Reliability and quality of YouTube videos as a source of public health information regarding COVID-19 vaccination: cross-sectional study. JMIR Public Health and Surveillance. 2021;7(7):e29942.
11. Paden CR, Tao Y, Queen K, Zhang J, Li Y, Uehara A, et al. Rapid, sensitive, full-genome sequencing of severe acute respiratory syndrome coronavirus 2. Emerging infectious diseases. 2020;26(10):2401.
12. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. The New England journal of medicine. 2021;384(24):2273-82.
13. Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet (London, England). 2021;398(10309):1407-16.
14. Lagan BM, Sinclair M, Kernohan WG. Internet use in pregnancy informs women's decision making: a web-based survey. Birth (Berkeley, Calif). 2010;37(2):106-15.
15. Madathil KC, Rivera-Rodriguez AJ, Greenstein JS, Gramopadhye AK. Healthcare information on YouTube: A systematic review. Health informatics journal. 2015;21(3):173-94.
16. Yuksel B, Cakmak K. Healthcare information on YouTube: Pregnancy and COVID-19. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2020;150(2):189-93.
17. Roberts M, Callahan L, O'Leary C. Social Media: A Path to Health Literacy. Studies in health technology and informatics. 2017;240:464-75.
18. Moorhead SA, Hazlett DE, Harrison L, Carroll JK, Irwin A, Hoving C. A new dimension of health care: systematic review of the uses, benefits, and limitations of social media for health communication. Journal of medical Internet research. 2013;15(4):e85.
19. Drozd B, Couvillon E, Suarez A. Medical YouTube Videos and Methods of Evaluation: Literature Review. JMIR medical education. 2018;4(1):e3.

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Bibliometric Analysis of Publications on Vertebral Osteomyelitis Infections

Vertebral Osteomyelit Konulu Yayınların Bibliyometrik Analiz Yöntemi İle İncelenmesi

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Abstract

Aim Vertebral osteomyelitis is defined as an infection of the intervertebral disc and the disc space of the adjacent vertebrae, which causes mortality and morbidity. This disease has started to be detected more frequently due to increased diagnostic possibilities. In this study, we aimed to review the contribution of the increasing number of cases to the scientific literature.

Material and Method This bibliometric analysis study was carried out by searching the keywords "vertebral osteomyelitis (VO)" or "spondylodiscitis" in Scopus database of Elsevier. English was chosen for the searching language. The distribution of the number of publications by years was evaluated in terms of the institution in which the publications were made, the language of the publication, the country, the author, the institutions providing financial support, the number of citations and the journal in which they were published.

Results It was determined that there were 2679 publications on vertebral osteomyelitis(VO). First publication was published in 1911. While there was very few publication on this subject until 1937, the number of publications after year 1980s were increased (Graph 1). A total number of 1924 (71.81%) were published after the year 2000. The authors with the highest number of articles in this field were Louis Bernard (16 publications) and Aurélien Dinh (16 publications) from France. A total number of 2576 (96.15%) publications were published in the field of medicine. There were publications on VO in 20 different disciplines, from nursing to veterinary. The publications were consisted of 2123 (79.24%) articles, 261 (9.7%) of them are not categorized, 9 (0.33%) letters to the editor, 150 (5.59%) reviews, and 136 (5.07%) other types of studies (conference papers, notes, book chapters, etc.). The dominant language of publication was English (1992, 74.35%). The most scientifically productive countries on VO were United States (n=452, 16.87%), France (n=303, 11.31%) and Germany (n=248, 9.25%).

Conclusion It is necessary to support scientific activities on VO and increase the number of publications made globally.

Keywords Vertebral osteomyelitis, bibliometric analysis, Scopus database.

Özet

Amaç *Vertebral osteomyelit mortalite ve morbiditeye neden olan, intervertebral disk ve komşuluğundaki vertebraların disk alanı enfeksiyonu olarak tanımlanır. Bu hastalık artan tanısal imkanlar nedeniyle daha sık saptanmaya başlamıştır. Bu çalışmada, artan vaka sayılarının bilimsel literatüre katkısının gözden geçirilmesi amaçlandı.*

Gereç ve Yöntem *Bu bibliyometrik analiz çalışması Elsevier'e ait Scopus veri tabanı taraması ile gerçekleştirildi. Arama kelimesi olarak başlık kısmında "vertebral osteomyelit (VO)" veya " spondilodiskit" anahtar kelimeleri kullanıldı. Arama dili için İngilizce dili tercih edildi. Yıllara göre yayın sayılarının dağılımı, yayınların yapıldıkları kurum, yazı dili, ülke, yazar, finansal destek sağlayan kuruluşlar, atıf sayıları ve yayınlandıkları dergi açısından değerlendirildi.*

Sonuçlar *VO konusunda 2679 yayın olduğu, ilk yayının 1911 yılında yayınlandığı saptandı. 1937 yılına kadar bu konuda hiç yayın yokken, 1980'ler sonrası yayın sayısında artış olduğu saptandı (Grafik 1). Yayınların 1924'ü (%71,81) 2000 yılından sonra yayınlanmıştı. En fazla bu alanda makalesi bulunan çalışmacılar, Fransa'dan Louis Bernard (16 yayın) ve Aurélien Dinh (16 yayın) idi. Yayınların 2576'sı (% 96,15) tıp alanında yayınlanmıştı. Hemşirelikten veterinerliğe 20 farklı bilim dalında VO konusunda yayın vardı. 2123'ü (%79,24) makale, 270'i (10,07) 9'u (%0,33) editöre mektup, 150'si (%5,59) derleme ve 136'sı (%5,7) tanesi diğer tür çalışmalar (konferans bildirisi, not, kitap bölümü, vb) idi. Hakim yayın dili İngilizce idi (1992,%74,35). Amerika Birleşik Devletleri (n=452, %16,87), Fransa (n=303, %11,31) ve Almanya (n=248, %9,25) VO konusunda en bilimsel üretken ülkeler idi.*

Sonuç *VO konusundaki bilimsel faaliyetlerin desteklenmesi, global olarak yapılan yayın sayılarının arttırılması gerekmektedir.*

Anahtar Kelimeler *vertebral osteomyelit, bibliyometrik analiz, Scopus veri tabanı*

INTRODUCTION

Disc space infection of the intervertebral disc and adjacent vertebrae is defined as vertebral osteomyelitis (VO) or spondylodiscitis[1].

Its incidence has increased due to the increase in life expectancy, invasive procedures, and patients receiving immunosuppressive therapy. The disease is most common in people under the age of 20 and between the ages of 50 and 70.[1,2]

According to the microorganism causing the etiology VO is classified as pyogenic, granulomatous or parasitic[2]. The most common form is the pyogenic form, and the agent often reaches the vertebrae by the hematogenous route. The causative agents of pyogenic VO are often Staphylococcus aureus or Escherichia coli.

Granulomatosis VO usually progresses insidiously; brucellosis and tuberculosis are the most common etiologies(1). The agents most commonly reach the vertebral area either iatrogenically or hematogenously. Iatrogenic VO occurs as a result of epidural injection, lumbar surgery, lumbar puncture or lumbar trauma[3].

