Journal of

BIOTECHNOLOGY & STRATEGIC HEALTH RESEARCH (BSHR)

Cilt / *Vol*: **8**

Sayı / *Issue*: **2**

Ağustos / *August* : **2024**

e-ISSN 2587-1641

jbiosad@gmail.com

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

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

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 2023 yılından itibaren sadece İngilizce yazı kabul etmeye başlayacaktır.

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

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

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, Ağustos 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 8. Yılı, Ağustos'2024 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.

Editör
Prof. Dr. Mustafa ALTINDİŞ
Editor in Chief

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

KÜNYE

Deneysel, Biyoteknolojik, Klinik ve Stratejik Sağlık Araştırmaları Derneği
JOURNAL of BIOTECHNOLOGY and STRATEGIC HEALTH RESEARCH
Nisan, Ağustos ve Aralık aylarında olmak üzere yılda 3 sayı çıkar.
Three issues annually: April, August, December

Yayın dili: Türkçe ve İngilizcedir
Publishing Language: Turkish and English

http://dergipark.gov.tr/bshr

Sahibi (Owner)
Deneysel, Biyoteknoloji, Klinik ve Stratejik Sağlık Araştırmaları Derneği Adına Prof. Dr. Mustafa ALTINDİŞ
Experimental, Biotechnology, Clinical and Strategic Health Research Association on behalf of Mustafa ALTINDIS MD

Yazışma Adresi (Corresponding Address)
Prof. Dr. Mustafa ALTINDİŞ
Sakarya Üniversitesi Tıp Fakültesi Dekanlık Binası, KORUCUK, 54200, Sakarya

Dergi Yazı Gönderimi Sayfası: http://dergipark.gov.tr/bshr

E-posta: jbiosad@gmail.com, maltindis@gmail.com

Tel: +90 (264) 295 72 77 **Faks:** +90.264.295 6629

Dizin Bilgisi (Indexing)
JOURNAL OF BIOTECHNOLOGY AND STRATEGIC HEALTH RESEARCH(Biyoteknoloji ve Stratejik Sağlık Araştırmaları Dergisi); "Türkiye Atıf Dizini", "Türk Medline", "Google Scholar", "ASOS Index", "SOBIAD"ve "CrossRef" gibi ulusal ve uluslararası dizinlerde taranmaktadır. Makalelere DOİ verilmektedir.

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

KÜNYE

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

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 yayının 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 ν 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

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

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.

Yazışma Adresi (Corresponding Address)
Prof. Dr. Mustafa Altındiş
Sakarya Üniversitesi Tıp Fakültesi Dekanlık Binası,
KORUCUK, 54200, Sakarya

Dergi Yazı Gönderimi Sayfası:
http://dergipark.gov.tr/bshr

E-posta: jbiosad@gmail.com, maltindis@gmail.com
Tel: +90 (264) 295 72 77
Faks: +90.264.295 6629

e-ISSN 2587-1641

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.

Papers are accepted for publication on the understanding that they have not been published and are not going to be considered for publication elsewhere. Authors should certify that neither the manuscript nor its main contents have already been published or submitted for publication in another journal. The copyright release form, which can be found at http://dergipark.gov.tr/bshr after you started submission, and it must be signed by the corresponding author on behalf of all authors and must accompany all papers submitted. Please see the form for additional copyright details. After a manuscript has been submitted, it is not possible for authors to be added or removed or for the order of authors to be changed. If authors do so, their submission will be cancelled. The peer review process is double-blind, i.e. both authors and referees are kept anonymous. Manuscripts may be rejected without peer review by the editor-in-chief if they do not comply with the instructions to authors or if they are beyond the scope of the journal. Any manuscript that does not conform to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, as reported at http://www.icmje.org/icmje-recommendations.pdf, will also be rejected. After a manuscript has been accepted for publication, i.e. after referee-recommended revisions are complete, the author will not be permitted to make changes that constitute departures from the manuscript that was accepted by the editor. Before publication, the galley proofs are always sent to the authors for corrections. Mistakes or omissions that occur due to some negligence on our part during final printing will be rectified in an errata section in a later issue. This does not include those errors left uncorrected by the author in the galley proof.

The use of someone else's ideas or words in their original form or slightly changed without a proper citation is considered plagiarism and will not be tolerated. Even if a citation is given, if quotation marks are not placed around words taken directly from another author's work, the author is still guilty of plagiarism. Reuse of the author's own previously published words, with or without a citation, is regarded as self-plagiarism. All manuscripts received are submitted to iThenticate®, a plagiarism checking system, which compares the content of the manuscript with a vast database of web pages and academic publications. Manuscripts judged to be plagiarised or self-plagiarised, based on the iThenticate® report or Turnitin for theses, will not be considered for publication. It is suggested for you to determine the ratio in the iThenticate® report of your manuscript before you submit it. Editorial board decided that this ratio should be less than 30, and if not, then the manuscripts are not accepted and sent back to author(s).

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.

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

HEALTH RESEARCH

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-

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

HEALTH RESEARCH

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.

Corresponding Address

Prof. Dr. Mustafa Altındiş

Sakarya Üniversitesi Tıp Fakültesi Dekanlık Binası,

KORUCUK, 54200, Sakarya

Dergi Yazı Gönderimi Sayfası:

http://dergipark.gov.tr/bshr

E-mail:

jbiosad@gmail.com, maltindis@gmail.com

Phone: +90 (264) 295 72 77

Fax: +90.264.295 6629

e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

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

DERLEME / *REVIEW*

ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLES*

DOI:10.34084/bshr.1501965 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Review / Derleme

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

Birinci Basamak ve Bütünleşik Sağlık Hizmetleri

Primary Care and Integrated Health Services

Osman Hayran

[1] İstanbul Medipol Üniversitesi, Tıp Fakültesi, Halk Sağlığı Anabilim Dalı, İstanbul, Türkiye

ORCID ID: Osman Hayran: https://orcid.org/0000-0002-9994-5033

***Sorumlu Yazar / Corresponding Author:** Osman Hayran, **e-posta / e-mail:** ohayran@gmail.com

Geliş Tarihi / Received : 16-06-2024 **Kabul Tarihi / Accepted:** 23-06-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Hayran O. Primary Care and Integrated Health Services. J Biotechnol and Strategic Health Res. 2024; 8(2):76-82

Öz

Hizmetlerin girdilerinin, sunumunun, yönetiminin ve organizasyonunun erişim, kalite, kullanıcı memnuniyeti ve verimliliğin artırılması amacıyla bir araya getirilmesi olarak tanımlanan bütünleşik sağlık hizmetlerinin amacı birbirinden kopuk ve bağımsız sunulan bazı sağlık hizmetlerine bağlı olarak ortaya çıkabilecek hasta güvenliği sorunları ile maliyet sorunlarını azaltmaktır. Bütünleştirme yatay ya da dikey şekilde olabilmektedir. Hangi tür sağlık hizmetlerinin, hangi hizmet basamağında, hangi sağlık kuruluşları ve profesyonelleri tarafından bütünleşik şekilde sunulması gerektiği konusunda tüm toplumlara uyarlanabilecek standart formüller bulunmamaktadır. Ülkelerin, aynı ülkedeki farklı bölgelerin coğrafi, sosyal ve ekonomik koşullarına bağlı olarak farklı bütünleştirme yöntemleri uygulanabilmektedir. Teknolojik ve bilimsel gelişmelere bağlı olarak zaman içerisinde yeni hizmet türlerinin, yeni mesleklerin ortaya çıkması yeni örgütlenmeleri ve yeni iş birliklerini gerektirebildiğinden bütünleşik hizmet konusunu sabit bir uygulama olarak değil dinamik bir değişim süreci olarak görmek gerekir. Sağlık politikaları, yönetimi ve örgütlenmesi alanındaki karar vericilerin ve yetkili profesyonellerin bu konuda donanımlı olması önemlidir.

Anahtar Kelimeler: Birinci basamak sağlık hizmeti, dikey bütünleşme, bütünleşik sağlık hizmeti, yatay bütünleşme

Abstract

The aim of integrated health services, which is defined as bringing together the inputs, delivery, management and organization of services with the aim of increasing access, quality, user satisfaction and efficiency, is to reduce patient safety problems and cost problems that may arise due to some health services that are disconnected and independent from each other. Integration can be horizontal or vertical. There are no standard formulas that can be adapted to all societies about which types of health services, at which service level, by which health institutions and professionals should be provided in an integrated manner. Different integration methods can be applied depending on the geographical, social and economic conditions of countries as well as different regions within the same country. Since the emergence of new types of services and new professions over time due to technological and scientific developments may require new organizations and new collaborations, the issue of integrated services should not be seen as a fixed practice but as a dynamic process of change. It is important that decision-makers and authorized professionals in the field of health policies, management and organization are equipped in this regard.

Keywords: Primary care, vertical integration, integrated health care, horizontal integration

GİRİŞ

"Birinci Basamak Sağlık Hizmetleri", "Temel Sağlık Hizmetleri" ve "Koruyucu Sağlık Hizmetleri" birbirinden farklı hizmet türlerini ifade ettikleri halde sıklıkla karıştırılan ve yanlışlıkla aynı amaçla kullanılan kavramlardır. Sağlık politikaları, sağlık hizmetlerinin örgütlenmesi ve yönetimi ile ilgilenenlerin bu kavramları karıştırmaması önemlidir. Kavramların anlam farklılıklarını değişmez ansiklopedik tanım farklılıkları olarak düşünmek yerine sağlık hizmetlerinin örgütlenme ve yönetimi faaliyetlerinde ortak dil kullanılmasının aracı olarak görmek gerektiğinden önce bu kavramları netleştirmek gerekir.

Dünya Sağlık Örgütü (DSÖ) tanımına göre Birinci Basamak Sağlık Hizmetleri, hizmetlerle ilk temas noktasında, erişilebilirliği olan, sürekli, kapsamlı, koordine edilmiş ve insan-merkezli bir hizmet modelidir. Amacı tüm toplumsal grupların hizmetlere eşit erişimin sağlanması, eşitsizliklerin azaltılması ve toplumun sağlık düzeyinin optimize edilmesidir.[1]

Temel Sağlık Hizmetleri (TSH) daha bütüncül bir toplumsal yaklaşım olup, üç bileşeni bulunmaktadır:

- Birinci basamak sağlık hizmetleri ve temel halk sağlığı işlevleri
- Çok sektörlü politika ve eylemler
- Güçlendirilmiş bireyler ve topluluklar

Koruyucu Sağlık Hizmetleri ise Kişiye Yönelik ya da Çevreye Yönelik olarak iki grupta toplanan, primordial, birincil, ikincil, üçüncül ve dördüncül koruyucu hizmetleri ifade eden bir kavramdır.

Tanımlardan anlaşılacağı gibi Birinci Basamak Sağlık Hizmetleri, bir ülkede veya bölgede insanların sağlık sorunları için ilk başvuru birimlerinde sunulan hizmetler anlamında kullanılır. Kişilerin ihtiyacı olan ya da talep ettikleri hizmetleri kapsaması nedeniyle ağırlıklı olarak ayakta tanı-tedavi hizmetleri ile kişiye yönelik koruyucu hizmetlerin bir kısmından oluşan bir hizmet grubudur.

Temel Sağlık Hizmetleri ise, birinci basamak sağlık hizmetlerini de kapsayacak şekilde, ancak, "temel halk sağlığı işlevleri" ile ifade edilen ve kamu sağlığı açısından sunulması gerekli olan, ne olması gerektiği DSÖ tarafından 1978 Alma-Ata Bildirgesinde tanımlanmış olan ve daha sonra aralıklı olarak güncellenen sağlık hizmetleri paketi anlamına gelir. Bu hizmet paketinde çevreye yönelik bazı koruyucu hizmetler ile hastalık izlemi ve yönetimi işlevleri de olabilmektedir.

Örneğin, ülkemizde birinci basamak sağlık hizmetleri ile ifade edilen hizmetler Aile Sağlığı Merkezleri, Muayenehaneler, Evde bakım Hizmeti Birimleri, Seyahat Sağlığı Merkezleri, Verem savaş dispanserleri gibi örgütler tarafından sunulan hizmetlerdir. Temel Sağlık Hizmetleri ise, Aile Sağlığı Merkezleri hizmetleri de dahil olmak üzere İlçe Sağlık Müdürlükleri ve Toplum Sağlığı Merkezleri sorumluluğunda yürütülen Bulaşıcı Hastalıklarla Mücadele, Kanser Erken Tanı çalışmaları, Çevre Sağlığı hizmetleri, Besin-Su Güvenliğinin denetimi, Üreme Sağlığı Hizmetleri, Sağlık Eğitimi gibi faaliyetlerden oluşmaktadır. Sayılan bu hizmetlerin bazıları kişiye yönelik bazıları çevreye yönelik koruyucu hizmetlerdir ve kamusal nitelikte olanlar İlçe Sağlık Müdürlükleri ve Toplum Sağlığı Merkezlerince yürütülmektedir.

Birinci Basamak Sağlık Hizmetleri

Bu kavramlar konusunda kafa karışıklığı sadece bize özgü değildir. Konuyla ilgili uluslararası kaynaklar tarandığında ve farklı ülkelerdeki sağlık hizmetleri örgütlenme modelleri incelendiğinde Birinci Basamak Sağlık Hizmetleri için farklı yaklaşımların bulunduğu görülmektedir. Örneğin, ağırlıklı olarak Anglosakson ülkelerden oluşan bazı gelişmiş ülkelerde bu konuda başlıca üç yaklaşım bulunmaktadır. Hiyerarşik Normatif Model olarak bilinen birinci yaklaşıma göre bu kavram sağlık hizmetleri sunum sistemi içerisindeki bir basamak anlamındadır. İkinci yaklaşıma göre (Hiyerarşik Profesyonel Model) toplumun sıklıkla ihtiyacı olan hizmet ve faaliyetlerin bir araya getirilerek örgütlenmiş olmasıdır. Üçüncü yaklaşıma göre (Hiyerar-

şik Olmayan Profesyonel Model) ise hizmeti sunan meslek grupları ile tanımlanan ve genellikle pratisyen/aile hekimi, hemşire, fizyoterapist, ebe, sağlık memuru, toplum sağlıkçısı gibi mesleklerin yer aldığı hizmet türüdür.[2]

Başka bir deyişle birinci basamak tanımı için,

- Sistem odaklı: Hizmet sunan sağlık sisteminin bir basamağı,
- Hizmet odaklı: Temel sağlık hizmetlerinin bir kısmını da kapsayan bir paket,
- Meslek odaklı: Bazı sağlık mesleklerince sunulan hizmetler,

şeklinde farklı yaklaşımların olduğu görülmektedir.

Bu yaklaşımlara uygun hizmetlerin neler olacağı birbirinden kesin çizgilerle ayrılmadığı gibi durağan da değildir ve zaman içerisindeki gelişmelere bağlı olarak değişim gösterebilmektedir.

Sonuç olarak birinci basamak sağlık hizmetlerinin kapsamı ve örgütlenme biçimi için standart bir formül bulunmamaktadır. Her ülkenin hatta bir ülkenin farklı bölgelerinin kendine özgü coğrafi, kültürel, sosyal ve ekonomik koşulları bu anlamda belirleyici olmaktadır.

Birinci basamak hizmetlerin taşıması gereken özelliklerin ilk sırasında erişim kolaylığı gelmektedir. Sağlık sistemi ile ilk temas noktasını oluşturan bu hizmetlere erişim için coğrafi, ekonomik ve kültürel anlamdaki her türlü engel kaldırılmış ve erişim her birey için kolaylaştırılmış olmalıdır.

Coğrafi açıdan erişim sorunu olmamalı, hizmetler ihtiyacı olan bireylerin yaşadığı yerin yakınına kadar getirilmiş olmalıdır. Ekonomik açıdan sağlık güvencesi olan-olmayan, zengin-yoksul her birey ihtiyaç duyduğu hizmetleri alabilmelidir. Kültürel açıdan ise farklı dil, din, ırk, etnik grup gibi özellikler hizmete erişimi engellememelidir.

Erişim kolaylığı her türlü engeli olan bireyler, dezavantajlı gruplar için de düzenlenmiş olmalıdır. Erişim kolaylığı için söylenebilecek son ve en önemli özellik ise alınacak hizmetlerin zamanında ve bekleme süresi en az olacak şekilde düzenlenmiş olmaları gereğidir.

Birinci basamak hizmetlerinin kapsamı hizmet alacak toplumun koşullarına göre belirlenmelidir. Bazı toplumlarda ana-çocuk sağlığı, üreme sağlığı, bulaşıcı hastalıklardan korunma hizmetleri ön planda iken başka toplumlarda madde bağımlılığı ile mücadele, kronik hastalık yönetimi, palyatif bakım hizmetleri gibi hizmetlerin ön planda olması gerekebilir.

Bu hizmetleri sunacak sağlık insan gücünün kimlerden ve ne miktarda olacağı da doğal olarak hizmet türleri ve hizmet sunulacak toplumun koşulları ile yakından ilişkilidir. Örneğin, ana-çocuk sağlığı hizmetlerinin pratisyen hekimler, ebe ve hemşireler, kadın-doğum uzmanları ve pediatristler tarafından sunulması söz konusu olabileceği gibi, koşullar gerektirdiğinde geleneksel ebeler (ara-ebeleri) ve toplum sağlıkçıları tarafından sunulması da mümkün olabilmektedir.

Birinci basamak sağlık hizmetlerinin sayılan bu özellikleri dikkate alındığında ayakta hastalık tanı-tedavisi hizmetleri başta olmak üzere günlük yaşamda ihtiyaç duyulan enjeksiyon-pansuman, aşı-bağışıklama, üreme sağlığı, gebe-çocuk izlemi, bulaşıcı hastalık izlem ve filyasyonu, kronik hastalık izlem ve yönetimi, gibi farklı hizmet türlerinin disiplinler arası bir anlayış ve bütünleşik bir ekip hizmeti şeklinde sunulması gerektiği ortaya çıkmaktadır.

Bu noktada sağlık hizmetlerinde bütünleşme yani entegrasyon konusunu biraz açmak gerekir.

Bütünleşik Sağlık Hizmetleri

Bütünleşik sağlık hizmetleri kavramı aslında yeni olmayan ancak sağlık sistemlerindeki reform arayışları nedeniyle belirli aralıklarla ön plana çıkan önemli bir kavramdır. Farklı sağlık sistemlerine ilişkin uluslararası kaynaklarda

"bütünleşik sağlık hizmeti" anlamında kullanılan bazı kavramlar şu şekilde sıralanmaktadır: integrated health, coordinated care, comprehensive care, seamless care, interprofessional care, transmural care, managed care, shared care, disease management.

Kavramın ön plana çıkmasının başlıca nedeni bazı sağlık hizmetlerinin birbirinden kopuk ve bağımsız sunulmasına bağlı olarak ortaya çıkabilecek hasta güvenliği sorunları ile maliyet sorunlarını azaltmaktır.

Örneğin, ülkemizde ilk kez 1961 yılında sağlık Hizmetlerinin Sosyalleştirilmesi sürecinde ortaya çıkan bu yaklaşım ile o güne kadar tüm ülkede ayrı sağlık örgütlenmeleri şeklinde yürütülen Verem Savaşı, Sıtma Eradikasyonu, Ana-Çocuk Sağlığı, Frengi-Lepra ve Trahom Savaşı, Hükümet Tabiplikleri gibi sağlık kuruluşları birleştirilerek Sağlık Ocağı Tabiplikleri ve İl Sağlık Sosyal Yardım Müdürlükleri bünyesinde entegrasyon sağlanmıştır. Bu şekilde her hizmet grubu için ayrı personel, fiziki alt yapı, araç-gereç kullanmak yerine tüm kaynakların bir arada kullanılması yoluna gidilerek hem maliyet anlamında hem de hizmetlerin birbirini tamamlayacak şekilde verilmesi gerçekleştirilmiştir.

Bu uygulama o dönemde başka ülkelerde de (Örneğin İngiltere, Sovyetler Birliği, Çin Halk Cumhuriyeti gibi) ortaya çıkan ilerici ve yenilikçi bir anlayıştır. Ne var ki her değişime doğal olarak karşı çıkan statüko yanlısı kesimler tarafından hoş karşılanmayan bu yaklaşıma ülkemizde ideolojik yakıştırmalar getirilerek hükümetlerin kalıcı bir politikası haline gelmesi engellenmiştir. Daha sonra DSÖ'nün 1978 Alma-Ata Bildirgesi ile gündeme gelen "Temel Sağlık Hizmetleri", sonraki yıllarda Astana Bildirgesi ile gündeme gelen "Evrensel Sağlık Kapsayıcılığı" kavramları aslında ülkemizdeki sosyalleştirme uygulamalarının güncellenmiş birer şeklinden başka bir şey değildir. Nitekim geçen süre içerisinde hiçbir iktidar tarafından tam olarak uygulanamayan ama bir kenara da bırakılamayan Sosyalleştirme uygulamalarına benzer birinci basamak örgütlenmeleri önce 80'li yılların sonunda Dünya bankası destekli "Sağlık Reformları", daha sonra 2000'li yılların başında "Sağlıkta Dönüşüm" adı altında tekrar gündeme gelmiş ve sevk zincirinin olmaması gibi önemli bazı eksiklikleri dışında başarı ile uygulanmıştır.

Bütünleşik sağlık hizmetleri konusu bir yandan küreselleşme ve ticarileşme eğilimlerine bağlı olarak sağlık harcamalarındaki aşırı artış bir yandan da hizmet kalitesi, hasta güvenliği konularında daha yüksek sesli itirazların duyulur hale gelmesi nedeniyle belirli dönemlerde gündeme gelmeye devam etmektedir.

Başka bir deyişle bütünleşik şekilde sunulan bazı sağlık hizmetleri zaman içerisinde gelişen teknolojiler, uzmanlaşmalar gibi uygulama farklılıklarına bağlı olarak dallanıp budaklanarak birbirinden kopuk hale gelmekte, bu durum hem kalite hem de verimlilik sorunlarına neden olmakta, daha sonra yeni entegrasyon arayışları gündeme gelmektedir. Bu bir döngü olup sağlık hizmetlerindeki yeni bilgi, uygulama, uzmanlaşma ve maliyet artışı eğilimleri sürdükçe dönmeye devam edecektir. Tıpkı sağlık reformlarının da bir sonunun olmaması gibi.

Bütünleşik sağlık hizmetlerini "Hizmetlerin girdilerinin, sunumunun, yönetiminin ve organizasyonunun erişim, kalite, kullanıcı memnuniyeti ve verimliliğin artırılması amacıyla bir araya getirilmesi" şeklinde tanımlamak uygundur.[3,4]

Bu anlamda bütünleşmeyi (entegrasyonu) başlıca iki farklı yaklaşımla gerçekleştirmek mümkündür: Yatay ve dikey bütünleşme.

Yatay bütünleşme, sağlık sisteminin aynı basamağında hizmet sunan farklı meslekler ya da örgütler arasında iş birliği ve bütünleşme sağlanması demektir. Örneğin, birinci basamakta sunulan ayakta tanı-tedavi hizmetlerinin bağışıklama, üreme sağlığı, kronik hastalık yönetimi, sağlık eğitimi gibi koruyucu hizmetler ile birlikte sunulması gibi.