The disease is typically characterized by back pain that does not respond to treatment. The diagnosis of VO is quite difficult. Magnetic resonance imaging (MRI) is frequently used in diagnosis. MRI is the gold standard imaging method with 92% sensitivity and 96% specificity[4]. It also provides visualization of abscess formation. Diagnosis is based on clinical, radiological, laboratory, microbiological and histopathological data. Treatment is based on the elimination of the causative agent with antibiotics and in some cases vertebral surgery. The goals of VO treatment are to eliminate the infection, restore the patient's functionality, and relieve pain[1,3]. A recent study in Denmark showed that the incidence of VO increased from 2.2/100,000 per year in the year 1995 to 2008 period to 5.8/100,000 in recent years. The age-standardized incidence in Germany is estimated to be 30/250,000/case-year based on data from the Federal Statistical Office. This increase can be attributed to the development of diagnostic methods or increased awareness of the disease in recent years[4].

In this study, we aimed to give a vision to the researchers on this issue by evaluating the scientific literature published on VO.

MATERIALS and METHODS

This bibliometric analysis study was carried out by searching the keywords "vertebral osteomyelitis" or "spondylodiscitis on Scopus database of Elsevier. English was chosen for the search language. The distribution of the number of publications by years was evaluated in terms of the institution in which the publications were made, the language of the publication, the country, the author, the institutions providing financial support, the number of citations and the journal in which they were published.

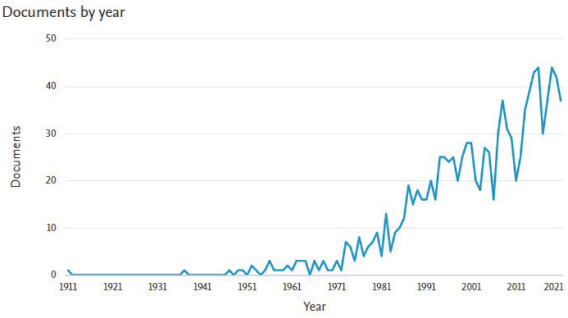
A statistical method was not used. Percentage and frequency values of descriptive data were calculated. Graphics provided by the Windows 10 program and graphics from the Scopus database were used for visualizations.

RESULTS

General analyzes

It was determined that there were 2679 publications, and the first publication was published by Fraser and McPherson in 1911[5]. While there was very few publication on this subject until 1937, there was an increase in the number of publications after the year 1980s. It was determined that 2016 and 2019 were the years with the highest number of publications (Graph 1). 1924 of the publications (71.81%) were published after 2000. The publications of 733 were published in open access (OA) journals. The authors with the most articles in this field were Louis Bernard (16 publications) and Aurélien Dinh (16 publications) from France. More than 100 researchers had publications on this subject. Publications of 137 were published in more than one

discipline; 2576 (96.15%) were in the field of medicine, 167 (6.23%) were in the field of immunology and microbiology, 74 (2.76%) were in the field of biochemistry, genetics and molecular biology. Publications were consisted of 2123 (79.24%) articles, 261 (9.7%) not categorized, 9 (0.33%) letters to the editor, 150 (5.59%) reviews, and 136 (5.07%) other types of studies (conference papers) , note, book chapter, etc.). Publications of 1992 (74.35%) were written in English, 258 (9.63%) in French, 143 (5.33%) in Spanish, 134 (5%) in German and 152 (5.67%)of them were written in other languages.

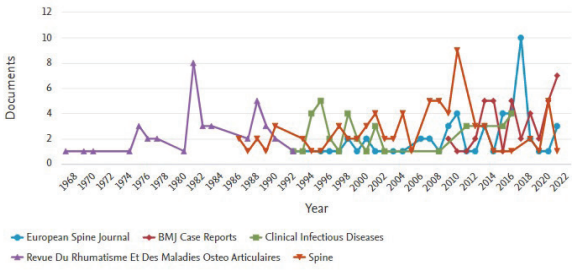


Graph 1. Number of publications by year.

The most articles on VO were published in 5 journals with the number of 76 publications in the Spine Journal, 55 in the European Spine Journal, 42 in the BMJ case reports, 39 in the Revue Du Rhumatisme Et Des Maladies Osteo Articulaires Journal and 39 in the Clinical Infectious Diseases Journal (Graph 2). AP-HP Assistance Public Hospital in Paris (France) (n=25, 0.93%), Catholic University del Sacro Cuore in Rome Campus (Italy) (n=25, 0.93%), VA Medical Center (United States) (n =20, 0.74%), Hospital Clinic Barcelona (Spain) (n=18, 0.67%), Chang Gung Memorial Hospital (Taiwan) (n=17, 0.63%) were the 5 most productive institutions in VO.

United States (n=452, 16.87%), France (n=303, 11.31%), Germany (n=248, 9.25%), Spain (n=161, 6.00%), Italy (n=156, 5.82%)), Japan (n=139, 5.18%), England (n=106, 3.95%), Turkey (n=94, 3.50), Switzerland (n=72, 2.68%), and India (n=70, 2.61%)) were the top 10 countries in scientific productivity on VO.

Studies of 107 (3.99%) were supported by the funding agency. Japan Association for the Promotion of Science (n=6), National Institute of Allergy and Infectious Diseases (n=6) (USA), China National Natural Science Foundation (n=6) and Korea National Research Foundation (n=5) were the institutions that provided the largest number of funds for VO researchs.



Graph 2. Distribution of the number of articles in the top 5 journals that published the most publications on vertebral osteomyelitis by years.

Citation analysis

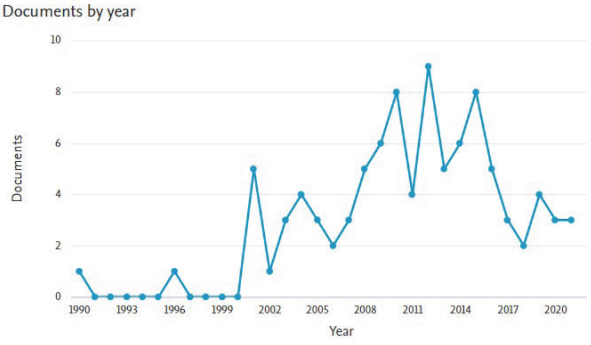
Publications of 714 (26.65%) were not cited at all. A publication received more than 500 citations; 8 publications 250, 51 publications 100, 149 publications 50, 339 publications 25, 778 publications more than 10. The analysis of the 10 most cited publications is given in detail in Table 1. The most cited article was about the effectiveness of MRI imaging of VO(6).

Table 1. Analysis of the 10 most cited publications [6-15].

Author,year of publication	Journal	Citation Number	Subject
Modic et al, 1985	Radiology	548	Efficiency of MRI Imaging
McHenry et al,2002	Clinical Infectious Diseases	402	Clinical results of patients
Gouliouris et al, 2010	Journal of Antimicrobial Chemotherapy	400	Compilation
Berbari et al,2015	Clinical Infectious Diseases	375	Diagnosis and treatment guide
Sapico et al,1979	Reviews of Infectious Diseases	356	Case series and compilation
Carragee EJ.1997	Journal of Bone and Joint Surgery - Series A	349	Clinical results of patients
Zimmerli, W.2010	New England Journal of Medicine	347	Case presentation
Mylona et al,2009	Seminars in Arthritis and Rheumatism	325	Systematic compilation
Eismont et al,1983	Journal of Bone and Joint Surgery - Series A	263	Clinical results of patients
Colmenero et al,1997	Annals of the Rheumatic Diseases	262	Clinical results of patients

Turkey's Contribution

There were 94 publications from our country on our study and Turkey was in the 8th place in the whole ranking. The first publication was published in 1990[16]. Publications on VO from our country also increased after the year 2000, in line with the global literature (Graph 3). On VO, 14 papers from Istanbul Medical Faculty, 7 from Atatürk University, 6 from Ege University, each five papers from Atatürk Training and Research Hospital and Van Yüzüncü Yıl University and each 4 papers from Trakya University, Fırat University, Dicle University and Baskent University were published. The most productive authors from our country were Prof Dr Reşat Özaras and Prof Dr Fehmi Tabak with four articles each.The publication published in the Journal of Infection in 2007 by Assoc. Dr. Tuba Yeter Turunç was the work with the highest number of citations (111 citations)[17].