Dikey bütünleşme ise farklı hizmet basamaklarında sunulan hizmetler ve/ya örgütler arasında iş birliği ve bütünleşme sağlanması anlamına gelir. Örneğin, birinci basamakta sunulan evde bakım hizmetleri, ayakta tanı-tedavi hizmetleri ile ikinci basamakta sunulan yatırılarak tedavi hizmetlerinin, üçüncü basamakta sunulan akademik sağlık hizmetlerinin birbiri ile eşgüdüm halinde, geri bildirimlerle destekleyecek şekilde sunulması gibi.[3]

Bütünleşmenin dinamiklerini ve yararlarını anlamak doğru politikalar belirlemek açısından önemlidir. Sağlık hizmetlerinin parçalı hale gelmesinin nedenleri arasında mesleki uygulamaların bağımsızlığı anlamına gelen otonomi yani özerklik konusu ilk sırada yer almaktadır. Uzmanlaşma, teknoloji ve yeni bilgilere bağlı olarak ortaya çıkan yeni tür sağlık hizmeti uygulamaları sağlık sisteminde yeni profesyonelleri ortaya çıkarmakta ve yeni mesleklerin özerk yapısına uygun olarak yeni güç alanları oluşturmaktadır. Bu alanın sahiplerinin artışı bir yandan uygulamaların daha da çeşitlenmesine diğer yandan yeni uygulamalar için yeni harcamalara ve doğal olarak bazı kesimler için fazladan yeni kazançlara yol açmaktadır. Yeni olan bu tür gelişmelerin süreç içerisinde neden olacağı hasta güvenliği ve maliyet sorunları yeterince dikkat çekici boyuta geldiğinde denetleyici ve düzenleyici mekanizmalara ihtiyaç duyulmakta ve bütünleşme devreye girmektedir. Bütünleşme, düzenlenmesi gereken hizmetlerin niteliğine bağlı olarak yatay veya dikey olabilmektedir. Bütünleşmenin başarısı sağlık mesleklerinin özerk yapıları dikkate alınarak güç alanları çatıştırılmadan uygun bir iş birliği ve koordinasyonla bir araya getirilmesine bağlıdır. Aksi halde iş hayatının doğal akışı içerisinde oluşmuş olan bütünleşik bir örgütsel yapının bile bir süre sonra parçalı hale gelmesi mümkündür.

Örneğin, ABD'de 2012 yılında dikey bütünleşme adına başlayan bir eğilim sonucu binlerce hekim muayenehanesi hastanelerle dikey bütünleşik hale gelmiş, iş birliğinin ötesinde hastaneler bunları satın almıştır. Bu yolla hem hizmet kalitesini arttırma hem de maliyetleri düşürme hedeflenmiş olmakla birlikte bir süre sonra bazı gruplarda aşırı büyüme oluşarak tekelleşme başlamış, tekelleşme keyfilik ve denetimsizliği arttırarak beklenenin tam aksine hizmetlerin maliyetlerinde artışlar, kalitesinde düşüşler ortaya çıkmıştır.[5,6] Bu durum sadece özel sektör için değil iyi planlanmadan bütünleşmeye giden kamu kurum ve kuruluşları için de söz konusu olabilmektedir.

Nasıl Bir Örgütlenme Olmalı?

Kurum ve kuruluşların işleyişi ve performansı arasındaki bağlantıyı analiz amacı ile sıklıkla başvurulan Durumsallık Teorisine (Olumsallık olarak da bilinir) göre örgütlenme ve yönetim konularında her duruma uyan tek bir "en iyi" yaklaşım yoktur. Zaten en iyi de iyinin düşmanıdır. En iyi yaklaşım, içinde bulunulan duruma ve koşullara göre değişmektedir. Bir kurumun performansı onun yapısal özelliklerinin ya da iş süreçlerinin sonucu olmaktan çok işleyişi ile büyüklüğü, geçmişi, çevresel koşulları gibi bir dizi durumsal özellikler arasındaki uyum sonucu gerçekleşmektedir.[7,8] Bu nedenle, örneğin en iyi birinci basamak örgütlenmesinin nasıl olması, kimlerden oluşması ve ne anlamda bütünleşik olması gerektiği gibi konular, hizmetlerden beklenen çıktılar ile eldeki imkân ve koşullar arasındaki uyuma bağlıdır.

Yapılan bir model incelemesine göre birinci basamak sağlık örgütlenmeleri genellikle hekim ya da hemşire merkezlidir ve hemşire merkezli örgütlenmelerin giderek artmakta olduğu dikkati çekmektedir.[9] Bazı ülkelerde lisans mezunu olup da pratisyen hemşire eğitimi almış hemşirelere sık görülen bazı hastalıklar konusunda tek başına tanı koyma, tedavi verme ve reçete yazma yetkisi verildiği görülmektedir. Örneğin, ABD'de yasal düzenlemelerle 26 eyalette bu tür bir yetkilendirme sağlanmıştır. Avusturalya'da[10], Kanada'da11 benzer uygulamalar bulunmaktadır. İrlanda12 ve İngiltere'de ise bu doğrultuda düzenleme yapılması tartışmalarının hız kazandığı görülmektedir.

ABD'de pratisyen hemşireler dışında hekim yardımcıları (PA), kiropraktik doktorlar, Çin'de geleneksel Çin tıbbı he-

kimleri, Rusya ve eski Sovyet ülkelerinde Feldsherler, Hindistan'da Ayushlar (AYUSH: Ayurvedic, Yoga, Naturopathy, Unani, Siddha and Homeopathy), Afrika'nın pek çok ülkesinde toplum sağlıkçıları birini basamakta tanı-tedavi hizmeti sunan meslek örnekleridir. Ülkemizde Refik Saydam dönemindeki uygulamalara ek olarak ebelerin rahim içi araç, MR uygulamaları da bu anlamda önemli örneklerdir.[13-15]

Bu örneklerin tam tersine birinci basamak sağlık hizmetleri için özel bir örgütlenme modeli bulunmayan, birinci ve ikinci basamak ayrımının belirsiz olduğu ülkeler de vardır. Bunun tipik örneği olan Japonya'da birinci basamak sağlık hizmetleri hem hastanelerde hem de toplum içerisinde sunulan hizmetlerdir. Japonya "süper-yaşlı" demografik yapısı ile dünyada doğumda beklenen yaşam süresi en uzun olan ve evrensel sağlık kapsayıcılığını 1960'lı yıllardan başlayarak tam anlamıyla gerçekleştirmiş bir ülkedir.[16] Ne var ki Japon sağlık sistemi COVID-19 pandemisi sırasında yetersiz kalmıştır. Yetersizliğin başlıca sorumlusunun son derece özgürce örgütlenmiş bir sağlık sistemi ile bağımsız biçimde finanse edilen özel hastaneler olduğu sonucuna varılmıştır. Ayrıca sağlık güvence sistemindeki seçme özgürlüğünün de bireylerin kapsayıcı hizmet almalarını, alınan hizmetlerin sürekliliğini engelleyici etkiler yaptığı anlaşılmıştır. Oysa yaşlı nüfusun hastane ağırlıklı tıbbi hizmetler yerine toplum odaklı bakım hizmetlerine ihtiyacı nedeniyle aile hekimliği mantığına dayalı ve çok disiplinli bir bakım ağı kurulması yolunda tartışmalar başlamıştır.[16,17]

Sağlık hizmetlerinin sunum biçimi ve örgütlenmesi konusunda küresel düzeyde güncel olan bir konu da e-Sağlık ve dijital sağlık konularıdır. COVID-19 pandemisi sırasında koşulların da zorlamasıyla yaygınlaşan tele-tıp uygulamaları sağlık hizmetlerinde dijitalleşmeyi hızlandırmıştır. DSÖ'ye göre dijital sağlık, sağlık sistemlerinin daha verimli ve sürdürülebilir olmasına yardımcı olarak kaliteli, uygun fiyatlı ve hakkaniyetli hizmet sunmalarını sağlayabilir. Bu uygulamalar özellikle orta ve düşük gelir düzeyindeki ülkeler için önem taşımaktadır. E-Sağlık ve dijital sağlık uygulamaları günümüzde sağlık alanında en hızlı büyüyen alanlardan biri olarak kabul edilmektedir.[18]

Sonuç olarak farklı basamaklarda yer alması gereken sağlık hizmetlerinin neler olacağı, hangi hizmetlerin kimler tarafından sunulacağı, bütünleşmenin nasıl yapılacağı konularında tek bir formül bulunmayıp çözümler her toplumun kendi olanakları ve koşullarına bağlı olarak belirlenmek zorundadır.

Çıkar Çatışması

Bu makale ile ilgili herhangi bir çıkar çatışması bulunmamaktadır.

Finansal Destek

Beyan edilecek mali destek yoktur.

Kaynaklar

1. https://www.who.int/teams/integrated-health-services/clinical-services-and-systems/primary-care (erişim:15.05.2024)
2. Bourgueil Y, Marek A, Mousquès J. Three Models of Primary Care Organisation in Europe, Canada, Australia and New-Zealand. Prospere/Irdes, Issues in health economics n° 141- April 2009.
3. Gröne O, Garcia-Barbero M. Trends in Integrated Care-Reflections on Conceptual Issues. World Health Organization, Copenhagen, 2002, EUR/02/5037864.
4. Kodner DL, Spreeuwenberg C. Integrated care: meaning, logic, applications, and implications – a discussion paper. International Journal of Integrated Care 2002; 2.
5. Baker LC, Bundorf MK, Kessler DP. Vertical integration: hospital ownership of physician practices is associated with higher prices and spending. Health Aff (Millwood) 2014; 33: 756-63.
6. Khullar D, Casalino LM, Bond AM. Vertical Integration and the Transformation of American Medicine. N Engl J Med 2024; 390:965-967. DOI:10.1056/NEJMp2313406. https://www.nejm.org/doi/full/10.1056/NEJMp2313406
7. Donaldson L. The normal science of structural contingency theory. Içinde: Clegg SR, Hardy C, Nord WR, eds. Handbook of Organization Studies. Thousand Oaks, CA: SAGE Publications, 1996:57–76.
8. Contandriopoulos D, Perroux M, Duhoux A. Formalisation and subordination: a contingency theory approach to optimising primary care teams. BMJ Open 2018;8: e025007. doi:10.1136/bmjopen-2018-025007.
9. Contandriopoulos D, Perroux M, Cockenpot A, et al. Analytical typology of multiprofessional primary care models. BMC Fam Pract 2018; 19:44.
10. https://www.nursingmidwiferyboard.gov.au/Codes-Guidelines-Statements/Professional-standards.aspx(erişim:15.05.2024)
11. https://web.archive.org/web/20200925090805/https://www.nurses.ab.ca/docs/default-source/document-library/standards/scope-of-practice-for-nurse practitioners.pdf?sfvrsn=ab5ce4b9_14 (erişim:15.04.2024)
12. https://www.independent.ie/regionals/sligo/news/changing-role-of-nursing-profession/39549757.html(erişim:15.05.2024)
13. Shrivastava SR, Shrivastava P. Integrating AYUSH in healthcare delivery system of India. Cukurova Medical Journal, 2019;44(4):1527-8, doi:10.17826/cumj.536761.
14. Wan G, Wei X, Yin, H. et al. The trend in primary health care preference in China: a cohort study of 12,508 residents from 2012 to 2018. BMC Health Serv Res. 2021; 21:768. https://doi.org/10.1186/s12913-021-06790-w
15. Jiang MZ, Fu Q, Xiong JY, Li XL, Jia EP, Peng YY, et al. Preferences heterogeneity of health care utilization of community residents in China: a stated preference discrete choice experiment. BMC Health Serv Res. 2020;20(1):430. https://doi.org/10.1186/s12913-020-05134-4.
16. Kato D, Ryu H, Matsumoto T, Abe K, Kaneko M, Ko M, Irving G, Ramsay R, Kondo M. Building primary care in Japan: Literature review. J Gen Fam Med. 2019;20(5):170-179. doi: 10.1002/jgf2.252.
17. Katori T. Japan's healthcare delivery system: From its historical evolution to the challenges of a super-aged society. Glob Health Med. 2024 Feb 29;6(1):6-12. doi: 10.35772/ghm.2023.01121.
18. OECD (2023), Health at a Glance 2023: OECD Indicators, OECD Publishing, Paris, https://doi.org/10.1787/7a7afb35-en.

DOI:10.34084/bshr.1490570. e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Klinik Örneklerden İzole Edilen *Staphylococcus aureus* Suşlarının Antibiyotiklere Direnç Oranlarının Araştırılması

Investigation of Antibiotic Resistance Rates of *Staphylococcus aureus* Strains Isolated from Clinical Samples

Zehra Varış Karakaş, Mustafa Behçet

Bolu Abant İzzet Baysal üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Bolu, Türkiye

ORCID ID: Zehra Varış Karakaş: https://orcid.org/0000-0002-9723-3112, Mustafa Behçet: https://orcid.org/0000-0002-5976-6983

***Sorumlu Yazar / Corresponding Author:** Mustafa Behçet, **e-posta / e-mail:** drmustafabehcet@gmail.com

Geliş Tarihi / Received : 28-05-2023 **Kabul Tarihi / Accepted:** 06-06-2023 **Yayın Tarihi / Online Published:** 31-08-2024

Varış-Karakaş Z., Behçet M. Investigation of Antibiotic Resistance Rates of Staphylococcus aureus Strains Isolated from Clinical Samples. J Biotechnol and Strategic Health Res. 2024;8(1):83-90

Özet

Amaç Hastane ve toplum kökenli enfeksiyonların en önemli etkenleri arasında yer alan Staphylococcus aureus (S. aureus) deri-yumuşak doku enfeksiyonları başta olmak üzere osteomyelit, septik artrit, endokardit, pnömoni ve bakteriyemiye neden olabilen ve antibiyotiğe direnç bakımından en inatçı patojenlerden biridir. Bu çalışmada klinik örneklerden S. aureus izolatlarının antibiyotik direnç profil lerinin belirlenerek ampirik tedavi ve antibiyotik kullanım politikalarına katkı sağlanması amaçlanmıştır.

Gereç ve Yöntem S. aureus izolatlarının bakteri tanımlanmasında konvansiyonel yöntemler ve otomatize yöntemler antibiyotik duyarlılık testi için ise yalnızca otomatize yöntemler kullanılmıştır. Antibiyotik duyarlılık testleri EUCAST kriterlerine göre değerlendirilmiştir.

Bulgular Toplam 513 S. aureus izolatının %34,1'i yara, %29,2'si kan, %15'i balgam ve %21,7'si diğer örneklerden elde edilmiş ve izolatların %25,5'i Metisiline dirençli Staphylococcus aureus (MRSA) olarak saptanmıştır. Metisilin direnci 2020 yılında 2018 yılına göre artmış, 2021 yılında ise 2020 yılına göre azalmıştır. MRSA izolatlarında 2020, 2021 yıllarında ko-trimoksazol ve 2021 yılında levofloksasin direncinin diğer yıllara göre azaldığı görülmüştür. MSSA ve MRSA'da linezolid, vankomisin, teikoplanin, tigesiklin, daptomisine ve ek olarak MSSA'larda gentamisin'e karşı direnç gelişmediği saptanmıştır.

Sonuç Günümüzde en önemli halk sağlığı sorunlarından biri olan antibiyotik direncini kontrol altına almak için her hastanenin ampirik tedavide her hastanenin antibi-yotik direnç profillerini belli aralıklarla takip etmesi, uygunsuz antibiyotik kullanımının engellenmesi ve enfeksiyon kontrol önlemlerine uyulması bu bakterilerin direnç oranlarının azalmasına katkı sağlayacaktır.

Anahtar Kelimeler : Antibiyotik direnci, Staphylococcus aureus, MSSA, MRSA.

Abstract

Aim *Staphylococcus aureus (S. aureus) is among the most important causes of hospital-acquired and community-acquired infections, can cause osteomyelitis, septic arthritis, endocarditis, pneumonia and bacteremia, skin-soft tissue infections, and especially it is one of the most persistent pathogens in terms of antibiotic resistance. This study aimed to contribute to empirical treatment and antibiotic use policies by determining the antibiotic resistance profiles of S. aureus isolates from clinical samples.*

Materials and Methods *Conventional and automated methods were used for bacterial identification of S. aureus isolates and only automated methods were used for antibiotic susceptibility testing. Antibiotic susceptibility tests were evaluated according to EUCAST criteria.*

Results *Of the total 513 S. aureus isolates, 34,1% were obtained from wounds, 29,2% from blood, 15% from sputum and 21,7% from other samples, and 25,5% of the isolates were found to be Methicillin-resistant Staphylococcus aureus (MRSA). Methicillin resistance increased in 2020 compared to 2018 and decreased in 2021 compared to 2020. In MRSA isolates, co-trimoxazole resistance in 2020, 2021 and levofloxacin resistance in 2021 decreased compared to other years. Resistance to linezolid, vancomycin, teicoplanin, tigecycline, tigecycline, daptomycin in MSSA and MRSA and gentamicin in MSSA was not developed.*

Conclusion *In order to control antibiotic resistance, which is one of the most important public health problems today, monitoring the antibiotic resistance profiles of each hospital in empirical treatment at certain intervals, preventing inappropriate antibiotic use and complying with infection control measures will contribute to the decrease in the resistance rates of these bacteria.*

Keywors *Antibiotic resistance, Staphylococcus aureus, MSSA, MRSA.*

GİRİŞ

Hastane ve toplum kökenli enfeksiyonların en önemli etkenleri arasında yer alan *Staphylococcus aureus (S. aureus)* deri-yumuşak doku enfeksiyonları başta olmak üzere osteomyelit, septik artrit, endokardit, pnömoni ve bakteriyemiye neden olabilmektedir. Metisilin dirençli *S. aureus*'un (MRSA) enfeksiyonları hastaların hastanede yatış süresinin uzamasına yol açmakla birlikte yüksek morbidite ve mortaliteye neden olmaktadır.[1]

S. aureus, spektrumunda bulunan hemen tüm antimikrobiyal ajanlara karşı direnç geliştirmiştir. Penisilinin sık kullanımının ardından kısa sürede penisilin direnci; metisilin kullanımından bir yıl sonra da metisiline karşı direnç saptanmıştır. MRSA izolatlarının çoklu ilaç direncinden dolayı tedavide yol açtıkları sorunlar giderek artmaktadır.[2] MRSA suşları yeni sefalosporinlerden seft o biprol ve seft ar olin dışında diğer beta-laktam grubu antibiyotiklere dirençli olmanın yanısıra; makrolidler, linkozamidler, kinolonlar ve aminoglikozidlere de direnç gösterebilmektedir. Bu direnç gelişiminden dolayı MRSA enfeksiyonlarının tedavisinde vankomisin, teikoplanin, linezolid, daptomisin gibi antimikrobiyaller kullanılmaktadır.[3]

Antibiyotik direnç oranları coğrafi k bölgelere ve hastaneden hastaneye değişiklik gösterebilmektedir. Günümüzde en önemli sağlık sorunlarından biri olan antibiyotik direncini kontrol altına alabilmek için ampirik tedavide her hastanenin antibiyotik direnç profi llerini belli aralıklarla takip etmesi oldukça önemlidir.

Çalışmamızda çeşitli klinik örneklerden izole edilen *S. aureus* izolatlarının bazı antibiyotiklere karşı duyarlılıkları saptanarak ampirik tedavide klinisyenlere yardımcı olunması ve akılcı antibiyotik kullanım politikalarına katkıda bulunulması amaçlanmıştır.

GEREÇ ve YÖNTEM

Çalışmamızda Haziran 2018-Haziran 2021 tarihleri arasında Tbbi Mikrobiyoloji Laboratuvarına farklı kliniklerden gönderilen ve çeşitli klinik örneklerden izole edilen *S. aureus* suşlarının antibiyotik direnç profilleri retrospektif olarak incelenmiştir.

Kan ve steril sıvı örnekleri kan kültürü şişelerine alınarak laboratuvara gönderilmiş ve BacT/ALERT 3D (bioMérieux, Fransa) otomatik kan kültürü sisteminde inkübe edilmiştir. Bakteriyel üreme sinyali veren kan kültürü şişeleri ve laboratuvara gönderilen diğer tüm klinik örnekler %5 koyun kanlı ve eozin metilen mavisi (EMB) agara (RTA, Türkiye) ekilerek 35,5 °C'de 24-48 saat süreyle inkübe edilmiştir. Bakteri tanımlamada konvansiyonel yöntemlerin yanı sıra VITEK® 2 Compact sisteminde (bioMérieux, Fransa) GP tanımlama kartları, antibiyotik duyarlılıkları için ise AST 641 kartları kullanılmıştır. Antibiyotik duyarlılıkları Avrupa Antimikrobiyal Duyarlılık Testi Komitesi Standartlarına (EUCAST) göre değerlendirilmiştir.[4] İstatistiksel analizler için ortalama değerler, yüzde oranları ve oranların homojenliği testi kullanılmıştır. İstatistiki anlamlılık değeri olarak $p<0,05$ olarak kabul edilmiştir.

BULGULAR

Çalışmada 0-95 yaş aralığındaki toplam 513 hastanın yaş ortalaması 55,4 olarak saptanmıştır. İzolatların %74,5'i MSSA, %25,5'i MRSA olarak saptanmıştır. 131 MRSA izolatının %39,7'si kadın, %60,3'ü erkek; 382 MSSA izolatının %40,3'ü kadın, %59,7'si erkek hastalardan izole edilmiştir.

Çalışmamızda *S. aureus* izolatlarının %34,1'i yara, %29,2'si kan, %15'i balgam, %9,4'ü idrar, %5,3'ü abse ve %7'si diğer örneklerden izole edilmiştir (Tablo 1).

Tablo 1. MSSA ve MRSA izolatlarının örnek türlerine göre dağılımı

Örnek türü	MSSA n (%)	MRSA n (%)	Toplam n (%)
	n (%)	n (%)	n (%)
Yara	135 (35,3)	40 (30,5)	175 (34,1)
Kan	111 (29,1)	39 (29,8)	150 (29,2)
Balgam	55 (14,4)	22 (16,8)	77 (15,0)
İdrar	29 (7,6)	19 (14,5)	48 (9,4)
Abse	22 (5,8)	5 (3,8)	27 (5,3)
Konjuktiva sürüntüsü	6 (1,6)	3 (2,3)	9 (1,8)
Katater	8 (2,1)	0 (0)	8 (1,6)
Plevra sıvısı	3 (0,8)	1 (0,8)	4 (0,8)
Boğaz	2 (0,5)	1 (0,8)	3 (0,6)
Eklem sıvısı	11 (2,9)	1 (0,8)	12 (2,3)
Toplam	**382 (74,5)**	**131 (25,5)**	**513 (100)**

MRSA izolatlarının %38,2'si yatan hastalardan, %35,1'i ayaktan hastalardan ve %26,7'si yoğun bakımlardan izole edilmiştir.

Metisilin direnci 2020 yılında 2018 yılına göre artmış, 2021 yılında ise 2020 yılına göre azalmıştır (Tablo 2).

Tablo 2. Yıllara göre metisilin direnci

	2018 n (%)	2019 n (%)	2020 n (%)	2021 n (%)	Toplam n (%)	P
Metisilin direnci	23/121 (19)	41/152 (27)	54/161 (33,5)	13/79 (16,5)	**131/513 (25,5)**	**p<0,05**

MSSA ve MRSA'da linezolid, vankomisin, teikoplanin, tigesiklin, daptomisine ve ek olarak MSSA'larda gentamisin'e karşı direnç saptanmamıştır. MSSA'larda penisiline %79,9 ve eritromisine %13,0, MRSA'larda eritromisine %44,4 ve tetrasikline %39,2 direnç oranı saptanmıştır (Tablo 3,4).