Graph 3. Distribution of publications in our country by years.

DISCUSSION

Bibliometric analyzes are data analysis studies that enable the evaluation of publications, theses and scientific productivity in a field of science, and it has started to take place in the medical literature in recent years[18-23]. There are many works in this field by the researchers from our country[18,20,23]. With this method, the scientific literature is revealed and it may be possible to provide ideas to the researchers of the relevant subject. It is possible to make these studies from databases, which allow bibliometric data analysis, and even visualization. Scopus database belonging to Elsevier publishing house is one of these ready-made databases. In addition, it has been observed that analyzes were performed using databases such as Web of Science Core Collection (WoSCC) and Pubmed Medline in many studies[18-23]. In this study, the Scopus database was preferred because of its richer journal content.

VO is an infectious disease known since from ancient times[1]. The number of patients diagnosed with medical advances has increased, but it is a disease with unknowns[2-4]. Especially the increase in the possibilities in the field of radiology provides facilitates diagnosis. Although there is a limited number of bibliometric analyzes for specific VO publications in the available literature[24-27], no study providing an overview was found. In this study, we aimed to give a vision to those who will work on VO with the bibliometric analysis method over the Scopus database.

As a result of the study, it was determined that the country with the highest number of publications on VO was the USA, as in almost all other bibliometric analyzes[18-23]. In addition, the other countries with the highest number of articles on VO were France (n=303, 11.31%), Germany (n=248, 9.25%), Spain (n=161, 6.00%), Italy (n=156, 5.82%), Japan (n=139, 5.18%), England (n=106, 3.95%), Turkey (n=94, 3.50), Switzerland (n=72, 2.68%) and India (n=70, 2.61%). In a vertebral similar bibliometric analysis, it was determined that Australia and the Netherlands were in dominant positions with the main research power, establishing a cooperation relationship with Austria, Bangladesh, Germany and Switzerland. However, no collaboration analysis was performed in our current study. The reason for the highest number of publications in the current study can be attributed to the high number of researchers in the USA. Looking at the funders of the studies, 107 (3.99%) studies were supported by the funding institution, and the Japan Science Promotion Association (n=6), the National Institute of Allergy and Infectious Diseases (n=6) (USA), the National Natural Science Foundation of China (n=) 6) and the Korea National Research Foundation (n=5) were the largest funders for research on VO. However, studies on VO were found to be at a very low level when compared to publications in other bibliometric analyzes[18-23].

When the disciplines in which the publications were made were examined, it was determined that the management of this disease required a multidisciplinary approach, contributing to the VO literature from 20 different disciplines from nursing to veterinary.(cümle tekrarı olamaması adına değiştirilmiştir)

Considering the citation analysis, the article on the effectiveness of MRI in imaging the highest number of citations for VO was received[6]. This proves the effectiveness of MRI in proving the effectiveness of this groundbreaking method in both the diagnosis and treatment of VO. In addition, the increase in publications on VO after the 2000s can be attributed to the reflection of technological developments in radiology. Another most frequently cited subject was the publications investigating clinical features (Table 1).

CONCLUSİON

As a result, it is necessary to support scientific activities on VO and to increase the number of studies published in our country and globally.

Limitations of the study

A single database was searched in the study. Therefore, it may not reflect all the scientific literature on VO.

Ethics Committee Approval

Ethics committee approval was not obtained because there was no animal or human study and it was a document review study.

Declaration of Conflict of Interest:

There is only one author. The author declared no conflicts of interest with concerning to the authorship and/or publication of this article.

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References

1. Berbari EF, Steckelberg JM, Osmon DR. Osteomyelitis In: Mandell GL Bennett JE, Dolin R, Blaser MJ. Principles and practice of infectious diseases, vol 2, 8th edn. Churchill Livingstone, Philadelphia, 2015:1318-27.
2. Márquez Sánchez P. Spondylodiscitis. Espondylodiscitis. radiology 2016;58 Suppl 1:50-59. doi:10.1016/j.rx.2015.12.005
3. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, Schmitt SK, et al. Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis. 2015;61(6):e26-e46.
4. Herren C, Jung N, Pishnamaz M, Breuninger M, Siewe J, Sobottke R. Spondylodiscitis: Diagnosis and Treatment Options. Dtsch Arztebl Int. 2017;114(51-52):875-882.
5. Fraser F, McPherson T. Acute osteomyelitis of the vertebral column. The Lancet. 1911;178(4605):1543-1544.
6. Modic MT, Feiglin DH, Piraino DW, et al. Vertebral osteomyelitis: assessment using MR. radiology. 1985;157(1):157-166.
7. McHenry MC, Easley KA, Locker GA. Vertebral osteomyelitis: long-term outcome for 253 patients from 7 Cleveland-area hospitals. Clin Infect Dis. 2002;34(10):1342-1350.
8. Gouliouris T, Aliyu SH, Brown NM. Spondylodiscitis: update on diagnosis and management. J Antimicrob Chemother. 2010;65 Suppl 3:iii11-iii24.
9. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clin Infect Dis. 2015;61(6):e26-e46. doi:10.1093/cid/civ482
10. Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. Rev Infect Dis. 1979;1(5):754-76.
11. Carragee EJ. Pyogenic vertebral osteomyelitis. J Bone Joint Surg Am. 1997;79(6):874-80.
12. Zimmerli W. Clinical practice. Vertebral osteomyelitis. NEngl J Med. 2010;362(11):1022-9.
13. Mylona E, Samarkos M, Kakalou E, Fanourgiakis P, Skoutelis A. Pyogenic vertebral osteomyelitis: a systematic review of clinical characteristics. Semin Arthritis Rheum. 2009;39(1):10-7.
14. Eismont FJ, Bohlman HH, Soni PL, Goldberg VM, Freehafer AA. Pyogenic and fungal vertebral osteomyelitis with paralysis. J Bone Joint Surg Am. 1983;65(1):19-29.
15. Colmenero JD, Jiménez-Mejías ME, Sánchez-Lora FJ, Reguera JM, Palomino-Nicás J, Martos F, et al. Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases. Ann Rheum Dis. 1997;56(12):709-715.
16. Cengel M, Akyol, N, Akyol S, Turhan A, Alp H. A case of vertebral osteomyelitis due to spinal anesthesia. Bulletin of Gulhane Military Medical Academy.1990;32(2); 403-408.
17. Turunc T, Demiroglu YZ, Uncu H, Colakoglu S, Arslan H. A comparative analysis of tuberculous, brucellar and pyogenic spontaneous spondylodiscitis patients. J Infect. 2007;55(2):158-63.
18. Kucuk U, Alkan S, Uyar C. Bibliometric analysis of infective endocarditis. Iberoam J Med. 2021;3(4):350-355.
19. Dahdi SA, Ben Abdelaziz A, Baroumi T, Ba O, Diagana M, Dada L, et al. Bibliometry of biomedical scientific publications in Mauritania (Medline:1992- 2016). Tunis Med. 2018;96(10-11):834-43.
20. Alkan S, Dindar Demiray EK, Yıldız E, Özlü C. Analysis of scientific publications on Acinetobacter bacteremia in Web of Science. Infect Dis Clin Microbiol. 2021;3(1):39-44.
21. Jiang H, Nong B, Yang L, Zong S, Zhan X, Wei Q, et al. Assessing the evolution of scientific publications in orthopedics journals from mainland China, Hong Kong, and Taiwan: a 12-year survey of the literature. J Orthop Surg Res. 2016;11(1):69. doi: 10.1186/s13018-016-0404-z.
22. Aminian A, Daigle CR, Brethauer SA, Schauer PR. Citation classics: top 50 cited articles in bariatric and metabolic surgery. Surg Obes Relat Dis. 2014;10(5):898-905. doi: 10.1016/j.soard.2013.12.021.
23. Öntürk H, Dindar Demiray EK, Alkan S. Network analysis of nursing publications in the COVID 19 era. J Clin Med Kaz. 2021;18(4):27-31.
24. Wang Y, Wang Q, Zhu R, Yang C, Chen Z, Bai Y, Li M, Zhai X. Trends of spinal tuberculosis research (1994-2015): A bibliometric study. Medicine (Baltimore). 2016;95(38):e4923.
25. Yang G, Li Z, Ye W, Huang S, Liu S, Liu K, Tan Q. Bibliometric Analysis of the 100 Most Cited Articles on Intervertebral Disc Research: From 1900 to 2017 Year. Clin Spine Surg. 2020;33(3):104-110.
26. Wang B, Zhao P. Worldwide research productivity in the field of back pain: A bibliometric analysis. Medicine (Baltimore). 2018; 97(40):e11566.
27. Figueiredo GC, Figueiredo ECQ, Tavares-Neto J. Aspectos clínicos e terapêuticos da osteomielite vertebral por fungos - análise secundária de dados. Revista Brasileira de Reumatologia. 2007;47:34-41.
28. Weng LM, Zheng YL, Peng MS, Chang TT, Wu B, Wang XQ. A Bibliometric Analysis of Nonspecific Low Back Pain Research. Pain Res Manag. 2020 9; 2020:5396734.