Tablo 3. MSSA izolatlarında antibiyotik direnç oranları

Antibiyotikler	2018 n (%)	2019 n (%)	2020 n (%)	2021 n (%)	Toplam n (%)	P
Linezolid	0/97 (0)	0/111 (0)	0/107 (0)	0/66 (0)	0/381 (0)	N/A
Vankomisin	0/93 (0)	0/109 (0)	0/105 (0)	0/65 (0)	0/372 (0)	N/A
Tigesiklin	0/61 (0)	0/111 (0)	0/106 (0)	0/66 (0)	0/344 (0)	N/A
Teikoplanin	0/58 (0)	0/110 (0)	0/106 (0)	0/66 (0)	0/340 (0)	N/A
Gentamisin	0/97 (0)	0/111 (0)	0/106 (0)	0/66 (0)	0/380 (0)	N/A
Daptomisin	0/97 (0)	0/106 (0)	0/105 (0)	0/66 (0)	0/374 (0)	N/A
Ko-trimoksazol	4/98 (4,1)	3/111 (2,7)	3/106 (2,8)	2/66 (3,0)	12/381 (3,1)	p>0,05
Levofloksasin	1/94 (1,1)	4/91 (4,4)	6/105 (5,7)	4/64 (6,3)	15/354 (4,2)	p>0,05
Klindamisin	6/92 (6,5)	5/97 (5,2)	7/100 (7)	1/60 (1,7)	19/349 (5,4)	p>0,05
Tetrasiklin	7/95 (7,4)	9/110 (8,2)	16/107 (15)	6/66 (9,1)	38/378 (10,1)	p>0,05
Siprofloksasin	1/93 (1,1)	10/110 (9,1)	7/107 (6,5)	4/66 (6,1)	22/376 (5,9)	p>0,05
Eritromisin	9/91 (9,9)	16/110 (14,5)	14/103 (14)	9/66 (13,6)	48/370 (13,0)	p>0,05
Penisilin	50/62 (80,6)	87/111 (78,4)	82/105 (78,1)	56/66 (84,8)	275/344 (79,9)	p>0,05

N/A: Direnç gelişimi gözlenmediğinden istatistiksel değerlendirmeye alınmadı

Tablo 4. MRSA izolatlarında antibiyotik direnç oranları

Antibiyotikler	2018 n (%)	2019 n (%)	2020 n (%)	2021 n (%)	Toplam n (%)	P
Linezolid	0/23 (0)	0/40 (0)	0/54 (0)	0/13 (0)	0/130 (0)	N/A
Vankomisin	0/23 (0)	0/41 (0)	0/54 (0)	0/11 (0)	0/129 (0)	N/A
Tigesiklin	0/15 (0)	0/41 (0)	0/54 (0)	0/13 (0)	0/123 (0)	N/A
Teikoplanin	0/14 (0)	0/37 (0)	0/50 (0)	0/12 (0)	0/113 (0)	N/A
Daptomisin	0/23 (0)	0/38 (0)	0/54 (0)	0/13 (0)	0/128 (0)	N/A
Gentamisin	3/20 (15)	3/41 (7,3)	3/54 (5,6)	0/13 (0)	9/128 (7,0)	p>0,05
Ko-trimoksazol	5/20 (25)	10/41 (24,4)	1/51 (2,0)	0/13 (0)	16/125 (12,8)	**P<0,05**
Klindamisin	2/19 (10,5)	5/29 (17,2)	4/32 (12,5)	2/7 (28,6)	13/87 (14,9)	p>0,05
Siproflok-sasin	9/22 (40,9)	7/41 (17)	10/54 (18,5)	1/13 (7,7)	27/131 (20,6)	p>0,05
Levoflok-sasin	9/22 (40,9)	6/37 (16,2)	12/52 (23,1)	0/13 (0)	27/111 (24,3)	**P<0,05**
Tetrasikline	8/20 (40)	17/40 (42,5)	21/53 (39,6)	3/12 (25)	49/125 (39,2)	p>0,05
Eritromisin	4/20 (20)	18/40 (45)	29/54 (53,7)	5/12 (41,7)	56/126 (44,4)	p>0,05

N/A: Direnç gelişimi gözlenmediğinden istatistiksel değerlendirmeye alınmamıştır.

MRSA izolatlarında 2020 ve 2021 yıllarında ko-trimoksazol direnci (p=0,001) ve 2021 yılında ise levofloksasin direnci azalmış olarak saptanmıştır (p=0,028). MRSA ve MSSA izolatlarında çalışmadaki diğer antibiyotiklerdeki direnç oranlarında istatistiksel olarak bir fark saptanmamıştır.

TARTIŞMA

Stafilokok enfeksiyonları ülkemizde ve dünyada gittikçe artan sıklıkta görülmekte değişik organ ve sistemleri tutarak ciddi enfeksiyonlara yol açmaktadır.[5]

S. aureus izole edilen klinik örnekler literatürde farklı oranlarda bildirilmiştir. *S. aureus* suşları ülkemizde yapılan birçok çalışmada (%30,4-56), çalışmamızda (%34,1) olduğu gibi en sık yara yeri örneklerinden izole edilirken ikinci sıklıkta izole edilen kan örnekleri (%29,2)ise bazı çalışmalarda en sık (%51,8-52,9) olarak saptanmıştır.[3,6-8] Stafilokok enfeksiyonları yoğun bakım ünitelerinde yatan hastalarda gittikçe artan sıklıkta karşımıza çıkmaktadır. Bu hastalara invaziv girişimlerin (endotrakeal tüp, santral venöz ve üriner kateterlerin kullanımı gibi) yapılması, uzamış yatış süresi, geniş spektrumlu antibiyotiklerin kullanımı ve genel durum bozukluğu gibi nedenlerle dirençli bakterilerde artış görülmektedir.[9]

Bakteriyel bulaşıcı hastalıkların tedavisinde antibiyotik direnç gelişimi Dünya Sağlık Örgütü tarafından en büyük tehditlerden biri olarak görülmektedir. Dünya genelinde hastane kaynaklı enfeksiyonların yaklaşık yarısını çok ilaca dirençli patojenler oluşturmaktadır. Nozokomial kaynaklı enfeksiyonlara neden olan MRSA izolatları antibiyotiğe direnç bakımından en inatçı etkenlerden biridir.[10]

Metisilin direnciyle ilgili ülkemizde birçok çalışma yapılmıştır. Çalışmamızda saptadığımız %25,5 oranındaki metisilin direnci bu çalışmalarda saptanan metisilin direnç oranları (%17,9-76,5) aralığındadır.[6,11] Son zamanlarda invazif MRSA enfeksiyon sıklığında düşüş gözlenmekte ve bu durum bazı çalışmalarda bildirilmiştir. EARS-Net' in 2022 verilerine göre Avrupa birliği ülkelerinde kan dolaşımı enfeksiyonlarında görülen MRSA sıklığında 2022 yılında 2019 yılına göre tahmini olarak %12,2 oranında bir azalma olduğu rapor edilmiştir.[12]

Ülkemizde yapılan bazı çalışmalarda yoğun bakımlarda izole edilen MRSA oranları %40-72 arasında değişmektedir.[13,14] Çalışmamızda bu çalışmalara kıyasla hastanemiz yoğun bakımlarında izole edilen MRSA oranı nispeten daha düşük oranda (%26,7) bulunmuştur. Ayrıca metisilin direnci 2020 yılında 2018 yılına göre artmış, 2021 yılında ise 2020 yılına göre azaldığı saptanmış olup son yıllarda MRSA oranlarının azaldığını bildiren çalışmaları desteklemektedir.

Stafilokoklar, ilk antibiyotik olan penisiline başlangıçta duyarlıyken beta-laktamaz üretimiyle bu antibiyotiğe

karşı hızla direnç geliştirmiştir. Ülkemizde MSSA'larda penisilin direnç oranlarıyla ilgili yapılan bir çalışmada 2010-2015 yıllarında kliniklerde takip edilen hastaların klinik örneklerinden izole edilen toplam 21478 stafilokok izolatında penisilin direnci çalışmamızla (%79,9) benzer oranda %80,1 bulunmuştur.[15]

Ülkemizde MSSA'larda tetrasiklin direnci ile ilgili yapılan çalışmalarda; çalışmamızla (%5,8) uyumlu olarak Tanrıverdi ve ark.[16] %6, Sen ve ark.[15] %7,3 direnç bildirmişlerdir. Bunun yanında yapılan bazı çalışmalarda oranlar değişkenlik göstermektedir. Duran ve ark.[3] tetrasiklin direnci saptamaz iken yapılan bazı çalışmalarda ise direnç oranları %10,5-26 olarak bildirilmiştir.[6,17,18] MRSA'larda tetrasiklin direnci ile ilgili çalışmalar incelendiğinde çalışmamızda saptadığımız %39,2'lik direnç oranı; Özel ve ark.[6] (%33,3), Duran ve ark.[3] (%33,7) ve Tanrıverdi ve ark.[16] (%38,2)' nın saptadığı direnç oranlarıyla benzer olmakla birlikte yapılan bazı çalışmalarda ise yüksek tetrasiklin direnci (%54,3- 88,2) bildirilmiştir.[15,19]

Ülkemizde MSSA'larda eritromisin direnci ile ilgili yapılan bazı çalışmalarda direnç oranları çalışmamızla (%13) benzer oranlarda (%8-17) saptanmıştır.[14,16,17] MRSA'larda ise eritromisin direnci ile ilgili yapılan çalışmalarda yüksek direnç oranları (%45,1-70) bildirilmiştir.[1,16,17] Kangül ve ark.[20] Diyarbakır'da yaptıkları bir çalışmada eritromisine karşı 2018, 2019, 2020 yıllarında sırasıyla %35, %55, %39 direnç saptamışlardır. Çalışmamızda 2018, 2019, 2020, 2021 yıllarında eritromisin direnci sırasıyla %20, %45, %53,7, ve %41,7 ve ortalama %45,5 oranında bu çalışmalar ile benzer bulunmuştur. Çalışmamızda 2018 yılında diğer yıllara kıyasla daha az görülen eritromisin direncinde (%20) istatistiksel olarak fark bulunamamıştır (p=0,08).

Metisilin direnci nedeniyle MRSA kaynaklı invaziv enfeksiyonların tedavisinde vankomisin de sıklıkla kullanılmakta ve bu kullanım sonucunda da vankomisine orta düzeyde duyarlı ve dirençli *S. aureus* suşlarının ortaya çıktığı bildirilmektedir.[1] Çalışmamızda olduğu gibi *S. aureus*'a karşı ülkemizde yapılan birçok çalışmada da glikopeptit direncine rastlanmamıştır.[1,3,6,7,11,14,16-18] Yine Ulusal Antimikrobiyal Direnç Sürveyans Sistemi (UAMDSS) 2016 ve Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) 2019 verilerinde ülkemizde MRSA izolatlarında vankomisin direnci bildirilmemiştir.[21,22] Bu verilere göre glikopeptitler halen *S. aureus* enfeksiyonlarına karşı etkinliğini korumaktadır.

Linezolid, özellikle MRSA kaynaklı deri-yumuşak doku, toplum ve hastane kökenli pnömoni enfeksiyonlarının tedavisinde vankomisine direncin artmasını engellemek amacıyla kullanılabilecek bir antibiyotiktir.[7] Bu çalışmada olduğu gibi ülkemizde yapılan çok sayıda çalışmada da *S. aureus* izolatlarında linezolid direncine rastlanmamıştır.[1,3,6,7,14,16,17,18] Shariati ve ark.[23] nın 25 farklı ülke verilerini değerlendirdiği bir çalışmada linezolid direncini %0,1 bildirmişlerdir.

Daptomisin, hem üreme fazındaki, hem de durağan fazdaki gram pozitif bakterilere etkili siklik bir lipopeptiddir.[14] Ülkemizde yapılan çalışmalarda MSSA'larda daptomisin direncine rastlanmamıştır.[3,14,17] Ancak MRSA izolatlarında MSSA izolatlarında olduğu gibi bazı çalışmalarda daptomisin direncine rastlanmaz iken[6,24], Arabacı ve ark.[14] %3, Sen ve ark.[15] %0,3, Duran ve ark.[3] %2,3 oranında daptomisin direnci bildirmişlerdir.

Çalışmamızla uyumlu olarak MSSA ve MRSA' larda tigesiklin direnciyle ilgili yapılan bazı çalışmalarda dirence rastlanmazken[6,14] MRSA'larda %2-9 oranında direnç bildirilen çalışmalar da bulunmaktadır.[14,25]

Ülkemizde MSSA'larda gentamisin direnci ile ilgili yapılan çalışmalarda çalışmamızla uyumlu olarak bazı çalışmalarda gentamisin direncine rastlanmazken[1,6]; %10'un üzerinde direnç bildirilen çalışmalar da vardır. Arabacı ve ark.[14] %13, Şanlı ve ark.[26] %21,7 oranında direnç bildirmişlerdir. MRSA'larda gentamisin direnciyle ilgili ülkemizde yapılan çalışmalarda (%9-96) çok farklı oranlar bildirilm-

iştir.[1,3,6,14-17,19,20,26]. Çalışmamızda saptadığımız gentamisin direnci (%7) bu çalışmalardan daha az orandadır. 2004-2019 yıllarında yapılan bir çalışmada MRSA'larda gentamisin için 2004 yılında saptanan %58,3 direnç oranı 2019 yılında %9,6 olarak bildirilmiş ve direncin zaman içerisinde azaldığı bildirilmiştir.[27] Çalışmamızda saptadığımız %7 gentamisin direnci bu çalışmayı desteklemekte ve çalışmamızdaki bu düşük oranın saptanmasında kısıtlı antibiyotik bildiriminin de etkisi olduğunu düşünmekteyiz.
Ülkemizde yapılan bazı çalışmalarda MSSA'larda ko-trimoksazole karşı %2-9,9 arasında değişen farklı direnç oranları saptanmıştır.[14,27] Çalışmamızdaki direnç oranı (%3,1) bu aralıkta yer almaktadır. MRSA'larda ülkemizde yapılan bazı çalışmalarda ko-trimoksazole karşı %6-33,3 arasında değişen farklı direnç oranları saptanmıştır.[6,28] Çalışmamızda 2018, 2019, 2020, ve 2021 yıllarında direnç oranları sırasıyla %25, %24,4, %2 ve %0 ve ortalama %12,8 oranında bulunmuştur. Ko-trimoksazole direnci MRSA'larda 2020 ve 2021 yıllarında, 2018 ve 2019 yıllarına göre azalmış olarak saptanmıştır (p=0,001). Benzer bir çalışmada Doğan ve ark.[29] 2001-2002 yıllarında %41,2, 2011-2012 yıllarında %18,5 direnç saptamışlar ve bu on yıllık dönemde direnç oranının düştüğünü belirtmişlerdir.

Kinolonlar geniş antibakteriyel spektrumları, gastrointestinal sistemden iyi emilimi ve iyi doku dağılımı nedeniyle geniş bir kullanım alanına sahiptir.[14] Bu sınıfta yer alan siprofloksasin için MSSA'larda çalışmamızda saptadığımız %5,9'luk direnç oranı ülkemizde yapılan bazı çalışmalarla benzer oranlarda (%3-11) bildirilmiştir.[1,3,6,14,16,17,28]

MRSA'larda ülkemizde siprofloksasin direnciyle ilgili yapılan çalışmalarda %16,7-92,2 aralığında oldukça farklı oranlarda saptanmıştır.[6,19]

Diğer bir florokinolon sınıfında yer alan levofloksasin direnciyle ilgili yapılan çalışmalarda MSSA'larda %4-9 arasında direnç oranları bildirilmiş ve çalışmamızda saptadığımız %4,2'lik direnç oranıyla uyumlu görünmektedir.[14,15,26] MRSA'larda levofloksasin için ülkemizde yapılan bazı çalışmalarda %50' den daha fazla direnç oranları bildirilmiştir.[14,15,17] Bu çalışmaların aksine Tanrıverdi ve ark.[16] Malatya' da (%26,3) çalışmamızla benzer (%24,3) oranda direnç saptamışlardır. Kangül ve ark.[20] 2018,2019,2020 yıllarında sırasıyla %18, %13, %7 direnç bildirmiş ve levofloksasin direncini 2020 yılında 2018 yılına göre azaldığını belirtmişlerdir. Çalışmamızda da benzer şekilde 2018, 2019, 2020 ve 2021 yıllarında sırasıyla %40,9, 16,2, 23,1 ve 0 oranlarında bulunmuş ve levofloxacin direnci MRSA'larda 2021 yılında, 2018, 2019 ve 2020 yıllarına göre azalmış olarak saptanmıştır (p=0,028). İzolat sayısının 2021 yılında diğer yıllara göre sayısının azlığı da bu düşük oranın görülmesinde etkili olmuş olabileceği de gözönünde bulundurulmalıdır.

Ülkemizde MSSA'larda klindamisin direnci ile ilgili yapılan çalışmalarda direnç oranları %1,4-17 arasında saptanmış olup çalışmamızla (%5,4) uyumlu bulunmuştur.[1,15] Yine ülkemizde MRSA'larda klindamisin direnci ile ilgili yapılan çalışmalarda ise yüksek direnç oranlarına (%34,9-55,4) rastlanmıştır.[3,17] Çalışmamızda ise klindamisin direnci daha düşük oranda (%14,9) saptanmıştır.

SONUÇ

Sonuç olarak klinik örneklerden izole edilen S. aureus izolatlarında MSSA (%74,5) oranı MRSA (%25,5)' lardan daha sık saptanmıştır. Daha kapsamlı çalışmalar gerektirmekle birlikte 2021 yılı sonuçları son yıllarda MRSA oranlarının düşme eğiliminde olduğunu bildiren çalışmaları desteklemektedir.

2018-2021 yıllarında MSSA ve MRSA'da linezolid, vankomisin, teikoplanin, tigesiklin, daptomisine ve ek olarak MSSA'larda gentamisin'e karşı direnç gelişmediği saptanmıştır.

Bu antibiyotiklerin yanısıra MSSA ve MRSA suşlarında; ko-trimoksazol (%3,1-12,8) klindamisin (%5,4-14,9) ve siprofloksasine (%5,9-20,6), MSSA suşlarında; levofloksa-

sin (4,2), tetrasiklin (%10,1) ve eritromisine (%13), MRSA suşlarında ise; gentamisin (%7)' e karşı düşük direnç oranları saptanmıştır.

MRSA suşlarında, ko-trimoksazol direnci 2020-2021 yıllarında azalmış olarak saptanmıştır. 2018-2021 yıllarında MRSA suşlarında levofloksasin direnci 2021 yılında azalmış olarak saptanmıştır.

Çalışmamızın kısıtlılığı tek merkezli bir çalışma olması ve verilerin sadece bir üniversite hastanesinin yaklaşımını yansıtmasıdır. Antibiyotik direnç oranları ülkelere, coğrafik bölgelere ve hastaneden hastaneye değişiklik gösterebilmesi nedeniyle, günümüzde en önemli sağlık sorunlarından biri antibiyotik direncini kontrol altına alabilmek için ampirik tedavide her hastanenin antibiyotik direnç profillerini belli aralıklarla takip etmesi, uygunsuz antibiyotik kullanımının engellenmesi ve enfeksiyon kontrol önlemlerine uyulması bu bakterilerin direnç oranlarının azalmasına katkı sağlayacaktır.

Teşekkür

İstatistiksel analiz için katkılarından dolayı Prof. Dr. Seyit Ali Kayış ve tez aşamasında katkı sunan Tıbbi Mikrobiyoloji Laboratuvarı çalışanlarına teşekkür ederiz.

Etik Onay

Bu çalışma için Bolu Abant İzzet Baysal Üniversitesi Klinik Araştırmalar Etik Kurulunda onay alınmıştır (2021/210). Bu çalışma yüksek lisans tezinden üretilmiştir.

Yazar Katkıları

Konsept: Z.VK., M.B. Dizayn: Z.VK., M.B. Veri Toplama ve İşleme: Z.VK. Analiz ve Yorumlama: Z.VK., M.B. Literatür Tarama: Z.VK. Makale Yazımı: Z.VK., M.B.

Çıkar Çatışması

Bu makale ile ilgili herhangi bir çıkar çatışması bulunmamaktadır.

Finansal Destek

Beyan edilecek mali destek yoktur.

References

1. Aksaray S, Arıcı N. Klinik örneklerden izole edilen Staphylococcus aureus suşlarının metisilin direncinin belirlenmesi ve antibiyotik duyarlılıklarının araştırılması. ANKEM Derg. 2019;33(2):70-76. doi:10.5222/ankem.2019.1922.
2. Sevgican E, Sınırtaş M, Özakın C, ve ark. Staphylococcus türlerinde metisilin direncinin farklı yöntemlerle saptanması. İnfeksiyon Dergisi. 2009;23(2):63-68.
3. Duran H, Çeken N, Atik TK. Çeşitli klinik örneklerden izole edilen Staphylococcus aureus suşlarının antibiyotik direnç oranları. Turk Mikrobiyol Cem Derg. 2021;51(3):233-238. doi:10.5222/TMCD.2021.72687.
4. The European Committee on Antimicrobial Susceptibility Testing: Breakpoint tables for interpretation of MICs and zone diameters Version 11.0, valid from 2021-01-01. https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_11.0_Breakpoint_Tables.pdf. Erişim tarihi: 25 Eylül 2022.
5. Şanlı K, Kömürcü SZM, Kansak N, ve ark. Staphylococcus aureus' un onbeş yılda metisilin direnç ve antibiyogram direnç profilinin ve görülme sıklığının değişimi. Turk Mikrobiyol Cem Derg. 2021;51(1):15-22. doi:10.5222/TMCD.2021.04706.
6. Özel Y, Büyükzengin KB, Yavuz MT. Klinik örneklerden izole edilen metisiline dirençli ve duyarlı Staphylococcus aureus suşlarının antibiyotik direnç profilinin araştırılması. ANKEM Derg. 2017;31(2):41-47. doi:10.5222/ankem.2017.041.
7. Coşkun M, Uslu H, Uyanik M, ve ark. Metisilin dirençli Staphylococcus aureus suşlarinda in vitro seftarolin etkinliğinin araştirilmasi. Ankem Derg. 2017;31(1):14-22. doi:10.5222/ankem.2017.014.
8. Telli M, Okulu Y, Pat Y. Staphylococcus aureus suşlarında metisiline direnç oranındaki değişim: Metisiline direnç azalıyor mu? Ankem Derg. 2018;32(3):103-108. doi: 10.5222/ankem.2018.1816.
9. Çikman A, Gündem NS, Karakeçili F, ve ark. Yoğun bakim Ünitesinde yatan hastalarin çeşitli klinik örneklerinden izole edilen mikroorganizmalar ve antibiyotik duyarliliklari. ANKEM Derg. 2012;26(3):131-6. doi:10.5222/ankem.2012.131.
10. Orhan Z. Metisiline dirençli Staphylococcus aureus tedavisinde kullanılan antibiyotiklerin genotipik direnç mekanizmaları. aktd. Eylül 2021;30(3):177-184. doi:10.17827/aktd.889472.
11. Namıduru M, Karaoğlan İ. Cerrahi yoğun bakım ünitesinde hastane infeksiyonu etkeni olan Staphylococcus aureus suşlarının antibiyotik dirençleri. Van Tıp Derg. 2003;10(3):72-75.
12. European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA (EARS-Net) - Annual Epidemiological Report 2022. Stockholm: ECDC; 2023.
13. Dinç F, Dinç FT, Akca B, ve ark. Kandan izole edilen metisiline dirençli Staphylococcus aureus (MRSA) suşlarının CLSI ve EUCAST kriterlerine göre vankomisin, tigesiklin, linezolid ve daptomisin in vitro duyarlılık sonuçları. Türk Mikrobiyol Cem Derg. 2011;41(3):120-126. doi:10.5222/TMCD.2011.120.
14. Arabacı Ç, Uzun B. Staphylococcus aureus izolatlarının çeşitli antibiyotiklere duyarlılıklarının değerlendirilmesi. Klimik Derg. 2021;34(1):69-71. doi:10.36519/kd.2021.12.
15. Sen P, Demirdal T, Özdemir R, et al. Antimicrobial resistance in staphylococci: A 6-year-evaluation. Medeniyet Med J. 2017; 32(4):205-211. doi: 10.5222/MMJ.2017.205.
16. Tanrıverdi ES, Duman Y, Tekerekoğlu MS. Bir üniversite hastanesi'nde 2018-2019 yıllarında izole edilen Staphylococcus aureus izolatlarının incelenmesi. Fırat Tıp Dergisi. 2020;25(4):184-188.
17. Kula-Atik T, Uzun B. Kan kültürlerinden izole edilen Staphylococcus aureus suşlarının metisiline ve diğer antimikrobiyal ajanlara direnç durumlarının değerlendirilmesi. Klimik Derg. 2020;33(2):132-136. doi: 10.5152/kd.2020.28.
18. Yüksekkaya Ş, Opuş A, Güvenç Hİ, ve ark. 2009-2013 Yillari arasinda Konya Eğitim ve Araştirma Hastanesi'nde kan kültüründen izole edilen Staphylococcus aureus suşlarinin antimikrobiyal ajanlara duyarliliklarinin değerlendirilmesi. Ankem Derg. 2017;31(1):1-6. doi:10.5222/ankem.2017.001.
19. Yıldız Ö, Çoban AY, Şener AG, et al. Antimicrobial susceptibility and resistance mechanisms of methicillin resistant Staphylococcus aureus isolated from 12 hospitals in Turkey. Ann Clin Microbiol Antimicrob. 2014(16);13:44. doi:10.1186/s12941-014-0044-2.
20. Kangül H, Atmaca S, Uzuner N, ve ark. Dicle Üniversitesi Tıp Fakültesi Hastanesi'nde yatan hastalardan 2018, 2019 ve 2020 yıllarında izole edilen metisiline dirençli Staphylococcus aureus suşlarının çeşitli antibiyotiklere karşı direnç oranları. ANKEM Derg. 2021;35(2):38-44 doi: 10.5222/ankem.2021.038.
21. Central Asian and European Surveillance of Antimicrobial Resistance Annual Report 2019 https://hsgm.saglik.gov.tr/depo/birimler/mikrobiyoloji-referans-laboratuvarlari-ve-biyolojik-urunler-db/Dokumanlar/Raporlar/CAESAR_Annual_Report_2019.pdf. Erişim tarihi:1 Ocak 2024.
22. Ulusal antimikrobiyal direnç sürveyans sistemi 2016 yıllık raporu. Ankara: T.C. Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu. https://hsgm.saglik.gov.tr/depo/birimler/mikrobiyoloji-referans-laboratuvarlari-ve-biyolojik-urunler-db/Dokumanlar/Raporlar/UAM-DSS_2016_Rapor.pdf. Erişim tarihi: 1 Ocak 2024.
23. Shariati A, Dadashi M, Chegini Z, et al. The global prevalence of daptomycin, tigecycline, quinupristin/dalfopristin, and linezolid resistant Staphylococcus aureus and coagulase–negative staphylococci strains: a systematic review and meta-analysis. Antimicrob Resist Infect Control. 2020 Apr 22;9(1):56. doi:10.1186/s13756-020-00714-9.
24. Hanci H, Uyanik MH, Bilici D, ve ark. Klinik örneklerden izole edilen metisiline dirençli stafilokok suşlarinda daptomisin etkinliğinin araştirilmasi. ANKEM Derg. 2013;27(2):64-69. doi:10.5222/ankem.2013.064.
25. Oksuz L, Gurler N. Susceptibility of clinical methicillin-resistant staphylococci isolates to new antibiotics. J Infect Dev Ctries. 2013;7(11):825-831. doi:10.3855/jidc.3867.
26. Şanlı K. Hastane kökenli ve toplum kaynaklı ID Staphylococcus aureus suşlarının çeşitli antimikrobiyallere duyarlılıkları. İstanbul Kanuni Sultan Süleyman Tıp Dergisi. 2020;12(2):188-193.
27. Haznedaroğlu T, Öncül O, Hoşbul T, ve ark. Yatan hastalardan soyutlanan Staphylococcus aureus suşlarında metisilin direnci: Üç yıllık trend. TAF Prev Med Bull. 2010; 9(6):585-590.
28. Yaman G, Çıkman A, Berktaş M, et al. The MLSB, fusidic acid and various antibiotic resistance rates of nosocomial Staphylococcus aureus isolates. ANKEM Derg. 2010;24(3):130-135.
29. Doğan M, Feyzioğlu B, Baykan M. On yıllık dönemde S. aureus suşlarının antibiyotik direnç durumundaki değişim. Abant Med J. 2014;3(3):237-241. doi:10.5505/abantmedj.2014.74946.

DOI:10.34084/bshr.1495495 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Investigation of Various Finishing/Polishing Procedures on Color Stability of Composite Resins

Farklı Bitim/Polisaj Sistemlerinin Rezin Kompozitlerin Renklenmesi Üzerine Etkisinin Değerlendirilmesi

Sevim Atılan Yavuz, Duygu Ergel, Ayşe Tuğba Ertürk Avunduk, Esra Cengiz Yanardağ

Mersin University, Faculty of Dentistry, Department of Restorative Dentistry, Mersin, Türkiye

ORCID ID: Sevim Atılan Yavuz: https://orcid.org/0000-0002-6192-4931, Duygu Ergel: https://orcid.org/0000-0001-7861-0499 Ayşe Tuğba Ertürk Avunduk: https://orcid.org/0000-0002-7879-8150, Esra Cengiz Yanardağ: https://orcid.org/0000-0002-2651-2755

***Sorumlu Yazar / Corresponding Author:** Sevim Atılan Yavuz, **e-posta / e-mail:** dtsevimatilan@gmail.com

Geliş Tarihi / Received : 04-06-2024 **Kabul Tarihi / Accepted:** 13-06-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Atılan-Yavuz S., Ergel D., Ertürk-Avunduk A.T., Cengiz-Yanardağ E. Investigation of Various Finishing/Polishing Procedures on Color Stability of Composite Resins. J Biotechnol and Strategic Health Res. 2024;8(1):91-99

Abstract

Aim The objective of this study was to assess the impact of various finishing and polishing systems on the color stability of composite resins treated with coffee.

Material and Method Fifty samples of each of nanohybrid and supra-nanohybrid composite resin materials were prepared and each material was randomly divided into 5 groups (n=10): Group 1: Control group (mylar strip), Group 2: One Gloss (one step), Group 3: One Gloss + polishing paste, Group 4: Soflex disk (multistep), Group 5: Soflex disk + polishing paste. The samples were colored in coffee solution for 144 hours to simulate six months of coffee consumption after polishing. The color of the samples before-after staining was measured with a spectrophotometer and ΔE00 values were calculated.

Results Material, polishing type and the interaction of these two parameters had a statistical effect on the color change values ($p< 0.001$). The ΔE00 values of supra-nanohybrid composite resin were higher than nanohybrid. Both materials exhibited color change above the thresholds of clinical perceptibility (PT> 0.8) and acceptability (AT> 1.8). In terms of polishing types, the highest ΔE00 was found in the control group and the lowest in the disk group. Th e additionally applied polishing paste caused a non-signifi cant decrease in the color change of the one-step polishing system ($p< 0.05$) and a statistically signifi cant increase in the multi-step polishing system ($p> 0.05$).

Conclusion Considering the limitations of the study, it can be concluded that the use of multi-step discs is more advantageous in preventing discoloration of composite resins.

Keywords Color stability, composite resin, finishing and polishing

Özet

Amaç *Çalışmanın amacı; farklı bitim/polisaj sistemlerinin kahve ile renklendirilen kompozit rezinlerin renk stabilitesi üzerine etkilerinin değerlendirilmesidir.*

Gereç ve Yöntem *Nanohibrit ve supra-nanohibrit kompozit rezin materyallerinin her birinden 50 adet numune hazırlandı ve her materyal rastgele beş gruba (n=10) ayrıldı: Grup 1: Kontrol grubu (mylar strip), Grup 2: One Gloss (tek aşama), Grup 3: One Gloss + Polisaj patı, Grup 4: Soflex disk (çok aşama), Grup 5: Soflex disk + Polisaj patı. Numuneler, cila sonrası altı aylık kahve tüketimini taklit etmek amacıyla 144 saat boyunca kahve çözeltisinde renklendirildi. Spektrofotometre cihazı ile renklendirme öncesi/ sonrası numunelerin rengi ölçülüp ΔE00 değerleri hesaplandı.*

Bulgular *Malzeme, cila tipi ve bu iki parametrenin etkileşimi renk değişim değerlerine istatistiksel olarak etkili olduğu görüldü ($p<0,001$). Supra-nanohibrit kompozit rezinin ΔE00 değerleri, nanohibrit kompozit rezinden yüksekti. Her iki materyal de klinik olarak algılanabilirlik (PT> 0,8) ve kabul edilebilirlik (AT>1,8) eşik değerlerinin üzerinde renk değişimi sergiledi. Polisaj türleri bakımından, en yüksek ΔE00 kontrol grubunda, en düşük değer ise yalnızca disk uygulanan grupta bulundu. İlave olarak uygulanan polisaj patı, tek aşamalı polisaj sistemin renk değişiminde anlamlı olmayan bir azalışa ($p< 0,05$), çok aşamalı polisaj sisteminde ise istatistiksel olarak anlamlı bir artışa neden oldu ($p> 0,05$).*

Sonuç *Çalışmanın limitasyonları göz önünde bulundurulduğunda, çok aşamalı disk kullanımının kompozit rezinlerde oluşan renklenmeyi önlemede daha avantajlı olduğu değerlendirilebilir.*

Anahtar Kelimeler *Renk stabilitesi, kompozit rezin, bitim ve cila*

INTRODUCTION

In contemporary dental practice, composite resins have gained widespread acceptance for the restoration of both anterior and posterior dental structures, owing to their enhanced physical characteristics and esthetic qualities. Unfinished and unpolished restoration surfaces cause plaque retention, caries, surface discoloration and inflammation in the surrounding soft tissues.[1] In addition, the finishing and polishing step is also important for the removal of the oxygen-inhibition layer formed as a result of the reaction of free radicals with oxygen in the air during polymerization in the top layer of the composite resin.[2]

Finishing is performed to create the ideal anatomical form of the tooth, to prevent fracture of the restoration and to provide the patient with the correct chewing function; polishing is performed to make the restoration look smoother, brighter and more esthetic.[1] This can be done in a one-step or multi-step.[3] In addition to finishing and polishing, polishing paste can also be applied to composite resins.[4] The abrasive particles of the polishing system used should be harder than the filler particles of the composite resin to be contacted. Otherwise, the polishing material will not be able to remove the filler particles, which are an area suitable for coloration on the surface, but only the soft resin matrix.[5]

The structure and organic monomer content of the composite resins have a direct impact on the smoothness and staining susceptibility of the surface.[6] The organic phase of composite resins; low viscosity triethylene glycol dimethacrylate (TEGDMA) co-monomer, high viscosity bisphenol glycidyl methacrylate (Bis-GMA) monomer and urethane dimethacrylate (UDMA) monomer with high adhesion color stability, ethoxy bisphenol A-dimethacrylate (BisEMA), decanediol dimethacrylate (DDDMA), urethane tetramethacrylate (UTMA) and bisphenol methacryloxy polyethonoxy phenylpropane (Bis-MEPP).[7]

The resin matrix and filler particles have different sizes and hardnesses, resulting in different polishability properties.[8] Nanofill composite resins consist of nanomers and nanoclusters obtained by nanotechnological methods in the range of 0,1-100 nanometers (nm), while supra-nano composite resins have 200 nm spherical particles with a wavelength lower than the wavelength of visible light.[9,10] Nano composites have many advantages such as low polymerization shrinkage, high mechanical properties, improved optical properties, high wear resistance and polishability.[11] The maintenance of color stability in dental restorative materials constitutes a significant determinant influencing the overall success of dental restorations. The color change in the structure of composite resins is intrinsic coloration, while the coloration caused by contamination due to external factors is extrinsic coloration. Color changes are observed in composite resins in relation to water absorption, degree of polymerization conversion, surface roughness of the restoration and diet.[12] Many studies have investigated the changes in composite resin materials caused by dark colored beverages such as tea, red wine and coffee.[13-15]

Within the existing literature, numerous investigations have delved into scrutinizing the influence of diverse polishing systems on the color stability of composite resins.[1,16,17] However, there are very few studies on the effectiveness of polishing pastes used in addition to different polishing systems.[18,19] The present study is the first in the literature to examine the effectiveness of a polishing paste used in addition to both one-step and multi-step polishing systems. The objective is to assess the impact of distinct finishing/polishing systems on the color stability of nano and supra-nanohybrid composite resins, specifically those subjected to coffee-induced discoloration. The null hypotheses in this study were; (1) composite resins with different fillers do not affect color change and (2) polishing paste used in addition to polishing systems do not affect color change.

MATERIALS and METHODS

In the present study, the composite resins containing filler

particles in two different sizes, nanohybrid (G-ænial Posterior, GC, Tokyo, Japan) and supra-nanohybrid (Palfique Estelite, Tokuyama Dental, Tokyo, Japan), were used. The properties of the composite resins and the finishing-polishing systems used in the study are shown in Table 1 and Table 2, respectively. Approval for this study was obtained from the Mersin University Clinical Research Ethics Committee, under the ethics committee permission number 2023/838.

Table 1. Properties of composite resins used in the study				
Composite resins	Manufacturers	Type	Organic matrix content	Inorganic filler
G-ænial Posterior	GC, Dental Products, Tokyo, Japan	Nanohybrid	UDMA and dimethacrylate co-monomer	Pre-polymerized fillers (16–17 μm). Silica, strontium and lanthanide fluoride. Silica and fluoroaluminosilicate >100 nm, micro silica <100 nm
Estelite® Sigma Quick	Tokuyama Dental, Tokyo, Japan	Supra-nanohybrid	Bis-GMA and TEGDMA	Supra-nano monodispersing spherical filler: SiO_2-ZrO_2. Average particle size is 0,2 μm and particle size is between 0,1 and 0,3 μm (71% by volume and 82% by weight)
*UDMA: Urethane dimethacrylate, BisGMA: Bisphenol glycidyl methacrylate, TEGDMA: Triethylene glycol dimethacrylate				

Table 2. Finishing and polishing systems used in the study				
Finishing and polishing system	Manufacturers	Type	Organic matrix content	Inorganic filler
One-Gloss	Shofu Inc., Kyoto, Japan	One-step polishing cups	Aluminium oxide and silicon dioxide	-
Sof-Lex	3M, ESPE, St. Paul, MN, USA	Multi-step polishing disks	Aluminium oxide coated disc	Coarse 60 μm Medium 29 μm Fine 14 μm Super fine 5 μm
Platina Hi-Gloss	PrevesDenpro, India	Polishing paste	Aluminium oxide	-

Preparation of Specimens

The study population was determined using the G*Power program (Version 3.1.9.4, Heinrich Heine University, Düsseldorf, Germany). With an established α of 0.05 and power (p) of 85%, the calculated minimum sample size was n = 90. To consider for potential dropouts, the sample size was increased by 10, resulting in a total of 100 subjects.

Specimens with a depth of 2 mm and a diameter of 6 mm were prepared from each composite resin (50 nanohybrid and 50 supra-nanohybrid composites) using a Teflon mold. The application of composite resins involved the use of a mouth spatula for precise placement within the mold. Subsequently, polymerization of all specimens was carried out for a duration of 20 seconds on both the upper and lower surfaces, employing a VALO LED (Ultradent Products Inc., South Jordan, UT, USA) in accordance with the manufacturer's instructions. Composite resins were polymerized using a 'mylar strip' to obtain a smooth surface. The output intensity of the curing light was measured for each group prior to polymerization using a radiometer (Blue-phase Meter II, Ivoclar Vivadent, Schaan, Liechtenstein). To ensure consistency, the distance between the light unit's tip and the specimen was standardized with transparent polyester tapes. The specimens were immersed in distilled water at 37°C for a duration of 24 hours. Subsequently, the two distinct composite resins were segregated into five subgroups, each comprising 10 specimens, for subsequent polishing procedures.

Group 1: Finished with mylar strip. No polishing or finishing procedures were applied (Control group).
Group 2: Al_2O_3 coated one-step polishing cups (One Gloss, Shofu, Kyoto, Japan) in flame-tipped form was applied to the specimens for 20 s under water cooling. **Group 3:** After the specimens were polished with Al_2O_3 coated one-step polishing cups (One Gloss, Shofu, Kyoto, Japan) in flame-tipped form under water cooling for 20 s, Al_2O_3 coated polishing paste (Platina Hi-Gloss, India) was applied to the specimen surfaces with a brush.
Group 4: Specimen surfaces were polished for 20 s without water cooling using a multi-steps polishing system (Sof-Lex, 3M ESPE, USA) with Al_2O_3 abrasive (coarse, medi-um, fine and super fine) polishing disks.
Group 5: The specimen surfaces were polished with a polishing discs (coarse, medium, fine and super fine) using a multi-step disc system (Sof-Lex, 3M ESPE, USA) con-taining Al_2O_3 abrasive for 20 s without water cooling and then polishing paste containing Al_2O_3 (Platina Hi-Gloss, India) was applied with a brush.

Color Measurement

Following the completion of the finishing and polishing procedures, the initial color values of each composite resin specimen were assessed with a spectrophotometer (Vita Easyshade V; VITA Zahnfabrik, Germany). Before measurements, the specimen were then placed on a neutral grey background under D65 light source, and the spectrophotometer tip was positioned in contact with and perpendicular to the middle third of the facial surface of the specimen taking care to ensure the same environment and the same time for each specimen. The "L*, C*, and H*" values were measured individually. Each measurement un-derwent three repetitions, and the resulting mean values were calculated. The spectrophotometer was recalibrated according to the manufacturer's instructions after every nine measurements.

Staining Procedure

After the initial measurements, the specimens were kept in coffee (Nescafé Classic, Switzerland) for 144 h, to sim-ulated 6 months of coffee consumption.[17] Coffee solution was prepared by adding 8 g of coffee to 100 ml of boiling water and kept at room temperature (37°C) to mimic the oral environment. The solution was renewed every 24 h. At the end of the 144th h, the specimens were removed from the solution, washed in distilled water and dried with a sponge. The L*, C*, H* values obtained after the second and final measurements were recorded. The preparation of the specimens, the experimental phase and the color

measurements were carried out by the one operator to ensure standardization of the study and to obtain subjective data. The color value difference data between two measurements (post-coloring and pre-coloring) were calculated according to the following CIEDE2000 (ΔE00) formula;

$$\Delta E_{00} = \left[\left(\frac{\Delta L}{k_L S_L}\right)^2 + \left(\frac{\Delta C}{k_C S_C}\right)^2 + \left(\frac{\Delta H}{k_H S_H}\right)^2 + R_T\left(\frac{\Delta C}{k_C S_C}\right)\left(\frac{\Delta H}{k_H S_H}\right)\right]^{1/2}$$

According to the literature we referenced, 50:50% perceptibility threshold (PT) ΔE00: 0.8 and 50:50% acceptability threshold (AT) ΔE00: 1.8.[20]

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS Inc., Version 23, Chicago, IL, USA). The hypotheses were evaluated at a significance level of α = 0.05. Descriptive statistics included the calculation of mean values and standard deviations. The Shapiro–Wilk test confir med that the data followed a normal distribution. A two-way analysis of variance (ANOVA) was employed to assess the signific ance of ΔE00, and multiple comparisons were performed using post-hoc Tukey's tests. The results are presented as mean ± standard deviation (SD), with a significance level set at p< 0.05.

RESULTS

According to the results obtained; it was seen that the results of the material, polishing type and the diff erence of these two parameters statistically affectedthecolor change (p< 0.001). Theresultsofcolorchangeaccording to mate-rial and polishing type are shown in Table 3. The supra-na-nohybrid composite resin group showed a higher ΔE00 value than the nanohybrid composite resin group.

Table 3. Results of color change according to materials and polishing systems

Factors	F	p
Materials	19.067	<0.001
Polishing systems	24.596	<0.001
Materials * polishing systems	20.674	<0.001

The mean value ±(SD) results of the color change values according to the experimental groups are shown in Table 4. Specimens from both composite groups exhibited color change values above the clinical PT (> 0.8) and AT (> 1.8). Th e control group (Group 1) utilizing mylar strip exhibited the highest ΔE00 value, whereas the multi-steps polishing system (Group 4) yielded the lowest ΔE00 value.

Table 4. Mean value ± standard deviation (SD) results of color change values according to experimental groups

	ΔE00		
Polishing systems	Materials		
	G-aenial Posterior (n=50)	Estelite Sigma Quick (n=50)	Total
Group 1 (n=10)	7,36 ± 3,53^{g}	18,11 ± 5,08^{c}	12,73 ± 6,97^{A}
Group 2 (n=10)	7,15 ± 1,43^{fg}	11,50 ± 2,39^{bcdg}	9,33 ± 2,94^{B}
Group 3 (n=10)	7,78 ± 1,66^{fg}	7,68 ± 2,99^{abdfg}	7,73 ± 2,35^{B}
Group 4 (n=10)	5,48 ± 0,96^{efg}	3,85 ± 0,77^{ag}	4,67 ± 1,19^{C}
Group 5 (n=10)	9,09 ± 1,57^{dfg}	7,20 ± 2,73$^{ab-defg}$	8,14 ± 2,37^{B}
Total	7,37 ± 2,27	9,67 ± 5,75	8,52 ± 4,50

*A-C: No difference between polishing types with the same letter.
**a-g: No difference between polishing types with the same letter.

There was a statistical difference between the two different polishing systems (p< 0.05). The additional application of polishing paste caused a non-significant decrease in color change in the one-step polishing system (Group 2 – Group 3) (p< 0.05) and a statistically significant increase in the multi-steps polishing system (Group 4 – Group 5) (p> 0.05).

DISCUSSION

The composite resins used in the present study exhibited color change depending on different polishing systems. Therefore, the first null hypothesis of the study was rejected. Since the polishing paste used in addition to the polish-

ing systems in the study showed different results according to the polishing system used together, the null second hypothesis of the study was partially accepted.

Regarding the color changes of composite resins composites, there is no definite value in the literature in terms of PT and AT values, and different values are used in the studies.[21,22] The critical parameters (AT and PT) for assessing the color stability of dental materials are reported with a ratio of 50:50%. Specifically, PT is indicated as ΔE00 (color difference) of 0.8, while AT is denoted as 50:50% with a ΔE00 of 1.8.[17]

In this study, composite type and composite type-polish material interaction were found to be effective on the color change value. In the literature, it has been reported that composite resins with small filler particle size can obtain smoother surfaces and therefore less discoloration.[23,24] However, in our study, contrary to this situation, higher color change was obtained in supra-nanohybrid composite resin specimens compared to nano hybrid specimens. We believe that the different content of composite resins is effective in these data.

Among the staining beverages consumed, coffee is one of the most commonly used agents to imitate the daily routine in a laboratory environment.[25] It causes adsorption and absorption of yellow colored substances present in the structure of coffee through the organic phase of resin-based composites and causes color change.[26] The literature stated that it takes an average of 15 minutes to drink a cup of coffee and the average daily consumption is 3.2 cups.[27] It is noted that a simulated coffee consumption duration of 72 hours corresponds to the equivalent of three months of daily consumption. On the other hand, it was determined that hot coffee solution was more effective in color change, and Hui et al.[28] reported that the amount of color change in composite resin specimens was proportional to the increase in temperature, confirming this situation.[29] To simulate oral conditions, a temperature of 37°C and continuous exposure to the staining solution without cycling have been suggested.[30] Considering these facts, in this study, the specimens were exposed to coffee solution for 144 hours in the incubator at a constant temperature of 37°C. This period corresponds to a person's 6 months of coffee consumption.

Discoloration of resin-based composites can be caused by intrinsic factors such as organic and inorganic phase and extrinsic factors such as absorption of coloring beverages by the composite resin.[20] It has been reported that the porous structure of the inorganic filler phase of the composite causes more coloration in dyeing solutions.[31,32] In addition, UDMA, one of the organic monomers, is known to be more resistant to staining than BisGMA and TEGDMA.[6] In many studies in the literature, more color change was obtained in composite resins containing TEGDMA and this was attributed to the high amount of water absorption of TEGDMA as it is a hydrophilic monomer.[10,33-36] Deljoo et al.[33] conducted a comparative analysis of color change between microhybrid and nanohybrid composites. The findings revealed a lesser degree of color change in the nanohybrid composite, which was attributed to the presence of the UDMA monomer within the nanohybrid composite formulation. In our study, the supra-nanohybrid (9,67 ± 5,75) composite group showed a higher ΔE00 value than the nanohybrid (7,37 ± 2,27) composite group and both composite types showed a perceptible (> 0,8) color change. This result is supported by the existing studies in the literature and that have assume it is related to the UDMA content of the nanohybrid composite and the TEGDMA content of the supra-nanohybrid composite.