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Identification Of Virulence Resistance Genes İn *Pseudomonas Aeruginosa* Strains İsolated From Blood Samples

Kan Örneklerinden İzole Edilen *Pseudomonas Aeruginosa* Suşlarında Virülans Direnç Genlerinin Belirlenmesi

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Abstract

Aim In this it is aimed to the determine the presence of virulence resistance genes (toxA, algD, plcN, lasB, plcH) in P. aeruginosa isolates isolated from blood samples.

Material and Method DNA extraction of the study isolates was done by boiling method. Optimization was done using positive control after DNA extraction. After optimization, the presence of virulence (toxA, algD, plcN, lasB, plcH) resistance genes was investigated by polymerase chain reaction (PCR) method.

Results As a result of PCR of the virulence gene regions (toxA, algD, lasB, plcN, plcH); Positive rates of KR 25 isolates were 80% (n=20), 100% (n=25), 100% (n=25), 100% (n=25), 96% (n=24) in KS 46 isolates. On the other hand, the positive rate distributions were found to be 93.47% (n=43), 100% (n=46), 100% (n=46), 100% (n=46), 97.82% (n=45).

Conclusion As a result of PCR of virulence gene regions (toxA, algD, lasB, plcN, plcH) of P. aeruginosa, it was determined that algD, lasB, plcN genes were found in all 25 carbapenem resistant (KR) and 46 carbapenem sensitive (KS) isolates.

Keywords P. aeruginosa, virulence, bactaremia

Özet

Amaç *Kan örneklerinden izole edilen P. aeruginosa izolatlarındaki virülans direnç genlerinin (toxA, algD, plcN, lasB, plcH) varlığının belirlenmesidir.*

Gereç ve Yöntem *Çalışma izolatlarının DNA ekstraksiyonu kaynatma yöntemiyle yapıldı. DNA ekstraksiyonundan sonra pozitif kontrol kullanılarak optimizasyon yapıldı. Optimizasyondan sonra virülans (toxA, algD, plcN, lasB, plcH) direnç genlerinin varlığının polimeraz zincir reaksiyonu (PZR) yöntemi ile araştırıldı.*

Sonuçlar *Yapılan virülans gen bölgelerinin (toxA, algD, lasB, plcN, plcH) PZR işlemi sonucunda; karbapenem dirençli (KR) 25 izolatta pozitif oranları sırasıyla % 80 (n=20), % 100 (n=25), % 100 (n=25), % 100 (n=25), %96 (n=24) olduğu, karbapenem duyarlı (KS) 46 izolatta ise pozitif oran dağılımlarının % 93,47 (n=43), % 100 (n=46), % 100 (n=46), % 100 (n=46), %97,82 (n=45) olduğu saptanmıştır.*

Sonuç *P. aeruginosa'ın virülans gen bölgelerinin (toxA, algD, lasB, plcN, plcH) PZR işlemi sonucunda KR 25 ve KS 46 izolatların hepsinde algD, lasB, plcN genlerinin bulunduğu belirlenmiştir.*

Anahtar Kelimeler *P. aeruginosa, Virülans, bakteriyemi*

INTRODUCTION

Pseudomonas aeruginosa is an aerobic, non-sporeforming and oxidase-positive gram-negative bacillus.[1] Since it is hydrophilic, it can be isolated from many environmental environments and antiseptic solutions.[2] It is among the serious causes of blood infections associated with high mortality.[3] It is a major cause of hospital-acquired infections, especially in immune suppressed patients.[4] Also in terms of general hygiene of the hospital, this bacterium is known to cause epidemics by contaminating water resources.[5,6] *P. aeruginosa* quickly develops resistance due to its structural features and the effect of intense antibiotic stress in the hospital environment.[7]

The virulence factors determine the disease-causing capacity of the bacteria. These factors are such as structural components, toxins, and enzymes of *P. aeruginosa*.[8] Both cellular and extracellular factors play a role in the virulence of *P. aeruginosa*.