Discoloration of the surface of composite resins can be reduced by effective polishing procedures.[37] According to the literature, the lowest surface roughness was generally obtained in composites polymerized under mylar strip.[1,38] However, contrary to this, the highest ΔE00 values were obtained for mylar strip specimens in many studies.[17,19,36,39] This result was attributed to the presence of an oxygen-in-

hibition layer from the mylar strip. Our study aligns with previous research findings, as the mylar strip group exhibited the highest observed color change value, consistent with existing studies.[17,19,36,39]

Differences in the effectiveness of polishing systems are due to the type of abrasive (abrasives containing Al2O3, diamond particles), sizes and shapes (disk, spiral, conical, flame).[17] In many studies in the literature, Sof-Lex Disk polishing system, which gives better results compared to other polishing systems, is a multi-step polishing system containing grains of various sizes and has been reported to be less effective on convex surfaces due to its flat discs.[17,33,40] Another polishing system used in our study, One Gloss one-step polishing system, includes polishing tires in the form of disc, conical tip and flame tip. Similar to the results of many studies, the multi-steps polishing system showed less discoloration than the one-step system in our study.[17,41,42] It is related that the fact that the polishing cups in the form of a flame tip in the one-step polishing system is less effective on the flat surfaces of the composite samples compared to the multi-steps polishing system is effective in the high color change of the one-step polishing system in our study.

There are conflicting results about the effects of additional polishing paste applied to polishing systems on the color stability of restorative materials.[18,19,39] It has been reported that the effectiveness of polishing systems varies depending on the type of abrasives and smoother surfaces are obtained with diamond abrasives which are harder than Al2O3.[17] In a study Güler et al.[42] comparing the efficacy of a multi-step polishing system with the incorporation of a polishing paste, it was observed that the group utilizing the additional polishing paste exhibited a reduced degree of color change. The fact that the polishing paste used in our study was Al2O3 containing, whereas the study in the literature used diamond containing abrasive supports the contradiction in the results. In the study examining the effect of additional polishing paste in a one-step polishing system, the color change was observed to decrease in the group utilizing additional paste, aligning with the findings of our study.[18] In addition, in order to fully compare the effectiveness of the polishing systems used in our study, polishing paste was applied both one and multi-step polishing systems.

CONCLUSION

In this study, the effect of composite resin from 2 different manufacturers and 4 different polishing applications on color change was examined. The limitations of this in-vitro study include the fact that the study was conducted under laboratory conditions and could not fully simulate the intraoral environment, the samples were not subjected to thermal cycling, and no roughness study was performed to support the color change values. Therefore, further studies to compare this results using a more composite resins and polishing systems and including different parameters in the study are needed.

Considering the data obtained from the study within the limitations of this study; it was found that additional polishing paste application to polishing systems affected the color change of composite resins depending on the polishing systems used, the specimens in all composite resin-polishing systems combinations showed less discoloration than the specimens in the unpolished control group and regardless of the composite resin and polishing systems used, all specimens showed color change due to coffee solution.

Acknowledgement

The authors thank Assoc. Prof. Dr. Naci Murat for his kind support during the statistical analysis.

Ethical Approval

Approval for this study was obtained from the Mersin University Clinical Research Ethics Committee, under the ethics committee permission number 2023/838.

Peer-review

Externally and internally peer-reviewed.

Author Contributions

Concept: S.A.Y., A.T.E.A., Design: S.A.Y., A.T.E.A., Data collection or Processing: S.A.Y., D.E., A.T.E.A., Analysis or interpretation: S.A.Y., A.T.E.A., E.C.Y., Literature Search: S.A.Y., D.E., A.T.E.A., Writing: S.A.Y., D.E., A.T.E.A., E.C.Y.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

No funding was received to assist with the preparation of this manuscript.

References

1. Scheibe KGBA, Almeida KGB, Medeiros IS, Costa JF, Alves CMC. Effect of different polishing systems on the surface roughness of microhybrid composites. J Appl Oral Sci. 2009;17:21-6.
2. Schmidlin PR, Gohring T. Finishing tooth-colored restorations in vitro: an index of surface alteration and finish-line destruction. Oper Dent. 2004;29(1):80-6.
3. St-Pierre L, Martel C, Crépeau H, Vargas M. Influence of polishing systems on surface roughness of composite resins: polishability of composite resins. Oper Dent. 2019;44(3):E122-E32. https://doi.org/10.2341/17-140-L.
4. Saraç D, Saraç Ş, Külünk Ş, Kural Ç, Külünk T. Farklı inorganik doldurucu içerikli kompozit rezinlerin renk sabitliği üzerinde polisaj yöntemlerinin ve yüzey verniği uygulamasının etkisi. GÜ Diş Hek Fak Derg. 2006;23(3):169-75.
5. Reis AF, Giannini M, Lovadino JR, dos Santos Dias CT. The effect of six polishing systems on the surface roughness of two packable resin-based composites. Am J Dent. 2002;15(3):193-7.
6. Khokhar Z, Razzoog M, Yaman P. Color stability of restorative resins. Quintessence Int. 1991;22(9).
7. Craig RG, Powers J, Wataha J. Direct esthetic restorative materials. In: Sakaguchi R, Powers J, editors. Restorative Dental Materials. 11th ed. St. Louis: Mosby; 2000:244-67.
8. Larato DC. Influence of a composite resin restoration on the gingiva. J Prosthet Dent. 1972;28(4):402-4. https://doi.org/10.1016/0022-3913(72)90241-7.
9. Shortall A, Palin W, Burtscher P. Refractive index mismatch and monomer reactivity influence composite curing depth. J Dent Res. 2008;87(1):84-8. https://doi.org/10.1177/154405910808700115.
10. Ertas E, Gueler AU, Yuecel AC, Köprülü H, Güler E. Color stability of resin composites after immersion in different drinks. Dent Mater J. 2006;25(2):371-6. https://doi.org/10.4012/dmj.25.371.
11. Mitra SB, Wu D, Holmes BN. An application of nanotechnology in advanced dental materials. J Am Dent Assoc. 2003;134(10):1382-90. https://doi.org/10.14219/jada.archive.2003.0054.
12. Aydın N, Karaoğlanoğlu S, Oktay EA, Kılıçarslan MA. Investigating the color changes on resin-based CAD/CAM Blocks. J Esthet Restor Dent. 2020;32(2):251-6. https://doi.org/10.1111/jerd.12561
13. Cangül ÖÜS, Adıgüzel Ö, Ünal ÖÜS, Tekin S, Sonkaya E, Erpaçal B. Investigation of the color stability of kept composite resins in different coffee types. Yeditepe J Dent. 2020;16(2):117-22.
14. Fontes ST, Fernández MR, Moura CMd, Meireles SS. Color stability of a nanofill composite: effect of different immersion media. J Appl Oral Sci. 2009;17:388-91. https://doi.org/10.1590/S1678-77572009000500007.
15. Güler E, Gönülol N, Yücel AÇ, YILMAZ F, Ersöz E. Farklı içeceklerde bekletilen kompozit rezinlerin renk stabilitelerinin karşılaştırılması. J Dent Fak Ataturk Univ. 2013;23(1):24-9.
16. Korkut B. Cila Sistemlerinin Mikrohibrit ve Nanohibrit Rezin Kompozitlerin Renklenmesi Üzerine Etkisinin Değerlendirilmesi. Turkiye Klinikleri J Dental Scı. 2021;27(3):451-61.
17. Um CM, Ruyter I. Staining of resin-based veneering materials with coffee and tea. Quintessence Int. 1991;22(5).
18. Douglas RD, Steinhauer TJ, Wee AG. Intraoral determination of the tolerance of dentists for perceptibility and acceptability of shade mismatch. J Prosthet Dent. 2007;97(4):200-8. https://doi.org/10.1016/j.prosdent.2007.02.012.
19. O'brien W, Groh CL, Boenke KM. A new, small-color-difference equation for dental shades. J Dent Res. 1990;69(11):1762-4. https://doi.org/10.1177/00220345900690111001.
20. Nasim I, Neelakantan P, Sujeer R, Subbarao C. Color stability of microfilled, microhybrid and nanocomposite resins—an in vitro study. J Dent. 2010;38:e137-e42. https://doi.org/10.1016/j.jdent.2010.05.020.
21. Choi M-S, Lee Y-K, Lim B-S, Rhee S-H, Yang H-C. Changes in surface characteristics of dental resin composites after polishing. J Mater Sci Mater Med. 2005;16:347-53.
22. Tuncer S, Demirci M, Tiryaki M, Ünlü N, Uysal Ö. The effect of a modeling resin and thermocycling on the surface hardness, roughness, and color of different resin composites. J Esthet Restor Dent. 2013;25(6):404-19. https://doi.org/10.1111/jerd.12063.
23. Reis AF, Giannini M, Lovadino JR, Ambrosano GM. Effects of various finishing systems on the surface roughness and staining susceptibility of packable composite resins. Dent Mater. 2003;19(1):12-8. https://doi.org/10.1016/S0109-5641(02)00014-3.
24. Villalta P, Lu H, Okte Z, Garcia-Godoy F, Powers JM. Effects of staining and bleaching on color change of dental composite resins. J Prosthet Dent. 2006;95(2):137-42. https://doi.org/10.1016/j.prosdent.2005.11.019
25. Barutcigil Ç, Yıldız M. Intrinsic and extrinsic discoloration of dimethacrylate and silorane based composites. J Dent. 2012;40:e57-e63. https://doi.org/10.1016/j.jdent.2011.12.017
26. Guler AU, Yilmaz F, Kulunk T, et al. Effects of different drinks on stainability of resin composite provisional restorative materials. J Prosthet Dent. 2005;94(2):118-24. https://doi.org/10.1016/j.prosdent.2005.05.004
27. Rajkumar K, Kumar S, Mahalaxmi S, et al. Colour stability of resin composites after emersing in coffee of different temperature-an in vitro study. SRM Univ J Dent Sci. 2011;2(2):91-5.
28. Hui R, Choi IH, Hussein I, et al. The effect of drinks and temperature on the staining of resin composites coated with surface sealants. J Dent Biomater. 2014;1(1):16-22.
29. Mundim FM, Garcia LdFR, Pires-de-Souza FdCP. Effect of staining solutions and repolishing on color stability of direct composites. J Appl Oral Sci. 2010;18:249-54.
30. Hepdeniz OK, Temel UB, Ugurlu M, et al. The effect of surface sealants with different filler content on microleakage of Class V resin composite restorations. Eur J Dent. 2016;10(02):163-9. https://doi.org/10.4103/1305-7456.178315.
31. Barakah HM, Taher NM. Effect of polishing systems on stain susceptibility and surface roughness of nanocomposite resin material. J Prosthet Dent. 2014;112(3):625-31. https://doi.org/10.1016/j.prosdent.2013.12.007.
32. Turkun L, Turkun M. The effect of one-step polishing system on the surface roughness of three esthetic resin composite materials. Oper Dent. 2004;29(2):203-11.
33. Deljoo Z, Sadeghi M, Azar MR, Bagheri R. The effect of different polishing methods and storage media on discoloration of resin composites. J Dent Biomater. 2016;3(2):226.
34. Ergücü Z, Türkün LS, Aladag A. Color stability of nanocomposites polished with one-step systems. Oper Dent. 2008;33(4):413-20. https://doi.org/10.2341/07-107.
35. Sadeghi M, Deljoo Z, Bagheri R. The influence of surface polish and beverages on the roughness of nanohybrid and microhybri resin composite. J Dent Biomater. 2016;3(1):177-85.
36. Ereifej N, Oweis Y, Eliades G. The effect of polishing technique on 3-D surface roughness and gloss of dental restorative resin composites. Oper Dent. 2012;38(1):E9-E20. https://doi.org/10.2341/12-122-L.
37. Gönülol N, Yılmaz F. The effects of finishing and polishing techniques on surface roughness and color stability of nanocomposites. J Dent. 2012;40:e64-e70. https://doi.org/10.1016/j.jdent.2012.07.005.
38. Karakas SN, Kuden C. Farklı Polisaj Sistemlerinin Yeni Alkasit Restoratif Materyalin Renk Değişimine Etkisinin Değerlendirilmesi. Value Health. 2022;12(3):411-6.
39. Marufu C, Kisumbi BK, Osiro OA, Otieno FO. Effect of finishing protocols and staining solutions on color stability of dental resin composites. Clin Exp Dent Res. 2022;8(2):561-70. https://doi.org/10.1002/cre2.555.
40. Yilmaz MN, Gül P, Uygun LA. The Role of Polishing Systems on the Staining Susceptibility of Composite Resins. Turkiye Klinikleri J Dental Sci. 2020;26(1):86-93. https://doi.org/10.5336/dentalsci.2018-64331.
41. Aydin N, Karaoglanoglu S, Oktay E, Ezros B. Effect of Additional Polishing Application on the Surface Roughness and Color Change of Composite Resins. J Dent Sci. 2021;27:462-9.
42. Güler AU, Güler E, Yücel AÇ, Ertaş E. Effects of polishing procedures on color stability of composite resins. J Appl Oral Sci. 2009;17:108-12. https://doi.org/10.1590/S1678-77572009000200007.

DOI:10.34084/bshr.1496654 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Evaluation of Healthcare-Associated Infections in Intensive Care Units

Yoğun Bakım Ünitelerinde Sağlık Hizmetiyle İlişkili Enfeksiyonların Değerlendirilmesi

Murat Aydın[1], Nurten Nur Aydın[1], Gülseren Savaş[1], Sibel İba Yılmaz[1], Dursun Murat Alada[2]

1 Erzurum Regional Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Erzurum, Türkiye

[2] Erzurum Regional Education and Research Hospital, Medical Microbiology Laboratory, Erzurum, Türkiye

ORCID ID: Murat Aydın: https://orcid.org/0000-0002-0167-0802, Nurten Nur Aydın: https://orcid.org/0000-0003-4138-2490 Gülseren Savaş: https://orcid.org/0009-0003-1902-7641, Sibel İba Yılmaz: https://orcid.org/0000-0002-4123-0828, Dursun Murat Alada: https://orcid.org/ 0000-0002-7429-7471

***Sorumlu Yazar / Corresponding Author:** Murat Aydın , **e-posta / e-mail:** kibamurat61@hotmail.com

Geliş Tarihi / Received : 06-06-2024 **Kabul Tarihi / Accepted:** 27-07-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Aydın M., Aydın N.N., Savaş G., İba-Yılmaz S., Alada D.M. Evaluation of Healthcare-Associated Infections in Intensive Care Units. J Biotechnol and Strategic Health Res. 2024;8(1):101-107

Abstract

Aim The aim of this study was to determine the healthcare-associated infections (HAIs), causative microorganisms and antibiotic resistance profiles in the tertiary intensive care unit of our hospital and, based on the results, to contribute to the rational administration of antibiotics.

Material and Method The study included patients who were followed up in the tertiary intensive care unit between January 2023 and December 2023 and were diagnosed with HAI. Patient data were obtained retrospectively from infection control nurse records and patient files.

Results During the study period, 107 HAI episodes were identified in 99 of 2296 patients. The incidence rate of HAI was 4.7% and the incidence density was 5.2 per thousand. Central line-associated bloodstream infections (43%) were the most common HAI associated with invasive devices. The next most common were ventilator-associated pneumonia (42%) and catheter-associated urinary tract infection (15%). Gram negative bacteria were isolated in 83.2%, fungi in 10.3%, and gram positive bacteria in 6.5% of patients diagnosed with HAI. The most common gram negative bacteria were Acinetobacter baumannii (34.6%) and Pseudomonas aeruginosa (19.6%). A colistin resistance rate of 8.1% was determined for Acinetobacter baumannii. Carbapenem resistance was 91.9% for Acinetobacter baumannii and 76.2% for Pseudomonas aeruginosa. Methicillin resistance was found in 66.7% of Staphylococcus aureus, the most commonly isolated gram positive bacterium.

Conclusion Monitoring HAIs, causative microorganisms and antibiotic resistance rates in intensive care units is of great importance for both infection prevention and the rational use of antibiotics.

Keywords Antimicrobial resistance, healthcare associated infection, intensive care unit

Özet

Amaç *Bu çalışmada, hastanemizin üçüncü basamak yoğun bakım ünitesinde gelişen sağlık hizmetiyle ilişkili enfeksiyonların (SHİE), etken mikroorganizmaların ve antibiyotik direnç profillerinin belirlenmesi ve bulgular ışığında akılcı antibiyotik uygulanmasına katkı sağlanması amaçlanmıştır.*

Gereç ve Yöntem *Çalışmaya Ocak 2023-Aralık 2023 tarihleri arasında üçüncü basamak yoğun bakım ünitesinde takip edilen ve SHİE tanısı koyulan hastalar dahil edilmiştir. Hasta verileri, enfeksiyon kontrol hemşireleri tarafından tutulan kayıtlardan ve hasta dosyalarından retrospektif olarak elde edilmiştir.*

Bulgular *Çalışma boyunca 2296 hastanın 99'unda 107 SHİE epizodu tanımlanmıştır. SHİE insidans hızı %4,7, insidans dansitesi binde 5,2 olarak olarak saptanmıştır. İnvazif araçla ilişkili SHİE içerisinde santral venöz kateter ilişkili kan dolaşımı enfeksiyonu (%43) ilk sırada yer almıştır. İkinci sıklıkta ventilatör ilişkili pnömoni (%42) ve sonrasında kateter ilişkili üriner sistem enfeksiyonu (%15) saptanmıştır. SHİE tanısı alan hastalardan %83,2'sinde gram negatif bakteriler, %10.3'ünde funguslar, %6.5'inde gram pozitif bakteriler izole edilmiştir. Gram negatif bakterilerden en sık Acinetobacter baumannii (%34,6) ve Pseudomonas aeruginosa (%19.6) saptanmıştır. Acinetobacter baumannii için kolistin direnci %8,1 olarak bulunmuştur. Karbapenem direnci Acinetobacter baumannii için %91,9, Pseudomonas aeruginosa için %76,2 olarak saptanmıştır. En sık izole edilen gram pozitif bakteri olan Staphylococcus aureus'un %66,7'sinde metisilin direnci tespit edilmiştir.*

Sonuç *Yoğun bakım ünitelerinde SHİE'lerin, etken mikroorganizmaların ve antibiyotik direnç oranlarının takip edilmesi ve hem enfeksiyonların önlenmesi hem de akılcı antibiyotik kullanımı açısından büyük önem taşımaktadır.*

Anahtar Kelimeler *Antimikrobiyal direnç, sağlık hizmeti ilişkili enfeksiyon, yoğun bakım ünitesi*

INTRODUCTION

Healthcare-associated infections (HAIs) represent an important health problem in intensive care units due to increasing mortality, impaired quality of life, increasing treatment costs, developing antibiotic resistance and placing additional burden on healthcare services.[1, 2]

Intensive care units (ICUs) are multidisciplinary units prepared for patients requiring specialized care and continuous follow-up in situations requiring advanced support. The incidence of HAI is higher than in other wards and ranges from 11% to 60%.[3] This difference is due to the presence of various risk factors that are unequally distributed in the healthcare system. The reasons for the high incidence of nosocomial infections, especially in ICUs, include the high frequency of invasive procedures, various comorbidities, suppression of the immune system and longer hospital stays.[4]

Nosocomial infections vary between different hospitals and units and these differences are due to various factors such as infectious agents and antibiotic resistance. Each hospital should identify the microorganisms and antibiotic resistance patterns that characterize its unique nosocomial flora. This information can be obtained through surveillance programs to determine the frequency and pathogens of infections.[5] In ICUs, the development of HAI is a dynamic process that changes continuously over time and requires constant monitoring. Therefore, it is crucial for each center to know the HAI rates, the causative microorganisms and antibiotic resistance profiles in their ICUs. This information can improve the treatment of nosocomial infections by enabling the development of infection control practices, the correct use of antibiotics, and a continuously informed approach.

The aim of this study was to identify the HAIs, causative microorganisms and antibiotic resistance profiles that developed in the intensive care unit of our hospital and to contribute to rational antibiotic administration according to these findings.

MATERIALS and METHODS

Among the 2296 patients followed up in the tertiary ICU of Erzurum Regional Training and Research Hospital between January 1, 2023 and December 31, 2023, patients aged 18 years and above who were diagnosed with HAI during their hospitalization were included in the study. Patients not diagnosed with HAI in ICUs and patients under 18 years of age were excluded from the study.

The 2017 National HAI Surveillance Guidelines, adapted from Centers for Disease Control and Prevention (CDC) criteria, were used to diagnose patients with HAIs.[6] Patient information was obtained retrospectively from infection control nurse records and patient files between the specified dates.

To identify and determine the antibiotic susceptibility of the infectious microorganisms isolated from the patients, conventional methods and the automated system VITEK 2 Compact (bioMérieux, France) were used.

The Phoenix ESBL test used five wells containing fixed concentrations of the following drugs or drug combinations: cefpodoxime, ceftazidime, ceftazidime plus clavulanic acid (CA), cefotaxime plus CA, and ceftriaxone plus CA. After inoculation with each of the isolates, the panel was placed in the instrument and continuously monitored for growth. At each decision point, the growth curve derived from each well was evaluated. Growth curves were evaluated using a series of functions describing their intensity and shape. A series of mathematical functions were used to determine a positive or negative growth response to a threshold; if the decision point was at the terminal node, the results were reported.

The Phoenix™ CPO Detection Test (BD), a qualitative, confirmatory, growth-based test aimed at phenotypically detecting carbapenemase enzyme expression in Entero-

bacteriaceae, P. aeruginosa, and A. baumannii, was used. Colistin resistance was determined by microdilution method (0.25-8).

The incidence rate of HAIs = (number of HAIs/number of patients) × 100, the incidence density = (number of HAIs/ number of patient days) × 1000 were calculated using the formula.

As part of the invasive device-related HAI rates, the rate of ventilator-associated pneumonia (VAP), the rate of central line-associated bloodstream infections (CLABSI) and the rate of catheter-associated urinary tract infections (CAUTI) were evaluated. VAP rate = number of VAPs / ventilation days x 1000, CLABSI rate = number of CLABSI / central line days x 1000, CAUTI rate = number of CAUTIs / urinary catheter days x 1000 were calculated using the formula. The formula was used to calculate the device usage rate = number of device days / patient days.

Ethical approval of this study was granted by the Ethics Committee of Erzurum Regional Training and Research Hospital (Decision No: 2024/01-06).

Statistical analysis

The statistical package program IBM SPSS 23.0 was used for data analysis. In the descriptive statistics of the evaluation results, numerical values (n) and percentage values (%) were given for categorical variables as well as mean and standard deviation (SD) values for numerical variables.

RESULTS

The study retrospectively analyzed 20,444 hospitalization days of 2296 patients followed up in the tertiary ICU over a one-year period. During this period, 107 HAI episodes were detected in 99 patients. Of the patients diagnosed with HAI, 59 (55%) were female and 48 (45%) were male. The mean age of the patients was 74.1 ± 14.4 years. Data on the patients' demographic characteristics, reasons for hospitalization, and comorbidities are shown in Table 1.

Table 1. Patient demographic characteristics, reasons for hospitalization, and comorbidities

	n	%
Male	48	45
Female	45	55
Mean age ± SD	74.1 ± 14.4	
Comorbidities		
Hypertension	48	44.9
Diabetes mellitus	27	25.2
Chronic obstructive pulmonary disease	15	14.0
Coronary artery disease	18	16.8
Congestive heart failure	11	10.3
Chronic kidney disease	9	8.4
Cerebrovascular disease	14	13.1
Alzheimer's disease	7	6.5
Malignancy	4	3.7
Reasons for hospitalisation		
Cerebrovascular accident	37	34.6
Acute coronary syndrome	9	8.4
Pulmonary causes	33	30.9
Trauma	16	15.0
Cardiac arrest	9	8.4
Other causes	16	15.0
Mean length of hospitalisation (days) ± SD	40.4 ± 41.7	

The incidence rate of HAI was 4.7% and the incidence density was 5.2 per thousand. The mechanical ventilator use rate was 56%, the VAP rate was 4 per thousand; the rate of urinary catheter use was 94%, the rate of CAUTI was 1 per thousand; The rate of central line use was 84% and the rate of CLABSI was 2.7 per thousand. The most common HAI associated with invasive devices was CLABSI (n: 46, 43%), followed by VAP (n: 45, 42%) and CAUTI (n: 16, 15%), respectively (Table 2).

Table 2. Days of invasive device use, frequency of invasive device use, and infection rates					
	Days of invasive device use	**Frequency of invasive device use (%)**		**Number of infections**	**Infection rate (per thousand)**
Central line	17.323	84	**CLABSI**	46	2.7
MV	11.505	56	**VAP**	45	4
UC	19.363	94	**CAUTI**	16	1

Th e causative agents of HAI and their distribution are listed in Table 3. Gram negative bacteria were isolated in 89 (83.2%), fungi in 11 (10.3%), and gram positive bacteria in 7 (6.5%) patients. *Acinetobacter baumannii* (n:37, 34.6%) and *Pseudomonas aeruginosa* (n:21, 19.6%) were the most commonly isolated gram negative bacteria. Staphylococcus aureus (n:6, 5.6%) was the most commonly isolated gram positive bacterium. *A. baumannii* (n:25, 55.6%) and *P. aeruginosa* (n:11, 24.4%) were the most common pathogens in VAP, *A. baumannii* (n:8, 17.4%) and *P. aeruginosa* (n: 5, 31.3%) were the most common pathogens in CAUTI.

Table 3. Healthcare-associated infectious agents and their distribution					
Microorganism	**VAP**	**CLABSI**	**CAUTI**	**Total number (n)**	**%**
Gram negative bacteria	**43**	**31**	**15**	**89**	**83.2**
Acinetobacter baumannii	25	8	**4**	37	34.6
Pseudomonas aeruginosa	11	5	**5**	21	19.6
Klebsiella pneumoniae	5	7	**2**	14	13.1
Pseudomonas putida	0	4	**0**	4	3.7
Escherichia coli	0	0	**4**	4	3.7
Stenotrophomonas maltophilia	1	3	**0**	4	3.7
Enterobacter cloacae	1	1	**0**	2	1.9
Klebsiella oxytoca	0	1	**0**	1	0.9
Moraxella species	0	1	**0**	1	0.9
Cedecea davisae	0	1	**0**	1	0.9
Gram positive bacteria	**2**	**4**	**1**	**7**	**6.5**
Staphylococcus aureus	2	4	**0**	6	5.6
Enterococcus faecium	0	0	**1**	1	0.9
Fungi	**0**	**11**	**0**	**11**	**10.3**
Candida albicans	0	6	**0**	6	5.6
Candida glabrata	0	2	**0**	2	1.9
Candida tropicalis	0	2	**0**	2	1.9
Candida parapsilosis	0	1	**0**	1	0.9
CAUTI: Catheter-associated urinary tract infections, CLABSI: Central line-associated bloodstream infections, VAP: Ventilator-associated pneumonia					

Extended spectrum beta-lactamase (ESBL) positivity for *Klebsiella pneumoniae* and *E. coli* was found to be 100%. Carbapenem resistance was 91.9% for *A. baumannii,* 76.2% for *P. aeruginosa* and 92.9% for *K. pneumoniae,* while no carbapenem resistance was detected in *Escherichia coli.* A colistin resistance rate of 8.1% was determined for *A. baumannii*. Susceptibility to ceft azidime-avibactam was examined in 46 bacteria and resistance to ceft azi-dime-avibactam was found in 28.3% of them. Th e most eff ective antibiotics according to susceptibility in gram negative bacteria were colistin for *Acinetobacter* spp. and *Pseudomonas* spp.; colistin, ceft azidime-avibactam and aminoglycosides for *Klebsiella* spp.; Carbapenems for E. coli and trimethoprim sulfamethoxazole for *Stenotrophomonas maltophilia*. Antimicrobial resistance rates of gram negative pathogens are shown in Table 4.

Table 4. Antimicrobial resistance rates of gram negative pathogens (%)

Antibiotic	A. baumannii (n: 37)	P. aeruginosa (n: 21)	K. pneumoniae (n: 14)
Ceftazidime	100.0	71.4	100.0
Ceftriaxone	-	-	100.0
Cefepime	-	90.4	92.9
Piperacillin tazobactam	100.0	81.0	85.7
Meropenem	91.9	76.2	92.9
Imipenem	91.9	76.2	92.9
Amikacin	83.8	33.3	35.7
Gentamicin	94.6	33.3	57.1
Ciprofloxacin	97.3	90.5	78.6
Levofloxacin	97.3	85.7	85.6
Trimethoprim-sulfamethoxazole	94.6	61.9	71.4
Colistin	8.1	9.5	21.4
Ceftazidime avibactam	-	23.8	35.7

Table 5: Antimicrobial resistance rates of gram positive pathogens (%)

Antibiotic	***S. aureus*** (n: 6)	***E. faecium*** (n: 1)
Oxacillin	66.7	-
Moxifloxacin	33.3	-
Trimethoprim sulfamethoxazole	16.7	-
Clindamycin	33.3	-
Linezolid	0	0
Teicoplanin	0	0
Vancomycin	0	0

S. aureus was the most commonly isolated gram positive bacterium and 66.7% were methicillin-resistant *S. aureus* (MRSA). 66.2% of *S. aureus* strains were isolated from blood and 33.3% from tracheal aspirate. The most eff ective antibiotics against gram positive bacteria were linezolid, vancomycin and teicoplanin. Antimicrobial resistance rates of gram positive pathogens are shown in Table 5.

All 11 fungal strains were isolated from blood. Of the Candida strains, 6 (%) were *C. albicans*, 2 (%) *C. tropicalis,* 2 (%) *C. glabrata* and 1 (%) *C. parapsilosis*.

DISCUSSION

In ICUs, where high-risk patients are followed for a long period of time and hospitalizations are frequent, nosocomial infections are common and become a serious problem. Nosocomial infections, particularly in ICUs, are known to increase the morbidity and mortality of patients in these units, prolong hospital stays and increase hospital costs.1 In our country, nosocomial infection rates in ICUs are related to surveillance methods, training status of staff, and compliance with infection control measures. The infection rates can vary between 5.3% and 88.9%.7,8 In our study, the rate and incidence density of HAI was found to be lower than national and international data. This reflects the eff ectiveness of the infection control measures implemented in our hospital. In the study by Çalangu et al. the nosocomial infection rate in ICU was reported as 16.8% and the incidence density as 25.9 per thousand.[9] Eggiman

et al. reported a nosocomial infection rate of 15.5% and an incidence density of 13.5 per thousand in 311 ICUs from 18 European countries.[10] Th ese results show that our hospital's infection control measures meet national and international standards and that these measures reduce the risk of infection.

Th e infectious agents of HAIs can vary from hospital to hospital and vary over time in the same department of the same hospital. In our study, gram negative bacteria were most frequently isolated among the HAI pathogens. In the study by Yılmaz et al. 82.8% of nosocomial infectious agents were gram negative bacteria.8 Köksaldı Motor et al. showed that 51% of the causative microorganisms were gram negative bacteria.[11] In the EPIC study, which analyzed ICU infections in 18 countries, it was reported that 53.1% of pathogens were gram negative, 49.2% were gram positive and 17.1% were fungal.[12] Th e EPIC II study reported that 62% of the causative agents of ICU infections were gram negative, 47% were gram positive bacteria, and 19% were fungi.[13] In our study, gram negative bacteria were found in 83.2%, fungi in 10.5%, and gram positive bacteria in 6.3%. Th ese results show that gram negative bacteria are an important pathogen group in ICUs and infection control measures for these bacteria should be strengthened.

Th e most frequently isolated agent among all microorganisms was *A. baumannii* (34.6%), followed by *P. aureginosa* (19.6%) and *K. pneumoniae* (13.1%). Leblebicioğlu et al. reported that 36.6% of nosocomial infection agents were caused by *A. baumannii.*[14] In the study conducted by Balın et al. *Acinetobacter* spp. (29.9%) was found to be the most common microorganism.[15] According to these results, it is thought that A. baumannii is a resistant pathogen frequently seen in ICUs and the choice of empirical treatment of moderate and serious infections developing in ICU should include especially gram negative bacteria and the antibiotic that acts on *Acinetobacter* spp. strains should be selected.

Th e prevalence of gram positive bacteria as pathogens of nosocomial infections in ICUs varies. Aly et al. report-ed that 27% of culture-confirmed nosocomial infections were caused by gram positive bacteria.[16] Similarly, Ak et al. reported that 68.8% of the isolates were gram negative bacteria and 27.6% were gram positive.[17] Doyle et al. reported that resistant *S. aureus* was reported less frequently compared to multidrug-resistant gram negative bacteria.[17] Th e se studies indicate that both gram positive and gram negative bacteria can be important causative agents of HAIs. Qadeer et al. reported that *Enterococcus* and MRSA were the two most common gram positive bacteria.[18] In our study, gram positive bacteria were observed at a rate of 6.5%, with *S. aureus* being the most commonly found. Th e frequency of active ingredients in HAIs also varies depending on the invasive instrument used. In the study by Ak et al. S. aureus was found to be the most common path-ogen in bloodstream infections, *P. aureginosa* in pneumonia, and *E. coli* in urinary tract infections.[17] In the study by Köksaldı Motor et al. *A. baumannii* was found to be the most common agent in VAP, Candida spp. for urinary tract infections and bloodstream infections.[11] In our study, *A. baumannii* was the most common pathogen in VAP and CLABSI, while *P. aureginosa* was the most common path-ogen in CAUTI.

Th e widespread use of antibiotics in the ICU leads to the colonization of resistant microorganisms in patients, resulting in treatment diffi culties and increased mortality rates in patients with infections. This problem is exacerbated by factors such as frequent use of antibiotics, prolonged ICU hospital stays, presence of comorbidities, lack of isolation practices, and easy spread of resistant pathogens, thereby increasing the burden of resistance in critically ill patients.[19] In the study by Gözütok et al. 82.7% of E. coli strains and 83.3% of *K. pneumoniae* strains were ESBL positive.[20] In the study conducted by Göktaş et al, ESBL positivity was found in 70% of *E. coli* and 93.7% of *Klebsiella* spp.[21] In our study, 100% ESBL positivity was found in E. coli and *K. pneumoniae*, and the carbapen-

em resistance rate was 92% for *A. baumannii,* 93% for *K. pneumoniae*, and 76% in P. aeruginosa. Th is situation is extremely worrying in the treatment of resistant gram negative bacteria and highlights the importance of new generation therapies. In the study by Gözütok et al. 96.6% of A. baumannii strains were resistant to imipenem and the most eff ective antibiotic was colistin, and no resistance to this antibiotic was detected.[20] In our study, carbapenem resistance was 91.9% and colistin resistance was 8.1% for A. baumannii. Furthermore, colistin was the most eff ective antibiotic against gram negative bacteria in our study. Th ese results indicate that carbapenem resistance is a serious treatment problem in intensive care units and the use of carbapenem should be limited and alternative antibiotics should be developed.

With the widespread use of antibiotics in ICUs, methicillin resistance rates in staphylococci are increasing. In previous studies, methicillin resistance in *S. aureus* was found to be 41.02% by Kula Atik et al. and 66.6% by Gözütok et al.[20,22] In our study, methicillin resistance was found to be 66.7%. Given that MRSA infections represent a serious treatment problem in ICUs, it should be borne in mind that measures such as MRSA screening, isolation and decolonization should be taken.

In the ICU, the frequency of fungal infections is increasing, which is associated with high mortality and morbidity. Candida species account for the majority of hospital-acquired fungal infections. Although C. albicans ranks fi rst among Candida species, there has been a recent increase in other Candida species.[23] In a study conducted in Turkey, *C. albicans* was reported to be the most frequently isolated, followed by *C. tropicalis* and *C. glabrata.*[24] Kerget et al. isolated C. parapsilosis most frequently in their study.[25] In our study, C. albicans was found most frequently.

In conclusion, the frequency, pathogens, and resistance profi les of H AIs developing in the ICUs of our hospital may diff er from similar studies in the literature. Th ese differences reflect our hospital's unique hospital flora, infection control practices, and antibiotic use policies. Therefore, each center should continuously monitor the development of nosocomial infections in its ICUs, determine the causative microorganisms and their antibiotic resistance profiles, develop infection control measures and ensure rational use of antibiotics. In this way, more successful results can be achieved in the prevention and treatment of HAIs.

Ethical Approval

Ethical approval of this study was granted by the Ethics Committee of Erzurum Regional Training and Research Hospital (Decision No: 2024/01-06).

Peer-review

Externally and internally peer-reviewed.

Author Contributions

Concept: M.A., N.N.A., Design: M.A., N.N.A., Data collection or Processing: G.S., N.N.A, Analysis or interpretation: M.A., S.İ.Y., D.M.A., Literature Search: M.A., N.N.A., Writing: M.A., N.N.A.

Conflict of Interest

No conflict of interest was declared by the authors.

Funding

The authors declared that this study received no financial support.

Informed Consent

Informed consent was not obtained since it was a retrospective study.

References

1. Manoukian S, Stewart S, Graves N, et al. Evaluating the post-discharge cost of healthcare-associated infection in NHS Scotland. J Hosp Infect. 2021;114:51-58.
2. Centers for Disease Control and Prevention. Healthcare-Associated Infections (HAIs) [Internet]. Available from: https://www.cdc.gov/healthcare-associated-infections/ Accessed: 05.06.2024
3. Choudhuri AH, Chakravarty M, Uppal R. Epidemiology and characteristics of nosocomial infections in critically ill patients in a tertiary care Intensive Care Unit of Northern India. Saudi J Anaesth. 2017;11(4):402-407.
4. Oliveira AC, Kovner CT, da Silva RS. Nosocomial infection in an intensive care unit in a Brazilian university hospital. Rev Lat Am Enfermagem. 2010;18(2):233-239.
5. Karabey S. Hospital infections: definitions. Hastane İnfeksiyonları. Doğanay M, Ünal S (Ed). Ankara. Bilimsel Tıp Yayınevi, 2013. p.35-57.
6. Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Rehberi Ankara 2024 [Internet] Available from: https://dosyaism.saglik.gov.tr/Eklenti/15719,ulusal-saglik- hizmeti-iliskili-enf-surveyansi-rehberipdf.pdf?0. Accessed: 05.06.2024
7. Arslan H, Gürdoğan K. Yoğun bakım ünitelerinde gözlenen hastane infeksiyonları. Hastane İnfeksiyonları Dergisi. 1999;3:165-170.
8. Yılmaz G, Çevik MA, Erdinç FŞ, Tülek N. Nöroloji yoğun bakım ünitesinde gelişen nozokomiyal infeksiyon risk faktörlerinin değerlendirilmesi. Hastane İnfeksiyonları Dergisi. 2002;6(1):24-31.
9. Çalangu S. Hastane infeksiyonlarının önemi. Sterilizasyon ve Dezenfeksiyon Hastane İnfeksiyonları SIMAD Yayınları. 2002;1:189-194.
10. Eggimann P, Pittet D. Infection control in the ICU. Chest. 2001;120(6):2059-2093.
11. Köksaldı Motor V, Evirgen Ö, Yula E, Erden EŞ, Ocak S, Önlen Y. Mustafa Kemal Üniversitesi Tıp Fakültesi Yoğun Bakım Ünitesi'nde 2011 yılında sağlık hizmeti ile ilişkili infeksiyonların değerlendirilmesi. ANKEM Derg. 2012;26(3):137-142.
12. Vincent JL, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. Jama. 1995;274(8):639-644.
13. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. Jama. 2009;302(21):2323-2329.
14. Leblebicioglu H, Rosenthal VD, Arikan OA, et al. Device-associated hospital-acquired infection rates in Turkish intensive care units. Findings of the International Nosocomial Infection Control Consortium (INICC). J Hosp Infect. 2007;65(3):251-257.
15. Balın ŞÖ, Şenol AA. Yoğun bakım ünitesinde gelişen hastane infeksiyonlarının değerlendirilmesi. Klimik Dergisi. 2017;30(3):108.
16. Aly NY, Al-Mousa HH, Al Asar el SM. Nosocomial infections in a medical-surgical intensive care unit. Med Princ Pract. 2008;17(5):373-377.
17. Ak O, Batirel A, Ozer S, et al. Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospective cohort study. Med Sci Monit. 2011;17(5):29-34.
18. Qadeer A, Akhtar A, Ain QU, et al. Antibiogram of Medical Intensive Care Unit at Tertiary Care Hospital Setting of Pakistan. Cureus. 2016;8(9):e809.
19. Paramythiotou E, Routsi C. Association between infections caused by multidrug-resistant gram-negative bacteria and mortality in critically ill patients. World J Crit Care Med. 2016;5(2):111-120.
20. Gözütok F, Sarıgüzel FM, Aydın B, ve ark. Kayseri eğitim ve araştırma hastanesi dahiliye yoğun bakım ünitesi'nde 2013 yılında gelişen hastane infeksiyonlarının değerlendirilmesi. Ankem Derg. 2014;28(3):86-93.
21. Göktaş U, Yaman G, Karahocagil M, ve ark. Anestezi yoğun bakım ünitesinde hastane enfeksiyonu etkenleri ve direnç profilinin değerlendirilmesi. Yoğun Bakım Derg. 2010;8(1):13-17.
22. Kula-Atik T, Uzun B. Kan Kültürlerinden İzole Edilen Staphylococcus aureus Suşlarının Metisiline ve Diğer Antimikrobiyal Ajanlara Direnç Durumlarının Değerlendirilmesi. Klimik Journal/Klimik Dergisi. 2020;33(2).
23. Edwards J. Candida Species. In: Mendel GL, Bennett JE, Dolin R, editors. Principles and Practice of Infectious Diseases. Elsevier. Churchill Livingstone, 2010.
24. Ergon MC, Yücesoy M. Evaluation of species distribution of yeasts isolated from intensive care units during the four years period. Mikrobiyol Bul. 2005;39(3):309-318.
25. Kerget F, Karaşahin Ö, Çelik N, ve ark. Yoğun bakım ünitesinde hasta örneklerinden izole edilen kandida türlerinin ve kandidemi risk faktörlerinin değerlendirilmesi. Bozok Tıp Dergisi. 2020;10(4):55-61.

DOI:10.34084/bshr.1498615 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Assessment of Diagnosis of Apical Root Fractures During Tooth Extraction Using Different Radiographic Techniques: An Ex-vivo Study

Diş Çekimi Sırasında Apikal Kök Kırıklarının Tanısının Farklı Radyografik Teknikler Kullanılarak Değerlendirilmesi: Ex-vivo Bir Çalışma

Kübra Öztürk[1], Turan Emre Kuzu[2], Fatma Akkoca[3], Hatice Cansu Kış[4]

[1] Nuh Naci Yazgan University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Kayseri, Türkiye

[2] Nuh Naci Yazgan University, Faculty of Dentistry, Department of Periodontology, Kayseri, Türkiye

[3] Dokuz Eylül University, Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, İzmir, Türkiye

[4] Tokat Gaziosmanpaşa University, Faculty of Dentistry, Department of Orthodontics, Tokat, Türkiye

ORCID ID: Kübra Öztürk: https://orcid.org/0000-0003-4447-0103, Turan Emre Kuzu: https://orcid.org/0000-0002-9478-1578, Fatma Akkoca: https://orcid.org/0000-0002-4522-656X, Hatice Cansu Kış: https://orcid.org/0000-0003-4956-7537

***Sorumlu Yazar / Corresponding Author:** Kübra Öztürk, **e-posta / e-mail:** kbrozturk89@gmail.com

Geliş Tarihi / Received : 10-06-2024 **Kabul Tarihi / Accepted:** 08-07-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Öztürk K., Kuzu T.E., Akkoca F., Kış H.C. Assessment of Diagnosis of Apical Root Fractures During Tooth Extraction Using Different Radiographic Techniques: An Ex-vivo Study. J Biotechnol and Strategic Health Res. 2024;8(1):108-116

Abstract

Aim This study aimed to examine the diagnostic ability of different imaging techniques for apical root fractures that occur during tooth extraction by specialist dentists in different branches.

Material and Method Dry human mandibles used for education at Faculty of Dentistry and teeth extracted for routine treatment were used. After the root lengths were measured using a periodontal probe, the samples were adjusted to different lengths. These specimens were placed on a dry human mandible, and images were obtained and recorded using a periapical device, panoramic device, and computed tomography. Radiographs and recordings were performed by an oral and maxillofacial radiologist. The evaluation process was performed by an oral and maxillofacial radiologist, periodontologist, and oral and maxillofacial surgeon.

Results The diagnosis of 1 mm root presence and absence on periapical radiographs showed significant agreement among all observers. In the presence of 2 mm and 3 mm roots, all observers stated that the roots were present. On the panoramic radiographs, moderate agreement was observed in teeth with a 1 mm root. However, poor agreement between observers was observed for teeth with 2 mm and 3 mm roots. Cone-beam computed tomography (CBCT) was effective for the diagnosis of all observers.

Conclusion Consistent with the literature, the present study showed a higher interobserver agreement in CBCT. However, considering the patient's anxiety during the procedure, the duration of local anesthesia, and the surgeon's fatigue, two-dimensional radiographs are generally preferred over CBCT, which has a longer image processing time. Diagnosis using periapical radiographs was more effective than that using panoramic radiographs.

Keywords Cone-Beam Computerized Tomography; Digital Radiography, Panoramic; Radiography; Tooth Fractures

Özet

Amaç *Bu çalışma, farklı branşlarda uzman diş hekimleri tarafından yapılan diş çekimlerinde meydana gelen apikal kök kırıklarının teşhisi için farklı görüntüleme tekniklerinin tanı yeteneğini incelemeyi amaçlamaktadır.*

Gereç ve Yöntem *Diş Hekimliği Fakültesi'nde eğitim amacıyla kullanılan kuru insan alt çeneleri ve rutin tedavi için çekilen dişler kullanılmıştır. Kök uzunlukları periodontal sonda kullanılarak ölçüldükten sonra örnekler farklı uzunluklara ayarlanmıştır. Bu örnekler kuru bir insan alt çenesine yerleştirilmiş ve bir periapikal cihaz, panoramik cihaz ve konik ışınlı bilgisayarlı tomografi (KIBT) kullanılarak görüntüler alınmış ve kaydedilmiştir. Radyografiler ve kayıtlar bir oral ve maksillofasiyal radyolog tarafından alınmıştır. Değerlendirme süreci bir maksillofasiyal radyolog, periodontolog ve oral ve maksillofasiyal cerrah olmak üzere üç kişi tarafından gerçekleştirilmiştir.*

Bulgular *Periapikal radyograflarda 1 mm kök varlığı/yokluğu konusunda tüm gözlemciler arasında yüksek düzeyde anlamlı uyum olduğu gösterilmiş olup 2 mm ve 3 mm köklerin varlığında, tüm gözlemciler radyografide köklerin görülebildiğini belirtmiştir. Panoramik radyograflarda 1 mm kök varlığı/yokluğu konusunda, tüm gözlemciler arasında orta düzeyde, 2 mm ve 3 mm kök varlığı / yokluğu tanısında ise gözlemciler arasında zayıf bir uyum olduğu gözlenmiştir. KIBT'de ise kök varlığı ve yokluğu tanısında gözlemciler arasında uyum konusunda anlamlı bir farklılık oluşmuştur.*

Sonuç *Literatürle uyumlu olarak, bu çalışma KIBT'de gözlemciler arasında daha yüksek uyum olduğunu göstermiştir. Ancak, işlem sırasındaki hastanın kaygısı, lokal anestezinin süresi ve hekimin yorgunluğu göz önüne alındığında, genellikle daha uzun bir görüntü işleme süresine sahip olan KIBT yerine genellikle iki boyutlu radyografiler tercih edilmektedir. Periapikal radyografiler kullanılarak yapılan tanıların, panoramik radyografiler kullanılarak yapılan tanılardan daha etkili olduğu görülmüştür.*

Anahtar Kelimeler *Konik Işınlı Bilgisayarlı Tomografi; Dijital Radyografi, Panoramik; Radyografi; Diş Kırıkları*

INTRODUCTION

In ideal tooth extraction, complete removal of the tooth with its roots and minimal trauma to the surrounding tissues is one of the most important treatment steps. However, in clinical practice, this goal may not always be achieved and undesirable complications such as fracture of the alveolar bone and/or fracture of the tooth root may occur during tooth extraction.[1] One of the frequently encountered complications during root extraction is root fracture. In such cases, it is the responsibility of the dentist to decide whether to remove the root. The dentist should evaluate the radiation dose required for radiographic follow-up, the distinguishability of the root if left in place, and the potential damage to the alveolar bone and periodontal soft tissues, as well as the resulting problems such as tissue collapse or inability to place implants if the root is extracted. Therefore, dentists should act appropriately.[1-4]

In current literature, it is widely accepted that if the length of the root remaining in the socket after extraction is less than 4-5 mm and the root is not infected or in a superficial position, it can be left in place.[5]

Anatomically, root fractures can be classified as horizontal and vertical root fractures.[6] Radiographic imaging is crucial for the diagnosis and follow-up of root fractures. The periodontal ligament space around the root and changes in trabeculation in the surrounding bone can be determining variables in the diagnosis of root fractures.[7,8] The radiographic diagnosis of horizontal root fractures is easier than that of vertical root fractures. Therefore, several studies have focused on the diagnosis and treatment of vertical root fractures. However, diagnosis of root fractures is challenging. The most affected teeth are mandibular molars and maxillary premolars.[6-8]

This study aimed to compare the diagnosability levels of apical root fractures of different sizes that occur during tooth extraction on periapical radiography, panoramic radiography, and cone beam computed tomography (CBCT) images by dentists with different specialties.