In particular, surface components such as pili, flagella and lipopolysaccharide adhere to the host cell surface, leading to the host immune response. In many animal model studies, it has been shown that proteases, toxins (exotoxin A and exoenzyme S) and hemolysins (phospholipase and rhamnolipid) play a role in the virulence of P. aeruginosa[9]. Exotoxin A encoded by the ToxA gene and has a role in inhibition of protein synthesis by inhibiting elongation factor 2 of eukaryotic cells. Alginates and algD genes of P. aeruginosa produce mucoid colonies which protects the bacterium from the antimicrobials and immun cells.[10] LasB elastase, is encoded by the LasB gene, and destroys collagen and elastin, help bacterium to invade tissues..[11] In addition, two phospholipase Cs which are encoded by hemolytic phospholipase C (plcH) and nonhemolytic phospholipase C (plcN) hydrolyse phospholipids in lung.[12,13]

P. aeruginosa has intrinsic resistance to numerous antimicrobial agents and also easily acquires resistance to many antibiotics.[14] Carbapenems are drug of choice for treatment of serious infections caused by *P. aeruginosa*.[15,16] Carbapenem resistance are involved in various mechanisms; such as intrinsic RND (Resistance-Nodulation- Division) efflux pump systems and lack of outer membrane porin (OprD). However, *P. aeruginosa* is becoming increasingly resistant against carbapenems have shown that recent study results.[17,18]

Antibiotic resistance status differ from region to region, even among patients hospitalized in different wards in the same hospital. Therefore, it is necessary to monitor the antibiotic resistance profiles of the isolates isolated in the hospital at regular intervals in each hospital, and to update the treatment protocols by looking at the resistance rates to the antibiotics used in the treatment.[19]

The distribution of carbapenemases shows differences between geographical area and clinical origins, and studies about the coexistence of carbapenem resistance and multiple virulence factors of in *P. aeruginosa* are limited.[20]

This study is aimed to determine the data results obtained by studying the presence of virulence genes (toxA, algD, plcN, lasB, plcH) in carbapenem resistant and susceptible P. aeruginosa isolates isolated from blood samples sent to the Medical Microbiology laboratory of hospitalized patients in Ondokuz Mayıs University hospital.

MATERIAL and METHOD

P. aeruginosa isolates (n: 71) obtained from blood samples sent to the Medical Microbiology laboratory of patients hospitalized in Ondokuz Mayıs University Hospital Medical Microbiology Laboratory at 01/01/2020 - 16/09/2021 were included in our study. The study was a retrospective study.

The blood cultures were incubated on BacT/Alert (Biomeriux, France) blood culture system until they signaled positive or for a maximum of five days. The Gram stains were done directly from positive blood culture bottles.

According to the result from the staining, specimen from the positive bottles were subcultured onto relevant agar plates. TIdentification of the isolates was performed by matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry (Vitek MS, Biomeriux, France). Antimicrobial susceptibilities were determined by Vitek2Compakt (Biomeriux, France) and evaluated according to the European Committee on Antimicrobial Susceptibility Testing. The isolates were stored at -20ºC until the studied.

Bacterial DNA extraction was done by boiling method that includes a heating step at 100˚C of colonies from Mueller-Hinton agar in a 500µl sterile distilled water for 15 min. followed by a centrifugation step of the cell suspension at 15000g for 20min, supernatant was used as template DNA. The DNA templets were stored at -20°C until the molecular study.

Determination of virulence genes

After DNA extraction, toxA was studied as uniplex PCR (polymerase chain reaction) and algD, lasB, plcN and plcH were studied as multiplex PCR. The primer sequences used in the study are given in Table 1.[21]

Table 1. toxA, algD, lasB, plcN, plcH primer sequences			
Forward Primer		Reverse Primer	
algD	5'-CGTCTGCCGCGAGATCGGCT-3'	5'-GACCTCGACGGTCTTGCGGA-3'	313
lasB	5'-GGAATGAACGAACGAAGCGTTCTC-CGAC-3'	5'-TTGGCGTCGACGAACACCTCG-3'	284
toxA	5'-CTGCGCGGGTCTATGTGCC-3'	5'-GATGCTGGACGGGTCGAG-3'	270
plcH	5'-GCACGTGGTCATCCTGATGC-3'	5'-TCCGTAGGCGTCGACGTAC-3'	608
plcN	5'-TCCGTTATCGCAACCAGCCCTACG-3'	5'-TCGCTGTCGAGCAGGTCGAAC-3'	481

Table 2. toxA, algD, lasB, plcN, plcH positivity rate in carbapenem susceptible P. aeruginosa isolates.					
	toxA	algD	lasB	plcN	plcH
Positive	43 (%93,4)	46 (%100)	46 (%100)	46 (%100)	45 (%97,8)
Negative	3	0	0	0	1
Total	46	46	46	46	46

Table 3. toxA, algD, lasB, plcN, plcH positivity rate in carbapenem resistant P. aeruginosa isolates					
	toxA	algD	lasB	plcN	plcH
Positive	20 (%80)	25 (%100)	25 (%100)	25 (%100)	24 (% 96)
Negative	5	0	0	0	1
Total	25	25	25	25	25

RESULTS

Twenty-five (35.2%) of the isolates included in the study were carbapenem resistant. The intensive care unit (22.5%) was the clinic where the most isolates sent. At the end of PCR of virulence gene regions (toxA, algD, lasB, plcN, plcH) of *P. aeruginosa,* algD, lasB and plcN virulence genes were detected in all isolates. ToxA and plcH virulence genes were found to be 88.7% and 97.2%, respectively. AlgD, lasB, and plcN gene regions were detected in all carbapenem-susceptible (CS) *P. aeruginosa* isolates, while toxA gene regions were detected in 93.4% and plcH gene regions in 97.8% of the isolates (Table 2). Similarly, algD, lasB, and plcN gene regions of carbapenem-resistant (CR) *P. aeruginosa* isolates were detected in all of them, while toxA gene regions were detected in 80% and plcH gene regions in 96% (Table 3).

DISCUSSION

Worldwide, *P. aeruginosa* isolates are an important pathogen responsible for 10-15% of hospital-acquired infections.[22,23] *P. aeruginosa* is among the most important pathogens infecting the lungs, urinary tract, blood circulation and soft tissue in intensive care units.[24] The main virulence factors of *P. aeruginosa* are exotoxin A, exoenzyme S, alginate, phospholipase and elastase.[25] Exotoxin A, alkaline protease, and elastase are documented as important virulence factors for systemic infections in immunocompromised patients.[26]

Ozer et al. stated that 68.8% of P. aeruginosa isolates were isolated from intensive care in their study.[27] In the European Prevalence Infection Intensive Care (EPIC) study, which included 1417 intensive care units from 17 different European countries, *P. aeruginosa* isolates isolated from blood samples were examined in terms of clinical services, and it was seen that they were most frequently isolated from the intensive care unit. *P. aeruginosa* isolates, which we isolated from blood samples in our study, were examined in terms of clinical services, it was seen that they were most frequently isolated from the intensive care unit. Intensive care units are wards where hospital infections are more common due to critically ill patients and invasive procedures in these units.[28]

Faraji et al., when comparing the positivity rates of resistance genes of P. aeruginosa isolate isolated from cystic fibrosis (CF) and burn patients; reported that toxA (63.1%), lasB (95.4%) and exoS (70.8%) genes were higher in patients with CF, and lasB (95.4%) was higher than other virulence genes. 21 In our study, it was determined that the presence of toxA and lasB was higher.

The distribution of algD, lasB, pilB, nan1 virulence regions in *P. aeruginosa* isolates showing multidrug resistance was examined and it was reported that lasB and algD gene regions were detected in all isolates, as in our study. It has been reported that there is a high correlation between chronic infections (urine, lower respiratory tract infection, urinary tract infection, blood and wound infections) and lasB and algD genes (100%).[29]

Wolska et al. in a study they conducted, the presence of six virulence genes (algae D, las B, tox A, plc H, plc N, exo S) was investigated in 49 *P. aeruginosa* isolates and they were detected algae D, las B, plc H in all isolates, while tox A and plc N on the other hand, it was determined in 91.8% of the isolates.[30] It was stated that the prevalence of virulence genes in *P. aeruginosa* among 143 isolates obtained from CF patients was 100% lasB, 100% plcB, and 96.5% plcH.31 The results of these studies are similar to the results of our study.

CR clinical *P. aeruginosa* ranks second based on most criteria for bacteria among 20 antidrug-resistant bacterial species by the World Health Organization reports.[17] Many studies reported that VIM gene is the most frequent MBL found in CR P. aeruginosa; however, IMP gene was the most common detected in a study conducted in Iran.[32,33,34] There have been limited data on of virulence genes in CR *P. aeruginosa* isolates. Bogiel et al. (2021), stated the toxA gene indicate highly common and between toxA genes

and algD genes; significant correlations between algD and lasB. Also altogether found in almost all of the examined strains were shown that a statistically significant correlation in the co-existence of lasB and both phospholipases genes (plcH, plcN).[35] In our study, KR isolates no CR gene was detected; however was detected that toxA, algD, lasB, plcN, plcH respectively 80%, 100%, 100%, 100%, 96%.

In the study by Ellapan et al. algD expression was detected in 93% of carbapenem resistant *P. aeruginosa* isolates, followed by algU (89%), rhlR (84%), lasR (81%) and exoS (76%). The lasB and plcH genes were detected in 94% and 92% of isolates, respectively.[32] And in a study by Park and Koo nine virulence factor genes (toxA, exoT, plcN, plcH, phzM, phzS, lasB, aprA, and algD) were identified in all of carbapenem resistant P. aeruginosa isolates.20 However, in those studies thay did not compare the presence of virulence genes in CR and CS *P. aeruginosa* isolates. In our study the coexistance of virulence genes in carbapenem resistant and susceptible isolates were found to be similar. One of the great challenges of modern medicine is the increase in antibiotic resistance in bacteria.[36] Because of their ability to develop rapid resistance to various virulence factors and antibiotics, they cause infections that are difficult to treat, especially in immunocompromised and hospitalized patients.[37]High prevalence of virulence factors and multiple resistance mechanism is worrisome in *P. aeruginosa* isolates. It is important to monitor the virulence and resistance mechanisms of *P. aeruginosa*, which is known to cause significant infections especially in intensive care patients.

CONCLUSION

In our study, algD, lasB, and plcN virulence genes were detected in both CS and CR *P. aeruginosa* isolates, and the presence of toxA and plcH was found to be slightly higher in CS isolates. The number of samples in our study was not high and blood samples were included because it caused serious infections. It would be useful to compare the presence of virulence genes in different sample types with more comprehensive studies.

Ethics approval

Ethical approve was taken from Ondokuz Mayıs University Medical Faculty Cinical Research Committee.

Conflict of interest

There is no conflict of interest.

Author contributions

Idea: IB, YTC; Study Design: IB, YTC; Literature review: IB; Laboratory work: IB, EBA; Editing: IB, YTC; Evaluation: YTC, AB; Review: YTC, AB

References

1. Palleroni NJ. Prokaryote taxonomy of the 20th century and the impact of studies on the genus Pseudomonas: a personal view. Microb. 2003;149(1):1-7.
2. Speert DP, Campbell ME, Davidson AGF, Wong LT. Pseudomonas aeruginosa colonization of the gastrointestinal tract in patients with cystic fibrosis. J Infect Dis. 1993;167(1):226-229.
3. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant Pseudomonas aeruginosa: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev. 2009;22(4):582-610.
4. Blanc DS, Petignat C, Janin B, Bille J, Francioli P. Frequency and molecular diversity of Pseudomonas aeruginosa upon admission and during hospitalization: a prospective epidemiologic study. Clin Microb Infect. 1998;4(5):242-247.
5. Varin A, Valot B, Cholley P, et al. High prevalence and moderate diversity of Pseudomonas aeruginosa in the U-bends of high-risk units in hospital. Int J Hyg Environ Health. 2017;220(5):880-885.
6. Witney A, Gould K, Pope C, et al. Genome sequencing and characterization of an extensively drug-resistant sequence type 111 serotype O12 hospital outbreak strain of Pseudomonas aeruginosa. Clin Microb Infect. 2014;20(10):609-618.
7. Öztürk C, Albayrak HT, Altinöz A, Ankarali H. Pseudomonas aeruginosa Suşlarinda Antibiyotiklere Direnç ve Beta-Laktamaz Oranları. Ankem derg. 2010;24(3):117-23.
8. Murray TS, Egan M, Kazmierczak BI. Pseudomonas aeruginosa chronic colonization in cystic fibrosis patients. Cur Opn Ped. 2007;19(1):83-88.
9. Wang Y, Dai Y, Zhang Y, Hu Y, Yang B, Chen S. Effects of quorum sensing autoinducer degradation gene on virulence and biofilm formation of Pseudomonas aeruginosa. Science in China Series C: Life Sciences. 2007;50(3):385-391.
10. Ra'oof WaM. Distribution of algD, lasB, pilB and nan1 genes among MDR clinical isolates of Pseudomonas aeruginosa in respect to site of infection. Tikrit Med J. 2011;17(2):148-160.
11. Jaffar-Bandjee MC, Lazdunski A, Bally M, Carrère J, Chazalette JP, Galabert C. Production of elastase, exotoxin A, and alkaline protease in sputa during pulmonary exacerbation of cystic fibrosis in patients chronically infected by Pseudomonas aeruginosa. J Clin Microb. 1995;33(4):924-929.
12. König B, Vasil M, König W. Role of haemolytic and non-haemolytic phospholipase C from Pseudomonas aeruginosa in interleukin-8 release from human monocytes. J Med Microb. 1997;46(6):471-478.
13. Ostroff R, Vasil A, Vasil M. Molecular comparison of a nonhemolytic and a hemolytic phospholipase C from Pseudomonas aeruginosa. J Bacteriol. 1990;172(10):5915-5923.
14. Livermore DM. Multiple mechanisms of antimicrobial resistance in Pseudomonas aeruginosa: Our worst nightmare? Clin. Infect Dis. 2002;34(5):634–640.
15. Bradley JS, Garau J, Lode H, Rolston KV, Wilson SE, Quinn JP. Carbapenems in clinical practice: a guide to their use in serious infection. Int J Antimicrob Agents. 1999;11(2):93–100.
16. Khosravi AD, Mihani F. Detection of metallo-beta-lactamase-producing Pseudomonas aeruginosa strains isolated from burn patients in Ahwaz, Iran. Diagn Microbiol Infect Dis. 2008;60(1):125–8.
17. Tacconelli E, Carrara E, Savoldi A, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis. 2018;18(3): 318-327.
18. Hu YY, Cao JM, Yang Q, et al. Risk Factors for carbapenem-resistant Pseudomonas aeruginosa, Zhejiang Province, China. Emerg Infect Dis. 2019;25(10):1861-1867.
19. Berrin U, Güngör S, Sezak N, Afşar İ, ŞERİFHAN-İLGÜN M, Demirci M. Yoğun bakım hastalarının kan kültürlerinden izole edilen Pseudomonas aeruginosa ve Acinetobacter baumannii izolatlarının antibiyotik direnç yüzdelerindeki değişim. Türk Hij Den Biy Derg. 2012;71(1):25-30.
20. Park Y, Koo SH. Epidemiology, Molecular Characteristics, and Virulence Factors of Carbapenem-Resistant Pseudomonas aeruginosa Isolated from Patients with Urinary Tract Infections. Infection and Drug Resistance, 2022;15:141.
21. Faraji F, Mahzounieh M, Ebrahimi A, Fallah F, Teymournejad O, Lajevardi B. Molecular detection of virulence genes in Pseudomonas aeruginosa isolated from children with Cystic Fibrosis and burn wounds in Iran. Microb Pathogen. 2016;99:1-4.
22. Maçin S, KITTANA FNA, YILMAZ YA. Çeşitli klinik örneklerden izole edilen pseudomonas aeruginosa suşlarının virulans faktörlerinin incelenmesi. Cukurova Med J. 2017;42(2):308-313.
23. Alvarez-Buylla A, Allen M, Betts D, et al. Multicentre study of the in vitro activity of ceftolozane/tazobactam and other commonly used antibiotics against Pseudomonas aeruginosa isolates from patients in the UK. J Antimicrob Chemother. 2020;2(2): doi:10.1093/jacamr/dlaa024
24. Trautmann M, Lepper PM, Haller M. Ecology of Pseudomonas aeruginosa in the intensive care unit and the evolving role of water outlets as a reservoir of the organism. Am J Infect Cont. 2005;33(5):S41-S49.
25. Alhede M, Bjarnsholt T, Givskov M, Alhede M. Pseudomonas aeruginosa biofilms: mechanisms of immune evasion. Adv Appl Microb. 2014;86:1-40.
26. Döring G. Significance of Pseudomonas aeruginosa virulence factors in acute and chronic Pseudomonas aeruginosa infections. Infect. 1987;15(1):47-50.
27. Özer B, Babayiğit C, Çolak S, Önlen C, Çimen F, Boyacıgil I, Akküçük Ş. Pnömoni Etkenleri ve Antimikrobiyal Direnç Durumları. Mustafa Kemal Üni Tıp Derg. 2016;7(27):45-53.
28. Sonmezer MC, Ertem G, Erdinc FS, Kaya Kılıc E, Tulek N, Adiloğlu A. Evaluation of risk factors for antibiotic resistance in patients with nosocomial infections caused by Pseudomonas aeruginosa. Can J Infect Dis Med Microb. 2016; doi.org/10.1155/2016/1321487.
29. Mitov I, Strateva T, Markova B. Prevalence of virulence genes among bulgarian nosocomial and cystic fibrosis isolates of Pseudomonas aeruginosa. Brazil J Microb 2010;41(3):588-595.
30. Wolska K, Szweda P. Genetic features of clinical Pseudomonas aeruginosa strains. Pol J Microbiol. 2009;58(3):255-260.
31. Pournajaf A, Razavi S, Irajian G, et al. Integron types, antimicrobial resistance genes, virulence gene profile, alginate production and biofilm formation in Iranian cystic fibrosis Pseudomonas aeruginosa isolates. Infez Med. 2018;26(3):226-236.
32. Ellappan K, Belgode Narasimha H, Kumar S. Coexistence of multidrug resistance mechanisms and virulence genes in carbapenem-resistant Pseudomonas aeruginosa strains from a tertiary care hospital in South India. J Glob Antimicrob Resist. 2018;12:37–43.
33. Al Dawodeyah HY, Obeidat N, Abu-Qatouseh LF, Shehabi AA. Antimicrobial resistance and putative virulence genes of Pseudomonas aeruginosa isolates from patients with respiratory tract infection. Germs. 2018;8(1):31–40.
34. Dogonchi AA, Ghaemi EA, Ardebili A, Yazdansetad S, Pournajaf A. Metallo-beta-lactamase-mediated resistance among clinical carbapenem-resistant Pseudomonas aeruginosa isolates in northern Iran: a potential threat to clinical therapeutics. Tzu-Chi Medical Journal. 2018;30(2):90–96.
35. Bogiel T, Prażyńska M, Kwiecińska-Piróg J, Mikucka A, Gospodarek-Komkowska E. Carbapenemresistant Pseudomonas aeruginosa strains distribution of the essential enzymatic virulence factors genes. Antibiotics. 2021;10(8): 1-10.
36. Andersson DI, Balaban NQ, Baquero F, et al. Antibiotic resistance: turning evolutionary principles into clinical reality. FEMS Microb Rev 2020;44(2):171-188.
37. Pseudomonas aeruginosa in healthcare settings. HAI/CDC [online]< https://www cdc gov/hai/organisms/pseudomonas html>[accessed 12 March 2022].