MATERIALS and METHODS

Ethical approval for this study was obtained from the Ethics Boards and Commissions (2022/8104). Dry human mandibles used for educational purposes at the Faculty of Dentistry, Nuh Naci Yazgan University, and extracted teeth with routine treatment indications from patients treated at the same faculty were utilized in the study. The roots of the maxillary anterior, mandibular anterior, and mandibular premolars were used as the jaw locations. With the patient's consent, the teeth were collected and stored in separate containers in neutral-buffered 10% formalin solution. Root lengths were measured using a periodontal probe (Nordent Manufacturing, Inc., IL, USA), and the roots were sectioned using a vibration saw (Dentsply Friadent, Mannheim, Germany) in an aqueous medium. Experimental root segments were created at different lengths, namely, 1, 2, and 3 mm from the apical portion of the extracted teeth. Fifteen root fractures were created for each group. These roots were placed in the edentulous socket in the molar region of the dry human mandible to obtain radiographic images using periapical, panoramic, and CBCT, which were recorded numerically. To mimic the soft tissue, a dry human mandible was coated with wax.

Image acquisition

A film holder was used for periapical radiography, and the recommended dose setting of 60 kVp, 7 mA, and 0.32 seconds of exposure time was applied by the imaging company (KaVo FOCUS, Tuusula, Uusimaa, Finland) (Figure 1). For panoramic radiography, –65-70 kVp, 10 mA, and 16 s exposure was used (Figure 1), and for the CBCT images, a 5 cm × 5 cm field of view (FOV) area was exposed at 80 kVp and 8 mAs using a KaVO OP 3D Pro machine (PaloDEx Group Oy, Tuusula, Finland). Sections with a thickness of 1 mm were obtained for image analysis (Figure 2). The images were evaluated on the same monitor (Dell, 32 inch, color, 1280x1024, 32 bit, LCD) and in the same room.

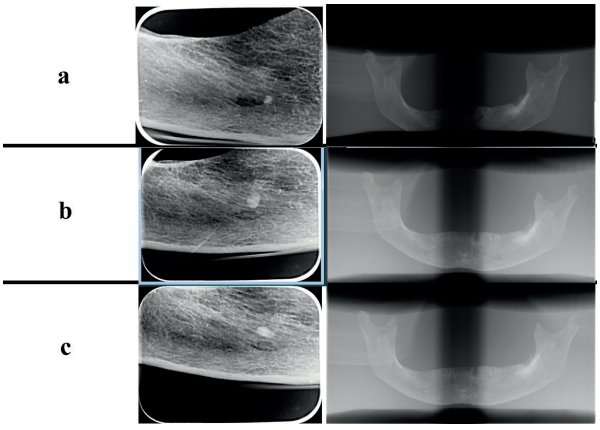

Figure 1. Periapical radiographs of the right third roots of different sizes; Panoramic radiography images of the left third roots of different sizes. a) Presence of 1 mm root (horizontal); b) Presence of 2 mm root (horizontal); c) Presence of 3 mm root (horizontal)

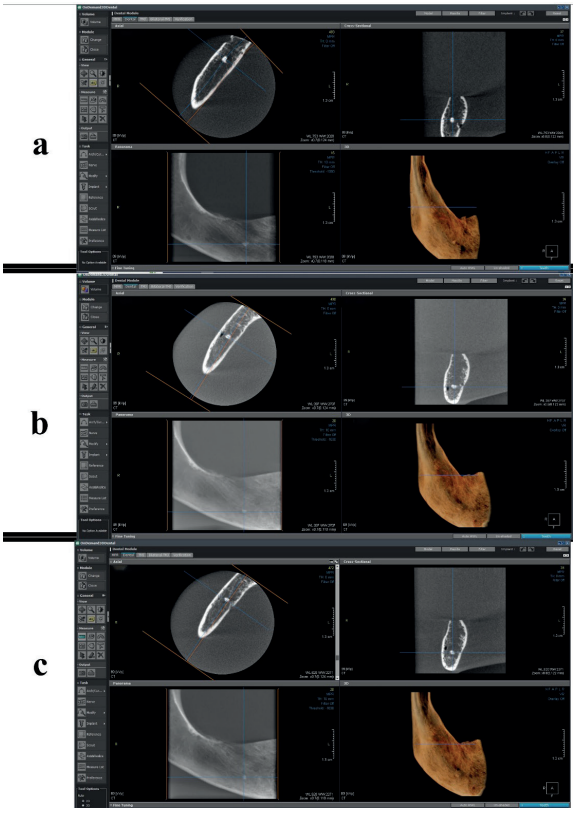

Figure 2. CBCT images of roots of different sizes. a) Presence of 1 mm root (horizontal); b) Presence of 2 mm root (horizontal); c) Presence of 3 mm root (horizontal)

Evaluation of the images

The X-ray imaging procedure and recording were performed by an oral, dental, and maxillofacial radiology specialist, with other observers having no knowledge about the image acquisition process. The radiologist responsible for obtaining the images did not participate in the evaluation. The radiologist who obtained the images did not present the unsuitable images for evaluation to the assessors. Only the images deemed suitable for evaluation were presented to the assessors, and the assessor's response regarding image quality was assessed. The evaluation process was performed by an oral and maxillofacial radiology specialist with 5 years of experience, a periodontics specialist, and an oral and maxillofacial surgeon. All the data were evaluated on the same computer screen in a dimly lit and quiet room. There was a 24-hour time interval between each observer's evaluation of the images. The evaluation criteria were based on the study by Yalda et al.9 The evaluators were asked to make assessments in two categories: the presence or absence of roots. Additionally, their confidence levels regarding the presence of roots were evaluated using a 5-point scale (definitely absent, probably absent, not sure, probably present, and definitely present). Finally, they were instructed to provide one of the three responses regarding image quality: sufficient, borderline, or insufficient. After all evaluations were completed, a random selection of 25% from each sample group was re-evaluated under the same conditions to assess the interobserver reliability.

Statistical analysis

GPower 3.1.9.4 program was used to calculate the sample size. When the effect size was taken as 0.5, α:0.05, β:0.82, the total number of samples for 3 groups was determined as 45.

IBM SPSS software (version 22.0) was used for the statistical analysis of the data. The Fleiss kappa (K) test was used to assess interobserver agreement (Table 1). In the interpretation of the κ statistic, the levels of agreement rec-

ommended by Landis and Koch (1977) were used in Table 1.10 A significance level of 0.05 was set for all analyses.

Table 1. Value Ranges for Interpretation of Kappa Statistic

Kappa Value	Interpretation
<0	Poor agreement
0.01-0.20	Slight agreement
0.21-0.40	Fair agreement
0.41-0.60	Moderate agreement
0.61-0.80	Substantial agreement
0.81-1.00	Almost perfect agreement

Examiner consistency

Five randomly selected images were observed again by the same investigator 2 weeks after the first round of observations. Examiner consistency was assessed for all variables. For three observers, variables were highly similar between the first and second rounds of observations, with correlation coefficients of 0.85–0.96.

RESULTS

There was significant interobserver agreement for the presence or absence of a 1 mm root on periapical radiographs (κ=0.722, p<0.001). For 2 mm and 3 mm roots, all observers reported the presence of roots. The Fleiss kappa values for the diagnosis of root presence on a five-point scale varied by category. The diagnosis of "root definitely present" showed poor interobserver agreement for 1 mm (κ=-0.154, p=0.399) and 2 mm (κ=-0.071, p=0.696) roots, but a significant substantial agreement for 3 mm roots (κ=0.712, p<0.001). The diagnosis of "root probably present" showed poor interobserver agreement for 1 mm (κ=-0.005, p=0.979) and 2 mm (κ=-0.034, p=0.850) roots, and insignificant fair agreement for 3 mm roots (κ=0.259, p=0.156). The diagnosis of "not sure" showed insignificant slight agreement for 1 mm (κ=0.100, p=0.584) and poor agreement for 2 mm and 3 mm roots (κ=-0.034, p=0.850). For the diagnosis of "root probably absent," there was a significant interobserver substantial agreement for 1 mm roots (κ=0.760, p<0.001), but no occurrence of this diagnosis for 2 mm and 3 mm roots. None of the observers reported a "root definitely absent" diagnosis. The image quality of periapical radiographs showed moderate agreement for borderline view and satisfactory view for 1 mm root presence (κ=0.524, p=0.004), fair agreement for inadequate view (κ=0.318, p=0.170), and insignificant slight agreement for satisfactory view (κ=0.050, p=0.785). For 2 mm root presence, all observers reported a satisfactory view, while for the 3 mm root presence, there was a moderate agreement for borderline and satisfactory views (κ=0.464, p=0.011) (Table 2).

Interobserver agreement on panoramic radiography was 1 mm (κ=0.441, p=0.016); moderate agreement in the presence of roots, 2 mm(κ=-0.111, p=0.543), and 3 mm(κ=-0.034, p=0.850) showed poor agreement in the presence of roots. According to the categories on the 5th scale, 3 mm (κ=0.659, p<0.001) in the diagnosis of "root definitely present," the presence of roots showed a significant substantial agreement and became the category with the highest agreement among all categories. The presence of 1 mm (κ=0.457, p=0.012) roots showed moderate agreement, while the presence of 2 mm (κ=0.330, p=0.070) roots showed fair agreement. Two mm(κ=0.365, p=0.046), and 3 mm(κ=0.280, p=0.125) for the diagnosis of "root probably present," a fair agreement was observed in the presence of the root, 1 mm(κ=-0.111, p=0.543)), and there was poor agreement in the presence of roots. For the diagnosis of "not time," 1 mm (κ=0.040, p=0.827), root presence is insignificant, 2 mm(κ=0.-200, p=0.273), and 3 mm(κ=0.-111, p= 0.543), there was poor agreement in the presence of root. The root probably absent "root probably absent" and "root definitely absent" diagnoses have no response for 2 mm and 3 mm, while "root probably absent" diagnosis in the presence of 1 mm root is a poor agreement (κ=-0.111 p=0.543), "root definitely absent" diagnosis was insignificant. (κ=0.464, p=0.011). The image quality of panoramic radiographs was moderate for 1 mm roots, with views of "sufficient" (κ=0.426, p=0.020) and "insufficient" (κ=0.583, p=0.012). "borderline" (κ=0.040,

p=0.827) showed insignificant agreement. In 2 mm roots, "insufficient" (κ=0.760, p<0.001) showed significant substantial agreement, "sufficient" (κ=0.330, p=0.070) showed fair agreement, and "borderline" showed insignificant agreement. In 3 mm roots, "sufficient" (κ=0.683 p<0.001) showed significant substantial agreement, while "insufficient" (κ=0.464, p=0.011) and "borderline" (κ=0.441, p=0.016) showed moderate agreement. (Table 3.)

Table 2. Statistical analysis of interobserver agreement for different root lengths on periapical radiographs (Fleiss kappa test)

PERIAPICAL			Root length			
Diagnosis	Yes	Fleiss kappa (%95 CI) p value	1 mm 0.722 (0.711-0.734) <0.001	2 mm All observer	3 mm All observer	Total 0.808 (0.801-0.814) <0.001
	of root	Fleiss kappa (%95 CI) p value	0.722 (0.711-0.734) <0.001	None	None	0.808 (0.801-0.814) <0.001
	Total	Fleiss kappa (%95 CI) p value	0.722 (0.711-0.734) <0.001	None	None	0.808 (0.801-0.814) <0.001
Diagnosis of root (Five point scale)	Root definitely present	Fleiss kappa (%95 CI) p-value	-0.154 (-0.165- -0.142) 0.399	-0.071 (-0.046- -0.060) 0.696	0.712 (0.700-0.723) <0.001	0.661 (0.654-0.667) <0.001
	Root probably present	Fleiss kappa (%95 CI) p-value	-0.005 (-0.016-0.007) 0.979	-0.034 (-0.046- -0.023) 0.850	0.259 (0.248-0.271) 0.156	0.200 (0.193-0.207) 0.058
	Not sure	Fleiss kappa (%95 CI) p-value	0.100 (0.089-0.111) 0.584	-0.034 (-0.046- -0.023) 0.850	-0.034 (-0.046- -0.023) 0.850	0.231 (0.224-0.237) 0.029
	Root probably absent	Fleiss kappa (%95 CI) p-value	0.760 (0.749-0.771) <0.001	None	None	0.788 (0.782-0.795) <0.001
	Root definitely absent	Fleiss kappa (%95 CI) p-value	None	None	None	None
	Total	Fleiss kappa (%95 CI) p-value	0.154 (0.147-0.161) 0.170	-0.053 (-0.062- -0.044) 0.713	0.439 (0.430-0.449) 0.004	0.461 <0.001
Image quality	Insufficient	Fleiss kappa (%95 CI) p-value	0.318 (0.307-0.330) 0.081	None	None	0.451 (0.445-0.458) <0.001
	Borderline	Fleiss kappa (%95 CI) p-value	0.524 (0.512-0.535) 0.004	None	0.464 (0.453-0.476) 0.011	0.586 ,(0.0579-0.592) <0.001
	Sufficient	Fleiss kappa (%95 CI) p-value	0.050 (0.038-0.061) 0.785	All observer	0.464 (0.453-0.476) 0.011	0.466 (0.579-0.592)
	Total	Fleiss kappa (%95 CI) p-value	0.283 (0.275-0.291) 0.030	None	0.464 (0.453-0.476) 0.011	0.499 (0.494-0.504) <0.001
Asymptotic 95% Confidence Interval p<0.05						

Table 3. Statistical analysis of interobserver agreement for different root lengths on panoramic radiographs (Fleiss kappa test)

PERIAPICAL			Root length			
Diagnosis of root	Yes	Fleiss kappa (%95 CI) p value	1 mm 0.441 (0.430-0.452) 0.016	2 mm -0.111 (-0.123- -0.100) 0.543	3 mm -0.034 (-0.046- -0.023) 0.850	Total 0.275 (0.268-0.282) 0.009
	of root	Fleiss kappa (%95 CI) p value	0.441 (0.430-0.452) 0.016	-0.111 (-0.123- -0.100) 0.543	-0.034 (-0.046- -0.023) 0.850	0.275 (0.268-0.282) 0.009
	Total	Fleiss kappa (%95 CI) p value	0.441 (0.430-0.452) 0.016	-0.111 (-0.123- -0.100) 0.543	-0.034 (-0.046- -0.023) 0.850	0.275 (0.268-0.282) 0.009
Diagnosis of root (Five point scale)	Root definitely present	Fleiss kappa (%95 CI) p-value	0.457 (0.446-0.468) 0.012	0.330 (0.319-0.342) 0.070	0.659 (0.648-0.671) <0.001	0.486 (0.479-0.492) <0.001
	Root probably present	Fleiss kappa (%95 CI) p-value	-0.111 (-0.123- -0.100) 0.543	0.365 (0.354-0.377) 0.046	0.280 (0.269-0.291) 0.125	0.275 (0.268-0.281) 0.009
	Not sure	Fleiss kappa (%95 CI) p-value	0.040 (0.029-0.051) 0.827	-0.200 (-0.211- -0.189) 0.273	-0.111 (-0.123- -0.100) 0.543	-0.079 (-0.86- -0.072) 0.454
	Root probably absent	Fleiss kappa (%95 CI) p-value	-0.111 (-0.123- -0.100) 0.543	None	None	-0.304 (-0.04- -0.028) 0.744
	Root definitely absent	Fleiss kappa (%95 CI) p-value	0.464 (0.453-0.476) 0.011	None	None	0.489 (0.482-0.495) <0.001
	Total	Fleiss kappa (%95 CI) p-value	0.202 (0.195-0.209) 0.059	0.219 (0.211-0.228) 0.106	0.372 (0.363-0.381) 0.008	0.277 (0.272-0.281) <0.001
Image quality	Insufficient	Fleiss kappa (%95 CI) p-value	0.583 (0.572-0.595) <0.001	0.760 (0.749-0.771) <0.001	0.464 (0.453-0.476) 0.011	0.640 (0.634-0.647) <0.001
	Borderline	Fleiss kappa (%95 CI) p-value	0.040 (0.029-0.051) 0.827	0.048 (0.036-0.059) 0.794	0.441 (0.430-0.452) 0.016	0.193 (0.186-0.199) 0.068
	Sufficient	Fleiss kappa (%95 CI) p-value	0.426 (0.414-0.437) 0.020	0.330 (0.319-0.342) 0.070	0.683 (0.671-0.694) <0.001	0.480 (0.473-0.487) <0.001
	Total	Fleiss kappa (%95 CI) p-value	0.372 (0.364-0.381) 0.006	0.331 (0.322-0.339) 0.015	0.557 (0.547-0.566) <0.001	0.421 (0.416-0.426) <0.001
Asymptotic 95% Confidence Interval p<0.05						

In CBCT examinations, all observers confirmed the presence of roots in all data, and the image quality was satisfactory.

DISCUSSION

This study provides information on the diagnostic ability of different imaging techniques for apical root fractures during tooth extraction. The results of this study show that dentists can diagnose apical root fractures more accurately on periapical radiographs. However, computed tomography images allow dentists to diagnose apical root fractures more accurately than panoramic radiography and periapical radiography.

Regarding root fractures, we came across the literature on vertical and horizontal root fractures, and radiological studies have focused on the diagnosis of these root fractures.[11,12] When the current literature is examined, no study has specifically focused on retained root fractures and apical root fractures that occur during tooth extraction. The literature primarily consists of in vitro and ex vivo studies that simulate root fractures using mechanical force with a hammer, or consider it as the gold standard.[13] In addition to vertical and horizontal root fractures, tooth roots can also fracture apically during tooth extraction. The clinician must then decide whether to leave the broken root fragment in place or to extract it. The decision to remove root fragments incidentally found on radiographs or those fractured during extraction procedures should be made based on the situation.[14] Although OPG and CBCT are not the first imaging methods applied in the clinical routine, an extra-oral film will be more atraumatic in case of a complication encountered during the procedure, considering both intra-oral bleeding and the patient's agitation.

Dentists and oral surgeons have developed various approaches for dealing with apical fractures that occur during tooth extraction, such as closed surgical techniques, open surgical techniques, the endodontic file technique, the local anesthetic needle technique, the vertical extraction technique, and the Benex device. Radiographic methods are important for analyzing the remaining roots. When dental imaging methods are compared in terms of radiation dose, periapical radiographs have the least radiation dose, while much less radiation dose is used in panoramic radiographs in full mouth imaging. Principles have been developed to reduce the radiation dose in CBCT radiographs. No matter which technique is preferred, movement of the patient during imaging negatively affects the image quality. To prevent this, it is necessary to fix the head. Its use is limited in some dental practices due to the sensitivity and contrast resolution of CBCT devices, artefacts and poor soft tissue image quality, as well as their high cost. Although CBCT with its increasing availability and popularity is more effective in analyzing the specific depth and location of remaining root fragments, traditional two-dimensional radiographs are still primarily preferred.[15-17] In this study, CBCT was found to be effective for diagnosis in all observers by the literature. However, in clinical practice, two-dimensional radiographs are often preferred over CBCT, which has a long image processing time, considering factors such as anxiety in the patient during the procedure, the duration of local anesthesia, and the fatigue of the surgeon. CBCT was compared with these radiographs to reflect clinical reality. Periapical radiographs showed more consistent results in the diagnosis by different observers on two-dimensional radiographs. Although this study tried to reflect soft tissue thickness, the patient factor should be taken into consideration in the clinic and head stabilization should be ensured. Aksever et al. found that CBCT images were more effective than periapical radiographs in an ex vivo study simulating horizontal root fractures.[18] However, no significant difference was found between conventional radiography, digital radiography, and CBCT images in the diagnosis of vertical root fractures in the anterior region of the mandible.[19]

Patient safety and radiation dose issues must be carefully considered when using CBCT. Although it reduces com-

plications and increases patient safety with 3D analysis of anatomical structures, the increase in radiation dose cannot be ignored. Application of low-dose CBCT protocols reduces this disadvantage while maintaining diagnostic performance.[20] Yalda et al. investigated the use of CBCT at different doses for diagnosing root fractures and attempted to develop a radiographic protocol for lower-dose usage. However, due to the ex-vivo model not reflecting soft tissue and anatomical variations seen in clinical settings, it was noted that a standard radiation dose suitable for clinical use could not be established and that reducing the recommended X-ray parameters by 20% would not affect the accuracy of diagnosis.[9] Ex-vivo studies do not reflect clinically ideal results. However, in vivo studies have ethical drawbacks due to excessive radiation exposure.[21] Due to ethical concerns, we could not perform this study in vivo. To minimize soft tissue deficiencies in the ex vivo study, we covered the dry mandible with wax.

In this study, observations of a periodontologist, radiologist, and oral and maxillofacial surgeon were analyzed. Selection bias from observers should also be considered in diagnostic studies. The experience and expertise of the observer can influence the results.[13] For this reason, observers with different areas of expertise and at least 5 years of experience in the field were determined.

The limitations of this study are as follows: The diagnoses may differ from those made in a real clinical setting. The radiographic images used in this study may differ from those obtained in clinical settings. Only the mandibular posterior region with a thick cortical bone was simulated in this study. Therefore, the results may vary among teeth in different regions. Root fractures were created in different sizes; however, different types of root fractures were not evaluated in this study.

CONCLUSION

Complications, such as root fractures, may arise during tooth extraction, and the dentist may have to decide whether to leave or remove the root. In these types of root fractures, CBCT was found to be more effective for diagnosis than two-dimensional radiographs, with periapical radiography being more effective than panoramic radiography.

Acknowledgements

Thank you to the radiology technicians at Nuh Naci Yazgan University.

Ethical Approval

The ethical approval of this study was approved by the Nuh Naci Yazgan University Scientific Research and Publication Ethics Committee in April 2022 with the decision number 2022/8104.

Peer-review

Externally and internally peer-reviewed.