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Telogen Effluvium After COVID-19 Infection: A Case Report

COVID-19 Enfeksiyonu Sonrası Gelişen Telogen Effluvium: Vaka Sunumu

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Abstract

Information on the period after COVID-19 infection has not yet been clarified. Every day, a new one is added to the post-COVID-19 symptoms. Hair loss can be seen in the clinical symptoms of many diseases, as well as after the disease has passed. Telogen effluvium (TE) is a condition characterized by widespread hair loss that occurs approximately 3-4 months after a stressor. In this article, a case who applied with the complaint of hair loss three months after suffering from COVID-19 infection is presented.

Keywords COVID-19, SARS-CoV-2, Telogen Effluvium

Özet

COVID-19 enfeksiyonu sonrası döneme ilişkin bilgiler henüz netlik kazanmadı. COVID-19 sonrası belirtilere her gün bir yenisi ekleniyor. Saç dökülmesi birçok hastalığın klinik semptomlarında görülebildiği gibi hastalık geçtikten sonra da görülebilmektedir. Telogen effluvium (TE), bir stres etkeninden yaklaşık 3-4 ay sonra ortaya çıkan yaygın saç dökülmesi ile karakterize bir durumdur. Bu yazıda COVID-19 enfeksiyonu geçirdikten üç ay sonra saç dökülmesi şikayeti ile başvuran bir olgu sunulmaktadır.

Anahtar Kelimeler *COVID-19, SARS-CoV-2, Telogen Effluvium*

GİRİŞ

COVID-19 infection caused by the SARS-CoV-2 is a life-threatening clinical situation, the data on the processes after it has not reached saturation yet. Every day, a new one is added to the post-COVID-19 symptoms.

Hair loss can be a clinical symptom of many diseases, but it can also occur after the disease has passed[1]. The hair follicle changes in three phases: the anagen (growth) phase, the catagen (regression leading to apoptosis) phase, and the telogen (resting) phase. It has been stated that there are an average of 100,000 hairs on the human scalp, and 10-15% of them are in the telogen phase and 85-90% in the anagen phase. The anagen phase lasts 2-6 years, while the catagen phase lasts 4-6 weeks and the telogen phase 3-4 months. Each hair follicle is independent of each other and can be in different phases. The hair follicle may enter the catagen phase and then the telogen phase with various factors[2].

Telogen effluvium (TE) has been defined as a condition characterized by widespread hair loss that occurs approximately 3-4 months after a stressor factor[3]. This condition, which is one of the common causes of diffuse hair loss, is characterized by the loss of hair in the telogen phase. The hair follicle is completely normal, only the change cycle of the hair is disrupted. It has been shown that TE is the most common form of hair loss with systemic diseases[1].

In this article, a case who presented with the complaint of hair loss three months after COVID-19 infection is presented.

CASE REPORT

A 49-year-old female patient applied to the family medicine outpatient clinic with the complaint of hair loss. The patient stated that this hair loss has been happening for two weeks, and as she pulls her hair, hair clumps come in pieces. In the patient's history, it was learned that she was diagnosed with COVID-19 infection three months ago after complaints of fever and cough, she was treated with favipiravir, and he was not hospitalized.

In the vital signs of the patient whose general condition was good, oriented and cooperative; fever was 36.5 degrees Celsius, arterial blood pressure was 110/70 mmHg, heart rate was 90 beats/minute, respiratory rate was 18/minute, and oxygen saturation (in room air) was 97%.

There was no feature in her medical history. In the physical examination, diffuse hair loss areas were detected on the scalp, other system examinations were normal. (Figure-1,2) Hair pulling test was positive. (>50 hairs)

Figure 1. Hair thinning and decreased hair density

Figure 2. Diffuse reduction in hair density

Laboratory examination results of the patient are presented in the table.

No abnormal finding was detected in the thorax computed tomography and abdominal ultrasonography evaluation.

In the differential diagnosis of hair loss; iron deficiency anemia, thyroid dysfunction, vitamin B12 deficiency, 25-Hydroxy vitamin D deficiency, hyperprolactinemia, diabetes mellitus, folate deficiency, malignancy, hypomagnesemia, sudden weight loss, drug use were excluded as a result of anamnesis, examination, tests and imaging. TE was considered in the patient because he had a history of COVID-19 infection, which could be a stressor, 3 months ago. For this diagnosis, minoxidil 2% skin spray treatment was started on the scalp and the patient was called for control.

Table. Patient's Laboratory Examination Results	
White Blood Cell (WBC)	9.7 (4.60-10.20) K/uL
Hemoglobin	12.8 (12.20-18.10) g/dl
Mean Corpuscular Volume (MCV)	91.3 (80- 100) Fl
Lymphocyte (LYM)	2.72 (0.60-3.40) K/uL
Eosinophil (EOS)	0.35 (0.0-0.7) K/uL
Platelet (PLT)	224000 (100000-450000) K/uL
Glucose	80 (74-118) mg/dL
Sodium (Na)	140 (136-146) mmol/L
Potassium (K)	4.0 (3.5-5.1) mmol/L
Calcium (Ca)	9.6 (8 .8-10.6) mg/dL
Urea	33 (17-43) mg/dL
Creatinine	0.65 (0.67-1.17) mg/dL
D-dimer	50 (0-500)) µg FEU/L
C-reactive protein (CRP)	17.6 (0-5) mg/dL
Iron (Fe)	107 (37-158) µg/dL
Ferritin	74 (4.63-204)) ug/L
Thyroid Stimulating Hormone (TSH)	2.18 (0.35-4.94) uIU/mL
Free T4	1.03 (0.7-1.48) ng/dL
Vitamin B12	380 (187-883) pg/mL
25-Hydroxy vitamin D	35.2 ng/mL
Magnesium	2.4 (1.9-2.5) mg/dL
Prolactin	12.06 (1.2) -29.93) ng/mL
CA 125	6 (0-35) U/ml
CA 15-3	4 (0-31.3) U/ml
CA 19-9	7 (0-37) U/ml
HgA1c	4.7 (4-6) % NGSP
Folate	5.9 (3.1-20.5) ng/mL

DISCUSSION

TE was first reported by Kligman in 1961, it was defined as a non-cicatricial alopecia disease characterized by the simultaneous loss of many telogen hairs. TE is seen on the entire scalp and manifests as a sudden increase in hair loss[3]. The onset and progression of hair loss is rapid, and the hair pull test is usually positive[4].

It has been stated that TE is usually seen as an indicator

of an underlying condition and usually 3-4 months after the triggering factors. It has been shown to date that many bacterial and viral diseases can cause TE. However, it has not been revealed exactly how these factors change the biorhythm of the hair[5].

Studies have reported that TE occurs after dengue virus and Rickettsia conorii infection[6,7]. Xiong et al. stated in their study that hair loss developed after SARS-CoV-2 infection[8]. Moreno-Arrones et al. showed that they included 214 patients with acute TE in their prospective study and that 191 (89.7%) of these patients had a previously confirmed SARS-CoV-2 infection[9]. Lv et al. stated in their case report that a 38-year-old female patient had a diagnosis of TE and that one of the factors that could lead to this situation was SARS-CoV-2 infection[5]. In current case, the detection of TE 3 months after COVID-19 infection suggests that the likely cause may be SARS-CoV-2.

Studies have reported that people with severe COVID-19 have higher levels of proinflammatory cytokines, which may be associated with a higher risk of TE. Jose et al. stated that the coagulation cascade was activated in response to COVID-19 infection, and the concentration of anticoagulant protein decreased due to decreased production and increased consumption[10]. Olds et al. reported that these factors may lead to the formation of microthrombus, which may prevent the feeding of the hair follicle. The presence of microthrombus formation and high levels of proinflammatory cytokines have been presented as two possible mechanisms to explain how SARS-CoV-2 infection may trigger TE[11].

Lv et al. stated that the COVID-19 pandemic creates various negative effects on people's social life, causes stress, anxiety and depression, and that some of these effects may pave the way for the emergence of TE[5].

It has been reported that the basis of the treatment of TE is to eliminate the underlying causes and stressor factors[11]. Although minoxidil is used in the treatment of most cases in the literature, the effectiveness of this treatment has not been fully demonstrated[12].

In this case report, it is emphasized that TE can be seen after COVID-19 infection, and systemic interrogation should be done in control examinations after COVID-19. Future studies and case series will contribute to clarify the relationship between COVID-19 and TE.

Informed consent was taken from the patient.

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Author Contributions

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References

1. Gathers RC, McMichael AJ. Hair disorders in systemic disease. Dermatological Signs of Internal Disease. 2009; 355–364.
2. Sperling LC. Hair and systematic disease. Dermatol Clin. 2001; 19: 711–726.
3. Malkud S. Telogen effluvium: A review. J Clin Diagn Res. 2015; 9: WE01–3.
4. Kavala M, Turkoglu Z, Can B. Hair and systemic diseases. Med J Goztepe Train Res Hosp. 2013; 26: 128–132.
5. Lv S, Wang L, Zou X, et al. A case of acute telogen effluvium after SARS-CoV-2 infection. CCID. 2021; 14: 385–387.
6. Veraldi S, Vaira F, Raia DD, et al. Telogen effluvium as first clinical presentation of dengue. G Ital Dermatol Venereol. 2017; 152: 184–185.
7. Rebora A, Ciccarese G, Drago F. Postfebrile telogen effluvium: hair fall after Rickettsia conorii infection. G Ital Dermatol Venereol. 2019; 154: 94–95.
8. Xiong Q, Xu M, Li J, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clin Microbiol Infect. 2021; 27: 89–95.
9. Moreno-Arrones OM, Lobato-Berezo A, Gomez-Zubiaur A, et al. SARS-CoV-2-induced telogen effluvium: a multicentric study. J Eur Acad Dermatol Venereol. 2021; 35: e181–e183.
10. Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med. 2020; 8: e46–e47.
11. Olds H, Liu J, Luk K, et al. Telogen effluvium associated with COVID-19 infection. Dermatol Ther. 2021; 34: e14761.
12. Stoehr JR, Choi JN, Colavincenzo M, et al. Off-label use of topical minoxidil in alopecia: A review. Am J Clin Dermatol. 2019; 20: 237–250.