Authorship Contributions

Concept: K.Ö., H.C.K.; Design: K.Ö., H.C.K.; Data collection or Processing: H.C.K; Analysis or interpretation: K.Ö., T.E.K., F.A.; Literature Search: K.Ö., F.A.; Writing: K.Ö.,T.E.K,F.A.

Conflicts of Interest Statement

There is no potential for bias or conflict.

Funding

This is research received no specific grant from any public, commercial, or for-profit funding agency.

Data Availability Statement

The datasets created and analyzed during the current study are available from the corresponding author upon request.

References

1. El-Kenawy MH, Ahmed WM. Comparison between physics and conventional forceps in simple dental extraction. J Maxillofac Oral Surg. 2015;14(4):949-955. doi:10.1007/s12663-015-0765-6.
2. Ahel V, Cabov T, Spalj S et al. Forces that fracture teeth during extraction with mandibular premolar and maxillary incisor forceps. Br J Oral Maxillofac Surg. 2015;53(10):982-987. doi: 10.1016/j.bjoms.2015.08.007.
3. Kapila S, Kaur T, Bhullar RS et al. Use of physics forceps in atraumatic orthodontic extractions of bilateral premolars: A randomized control clinical study. J Maxillofac Oral Surg. 2020;19(3):347-354. doi: 10.1007/s12663-020-01347-6
4. Krug R, Soliman S, Krastl G. Intentional replantation with an atraumatic extraction system in teeth with extensive cervical resorption. J Endod. 2019;45(11):1390-1396. doi: 10.1016/j.joen.2019.07.012.
5. Yoldaş S, Bodur H, Küçükkurt S. Horizontal kök kırıklı bir dişin dekoronasyon ile tedavisi: olgu bildirimi. Acta Odontologica Tursica. 2016;33(2):91-94. doi: 10.17214/aot.66530.
6. Popescu SM, Diaconu OA, Scrieciu M, et al. Root fractures: epidemiological, clinical and radiographic aspects. Rom J Morphol Embryol. 2017;58(2):501-506.
7. Lustig JP, Tamse A, Fuss Z. Pattern of bone resorption in vertically fractured, endodontically treated teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000;90(2):224-227. doi: 10.1067/moe.2000.107445.
8. Tamse A, Kaffe I, Lustig J et al. Radiographic features of vertically fractured endodontically treated mesial roots of mandibular molars. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(6):797-802. doi: 10.1016/j.tripleo.2005.09.014.
9. Andraws Yalda F, Theodorakou C, Clarkson RJ, et al. Determination of a cone-beam CT low-dose protocol for root fracture diagnosis in non-endodontically treated anterior maxillary teeth. Dentomaxillofac Radiol. 2022;51(2):20210138. doi: 10.1259/dmfr.20210138.
10. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;(1):159-174. doi: 10.2307/2529310.
11. Cohen S, Blanco L, Berman L. Vertical root fractures: clinical and radiographic diagnosis. The Journal of the American Dental Association. 2003;134(4):434-41. doi: 10.14219/jada.archive.2003.0192.
12. Kamburoğlu K, Ilker Cebeci A, Gröndahl HG. Effectiveness of limited cone-beam computed tomography in the detection of horizontal root fracture. Dental Traumatology. 2009;25(3):256-261. doi: 10.1111/j.1600-9657.2009.00770.x.
13. Salineiro FCS, Kobayashi-Velasco S, Braga MM et al. Radiographic diagnosis of root fractures: a systematic review, meta-analyses and sources of heterogeneity. Dentomaxillofac Radiol. 2017;46(8):20170400. doi: 10.1259/dmfr.20170400.
14. Nayyar J, Clarke M, O'Sullivan M et al. Fractured root tips during dental extractions and retained root fragments. A clinical dilemma? Br Dent J. 2015;218(5):285-290. doi: 10.1038/sj.bdj.2015.147.
15. Samur S. Dişhekimliğinde cone beam bilgisayarlı tomografi. ADO klinik bilimler dergisi. 2009;3:346-351.
16. Benton PN, Chang P. Oral Surgery, Extraction of Roots. [Updated 2023 Feb 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK589696/
17. Baş A, Derelioğlu SŞ. Çocuk diş hekimliğinde kullanılan farklı radyografi tekniklerinde radyasyon dozunu azaltıcı önlemler. Current Research in Dental Sciences.2022;32:231-238. doi: 10.17567/ataunidfd.1038856.
18. Avsever H, Gunduz K, Orhan K, et al. Comparison of intraoral radiography and cone-beam computed tomography for the detection of horizontal root fractures: an in vitro study. Clin Oral Investig. 2014;18(1):285-292. doi: 10.1007/s00784-013-0940-4.
19. Kambungton J, Janhom A, Prapayasatok S et al. Assessment of vertical root fractures using three imaging modalities: cone beam CT, intraoral digital radiography and film. Dentomaxillofac Radiol. 2012;41(2):91-95.
20. Kaaber L, Matzen LH, Spin-Neto R, et al. Low-dose, standard, and high-resolution cone beam computed tomography for alveolar bone measurements related to implant planning: An ex vivo study in human specimens. Clin Oral Implants Res. 2024. doi: 10.1111/clr.14326. Online ahead of print.
21. Keyzer C, Tack D, de Maertelaer V et al. Acute appendicitis: comparison of low-dose and standard-dose unenhanced multi-detector row CT. Radiology. 2004;232(1):164-172. doi: 10.1148/radiol.2321031115.

DOI:10.34084/bshr.1510840 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Evaluation of COVID 19 Patients Who Developed after COVID 19 Vaccination

COVID 19 Aşısı Sonrası Gelişen COVID 19 Hastalarının Değerlendirilmesi

Gülsüm Kaya[1], Pınar Özkan Oskay[2], Nesrin Kebabcı Mert[3], Şeyma Trabzon[4], Zeynep Ergenç[5], Hasan Ergenç[5], Osman Karakuş[6], ✉ Cengiz Karacaer[7]

[1] University of Health Sciences, İnstitute of Health Sciences, Dep. of Medical Microbiology; Dep. of Support and Quality Directorate, Yalova Training and Research Hospital, Türkiye.

[2]Sakarya Yenikent State Hospital, Infection Control Committee, Sakarya, Türkiye.

[3]Sakarya Yenikent State Hospital, Department of Infectious Diseases and Clinical Microbiology, Sakarya, Türkiye.

[4]Sakarya University Vocational School of Health Services, Emergency Medical Technician Program, Sakarya, Türkiye

[5]Yalova Training and Research Hospital, Department of Internal Medicine, Yalova, Türkiye

[6]Yalova Provincial Health Directorate, Anesthesia and Reanimation Department, Yalova, Türkiye

[7]Sakarya Training and Research Hospital, Department of Internal Medicine, Sakarya, Türkiye

ORCID ID: Gülsüm Kaya: https://orcid.org/0000-0003-2517-5512, Pınar Özkan Oskay: https://orcid.org/0000-0003-1327-6025, Nesrin Kebabcı Mert: https://orcid.org/0009-0001-3531-6414, Şeyma Trabzon: https://orcid.org/0000-0001-9030-7804, Zeynep Ergenç: https://orcid.org/0000-0001-7598-4508, Hasan Ergenç: https://orcid.org/0000-0002-1595-5825, Osman Karakuş: https://orcid.org/0009-0009-8590-8803, Cengiz Karacaer: https://orcid.org/0000-0001-6951-899X,

***Sorumlu Yazar / Corresponding Author:** Cengiz Karacaer, **e-posta / e-mail:** karacaerc@yahoo.com

Geliş Tarihi / Received : 04-07-2024 **Kabul Tarihi / Accepted:** 27-07-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Kaya G, Özkan-Oskay P., Kebabcı-Mert N., Trabzon Ş., Ergenç Z., Ergenç H., Karakuş O., Karacaer C. Evaluation of COVID 19 Patients Who Developed after COVID 19 Vaccination. J Biotechnol and Strategic Health Res. 2024;8(1):117-124

Abstract

Aim This study aims to evaluate the sociodemographic and clinical characteristics of patients with COVID-19 that developed after COVID-19 vaccination.

Material and Method The study was conducted retrospectively in a public hospital between July 5 and August 5, 2021. Patients whose SARS-CoV-2 positivity was confirmed by molecular methods and who were hospitalized due to COVID-19 and who had a history of COVID-19 vaccination were included. Sociodemographic information and clinical observation results of the patients were recorded.

Results 49.09% of the patients were female and the median age was 72.00 [62.00-79.00] years. 70.45% of patients had a chronic disease and 37.27% were constantly using medication. 82.73% of patients received the CoronaVac vaccine and 8.18% received COVID-19 mRNA vaccine; 9.09% had received both vaccines. 66.82% of patients received two doses of COVID-19 vaccine, 26.82% received three doses, 5.45% received one dose and 0.91% received four doses of COVID-19 vaccine. When the infection findings at the time of admission to the hospital are evaluated, the most common symptoms in patients are dyspnea (89.55%), cough (45.45%), weakness (37.73%), malaise (22.27%) and fatigue-exhaustion. (20.00%); 95% of them had COVID-19 findings in their lung imaging reports. 99.55% of patients receive oxygen therapy; 62.73% were connected to mechanical ventilation. 91.82% of patients were receiving steroid treatment, 89.09% were receiving favipiravir treatment, and 98.64% were receiving anticoagulant; 96.82% had received antibiotic treatment. 38.64% of patients were discharged; 61.36% died.

Conclusion The average age of patients who contracted COVID-19 disease after the COVID-19 vaccine was high and the majority had chronic diseases. In addition, patients received the with a high rate of CoronaVac vaccine and received a maximum of two doses; It was observed that they did not receive the reminder dose of vaccination. Mortality and morbidity can be reduced by creating successful vaccination programs as well as protective measures in the fight against COVID-19.

Keywords COVID-19 disease, COVID-19 vaccine, patient characteristics, vaccine

Özet

Amaç *Bu çalışmanın amacı, COVID-19 aşısı sonrası gelişen COVID-19 hastalarının sosyodemografik ve klinik özelliklerini değerlendirmektir.*

Gereç ve Yöntem *Çalışma, 5 Temmuz-5 Ağustos 2021 tarihleri arasında bir devlet hastanesinde retrospektif olarak gerçekleştirildi. SARS-CoV-2 pozitifliği moleküler yöntemlerle doğrulanan ve COVID-19 nedeniyle hastaneye yatırılan, COVID-19 aşısı yapılma öyküsü olan hastalar dahil edildi. Hastaların sosyodemografik bilgileri ve klinik gözlem sonuçları kaydedildi.*

Bulgular *Hastaların %49,09'u kadındı ve ortanca yaş 72,00 [62,00-79,00] yıldı. Hastaların %70,45'inin kronik hastalığı vardı ve %37,27'si sürekli ilaç kullanıyordu. Hastaların %82,73'üne CoronaVac aşısı, %8,18'ine ise COVID-19 mRNA aşısı yapılmıştı; %9,09'u her iki aşıyı da almıştı. Hastaların yüzde 66,82'sine iki doz, yüzde 26,82'sine üç doz, yüzde 5,45'ine tek doz ve yüzde 0,91'ine dört doz aşı yapılmıştı. Hastaneye başvuru anındaki enfeksiyon bulguları değerlendirildiğinde hastalarda en sık görülen semptomlar nefes darlığı (%89,55), öksürük (%45,45), halsizlik (%37,73), kırgınlık (%22,27) ve yorgunluk-bitkinlikti. (%20,00). Hastaların %95'inin akciğer görüntüleme raporlarında COVID-19 bulguları vardı. Hastaların %99,55'i oksijen tedavisi alırken; %62,73'ü mekanik ventilasyona bağlanmıştı. Hastaların %91,82'si steroid tedavisi, %89,09'u favipiravir tedavisi, %98,64'ü antikoagülan alırken; %96,82'si antibiyotik tedavisi almıştı. Hastaların %38,64'ü taburcu olurken; %61,36'sı ex oldu.*

Sonuç *COVID-19 aşısı sonrası COVID-19 hastalığına yakalanan hastaların yaş ortalamasının yüksek olduğu ve çoğunluğunun kronik hastalığı vardı. Ayrıca hastaların CoronaVac aşısı olduğu ve en fazla iki doz aşı olup; hatırlatma dozu aşı olmadıkları görüldü. COVID-19 ile mücadelede korunma önlemlerinin yanında başarılı aşı programlarının oluşturulmasıyla mortalite ve morbidite azaltılabilir.*

Anahtar Kelimeler *COVID-19 hastalığı, COVID-19 aşısı, hasta özellikleri, aşı,*

INTRODUCTION

Vaccines are important tools to improve health around the world, but the burden of death and disease caused by infectious diseases remains unacceptable. Even if there are vaccines that can prevent infectious diseases, limitations such as high costs, logistics difficulties, limited cold chain capacity, and chronic conditions that will cause the immune response of patients to decrease may reduce the effectiveness of the vaccine's effectiveness.[1] COVID-19 is an infectious disease that causes a pandemic, and the total cumulative global number of cases as of May 2024 is 776 million.[2] Many complications such as lung involvement, acute respiratory distress syndrome (ARDS), cytokine release syndrome, septic shock, gastrointestinal disorders, kidney diseases, hematological, neurogenic, and psychogenic disorders have been reported in association with this infectious disease, and multiple organ failure has been reported most frequently in patients with predisposing diseases.[3] Antiviral, anti-inflammatory, immunomodulatory agents and anticoagulants have been used to treat COVID-19, which manifests itself in different clinical severities.[4-7] Despite all the efforts made in the management of COVID-19 infection, the lack of a specific pharmacotherapy causes difficulties.[8] COVID-19 vaccines are important to reduce and prevent the severity and contagiousness of SARS-COV-2 infection.[9]

As of January 2021, vaccines such as BNT162b2, Moderna mRNA-1273, vector-based vaccines ChAdOx1 nCoV-19 Oxfort-AstraZeneca, Gam-COVID-Vac Sputnik-V, Covilo/BBIBP-CorV/Sinopharm by Pfizer-BioNTech are for emergency use in many countries. It started to be implemented within the scope of permission.[10,11] Turkovac (ERUCoV) is an inactivated SARS-CoV-2 vaccine developed and started to be implemented in Turkey in February 2022.[12] The role of these introductory COVID-19 vaccines in preventing SARS-CoV-2 infection and/or reducing hospitalization and mortality rates has been confirmed.[13,14] After the introduction of vaccines, the emergence of new variants has raised concerns about the decrease in vaccine effectiveness as a result of increased contagiousness. Post-vaccination infections may induce nonsterile immune response by promoting vaccine escape mutations and pose a serious risk.[11] It has been stated that post-vaccination infection is less severe than in unvaccinated individuals, but mortality remains high in case of hospitalization.[15] In the United Kingdom, the mortality rate for individuals hospitalized with COVID-19 within 21 days of vaccination has been reported to be 27%, which is similar to mortality rates observed during vaccination.[16]

Assessment of individuals who contract COVID-19 after vaccination is important for clinical utility in facilitating identification of risk groups for intervention, estimating medical resource requirements, and informing appropriate testing guidelines. There are limited studies in the literature evaluating COVID-19 cases after vaccination. This study aims to evaluate patients with COVID-19 that developed after COVID-19 vaccination.

MATERIALS and METHODS

Place and time of the study

The study was conducted at Sakarya Yenikent State Hospital (SYDH) between July 5 and August 5, 2021. SYDH is a secondary care hospital with a total of 255 beds, including 50 intensive care unit (ICU) beds.

Collection of patient information

The population of the study consisted of patients hospitalized in the SYDH COVID-19 clinic and intensive care unit (ICU). To work; Patients who were i) vaccinated against COVID-19, ii) - whose SARS-CoV-2 positivity was confirmed by molecular methods, and iii) - who received inpatient treatment in a clinic or ICU due to COVID-19 in the hospital and whose file records were complete were included. Sociodemographic information of the patients, COVID-19 vaccine information, COVID-19 infection findings at the time of admission to the hospital, laboratory examination and radiological imaging data, and clinical observation results were taken from the hospital informa-

tion management system and recorded in the standard form created by the researcher.

Evaluation of data

Data analysis was performed by using SPSS 22 for Windows (Statistical Package for Social Science, SPSS® Corp., Armonk, NY, USA). The variables were analyzed in terms of normality distribution using the Kolmogorov-Simirnov test. Depending on the normality of the distribution, continuous variables were reported as mean and standard deviation or median and interquartile range. Categorical variables were expressed using frequency tables.

Ethics committee approval for this study was received from Sakarya University Faculty of Medicine Ethics Committee with number E-71522473-050.01.04-39900-357.

RESULTS

Of the 220 patients included in the study, 49.09% were women and the median age was 72.00 [62.00-79.00] years. 92.73 of the patients were primary school graduates and 79.09% lived in the district. 70.45% of the patients had a chronic disease, and the three most common chronic diseases were hypertension (76.13%), diabetes mellitus (50.32%) and heart failure (18.71%). 37.27% of the patients were constantly using medication (Table 1).

Table 1. Sociodemographic information of the patients and clinical information about COVID-19 infection

Features		n/mean (min-max)/median [Inter-quartile range]
The average age		7200 [62.00-79.00]
< 65		65 (29.54)
> 65		145 (70.46)
Age	18-34	2 (0.91)
	35-49	11 (5.00)
	50-64	52 (23.64)
	65-80	105 (47.73)
	> 80	50 (22.73)
Sex	Female	108 (49.09)
	Male	112 (50.91)
Educational background	Primary education	204 (92.73)
	High school	11 (5.00)
	University	5 (2.27)
Place of residence	Town center	43 (19.55)
	District	174 (79.09)
	Bay	3 (1.36)
Chronic Disease	Yes	155 (70.45)
	No	65 (29.55)
Distribution of chronic diseases	Hypertension	118 (76.13)
	Diabetes	78 (50.32)
	Heart failure	29 (18.71)
	Coronary artery disease	18 (1.61)
	COPD	10 (6.45)
	Malignancy	10 (6.45)
	Asthma	7 (4.52)
	Hypothyroidism	4 (2.58)
Continuous drug use	Yes	82 (37.27)
	No	138 (62.73)
Received COVID-19 vaccinations	Coronavac (Inactive vaccine)	182 (82.73)
	BNT162b2 (mRNA vaccine)	18 (8.18)
	Coronavac+ BNT162b2	20 (9.09)
COVID-19 vaccine doses	1 dose	12 (5.45)
		147 (66.82)
	3 doses	59 (26.82)
	4 doses	2 (0.91)
Vaccine doses in	1 doses	9 (4.09)
	COVID-19 cases	148 (67.27)
	3 doses	63 (28.63)
	4 doses	1 (0.45)

COVID-19 Clinic	Dyspnea	197 (89.55)
	Cough	100 (45.45)
	Weakness	83 (37.73)
	Disappointment	49 (22.27)
	Fatigue-Exhaustion	44 (20.00)
	Fire	28 (12.73)
	Unrest	11 (5.00)
	Confusion	11 (5.00)
	Muscle-Joint pain	8 (3.64)
	Pain in throat	5 (2.27)
	Chills-Trembling	5 (2.27)
	Sleep Disorders	4 (1.82)
	Stinging in chest	4 (1.82)
	Runny nose	4 (1.82)
	Insomnia	3 (1.36)
	Chest pain	2 (0.91)
	Fainting-Seizure	2 (0.91)
	Numbness	2 (0.91)
	Back-Waist pain	2 (0.91)
	Diarrhea	2 (0.91)
	Headache	1 (0.45)
	Blood pressure imbalance	1 (0.45)
	Sweating	1 (0.45)
	Nausea	1 (0.45)
	Visual impairment	1 (0.45)
	Loss of taste and smell	0
	Dry Mouth	0
	Stomach ache	0
	Heart palpitations	0
COVID-19 finding on CT	Yes	209 (95.00)
		11 (5.00)
SPO2 value		91.00 [86.00-95.00]
Oxygen therapy	Yes	219 (99.55)
	No	1 (0.45)
Intubation	Yes	138 (62.73)
	No	82 (37.27)
Taking steroids	Yes	202 (91.82)
	No	18 (8.18)
Faviripavir	Yes	196 (89.09)
	No	24 (10.91)
Antibiotic	Yes	213 (96.82)
	No	7 (3.18)
Anticoagulant	Yes	217 (98.64)
		3 (1.36)
Patient's outcome	Discharge	85 (38.64)
	Ex	135 (61.36)

82.73% of the patients received the CoronaVac (Sinovac Life Sciences, Beijing, China) vaccine, which is an inactive SARS-CoV-2 vaccine, and 8.18% received the COVID-19 mRNA vaccine (BNT162b2) developed in partnership with Pfizer-BioNTech; 9.09% had received both vaccines (Figure 1).

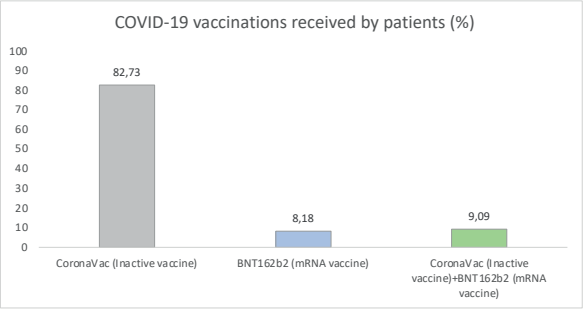

Figure 1. COVID-19 vaccinations received by patients

When the COVID-19 vaccine doses of the patients were evaluated, 66.82% received two doses, 26.82% received three doses, 5.45% received one dose and 0.91% received four doses of COVID-19 vaccine; 67.27% contracted COVID-19 infection after two doses of vaccine, 28.63% after three doses of vaccine, 4.9% after one dose of vaccine and 0.45% after four doses of COVID-19 vaccine. When the infection findings at the time of admission to

the hospital are evaluated, the most common symptoms in the patients are dyspnea (89.55%), cough (45.45%), weakness (37.73%), malaise (22.27%) and fatigue-exhaustion. (20.00%) (Table 1). 95% of the patients had COVID-19 findings in their lung imaging reports. 99.55% of patients receive oxygen therapy; 62.73% were connected to mechanical ventilation. 91.82% of the patients were receiving steroid treatment, 89.09% were receiving favipiravir treatment, and 98.64% were receiving anticoagulant; 96.82% had received antibiotic treatment. 38.64% of the patients were discharged; 61.36% died (Table 1). Information on the laboratory blood test parameters of the patients is shown in Table 2.

Table 2. Distribution of laboratory parameters of the COVID-19 patients

WBC K/uL	9.13 [6.14-12.06]	Glucose mg/dL	167.00 [120.25-224.00]
RBC M/uL	4.25 [3.81-4.60]	Urea mg/dL	55.50 [36.00-84.75]
HGB g/dL	12.05 [10.92-13.47]	Uric acid mg/dL	6.10 [4.70-8.00]
HCT %	37.00 [33.17-40.70]	Creatinine mg/dl	1.00 [0.74-1.52]
PLT K/uL	200.90 [155.00-257.00]	AST U/L	32.50 [24.00-49.75]
MCH pg	29.10 [27.70-30.40]	ALT U/L	22.00 [15.00-35.00]
MCHC g/dL	32.70 [32.00-33.20]	CK	88.50 [51.00-205.50]
RDW %	14.30 [13.70-15.80]	CK-MB	19.00 [13.00-25.00]
MCV fl	89.10 [85.20-92.10]	LDH U/L	342.00 [271.50-451.50]
MPV fl	10.70 [9.50-11.60]	D-Dimer ugFEU/L	1.41 [0.44-602.00]
PCT %	0.21 [0.16-0.27]	Ferritin	427.77 [194.11-836.67]
PDW	16.40 [16.10-16.70]	CRP mg/L	115.85 [67.25-183.54]
NEU%	86.10 [78.32-90.50]	Sedim 30 min	44.00 [23.00-67.50]
NEU K/uL	7.34 [4.94-10.52]	Sedim 1 hour	62.76±30.75 (9.00-149.00)
LYM %	9.35 [5.82-15.27]	Procalcitonin	0.32 [0.14-0.66]
LYM	0.79 [0.50-1.32]	INR	1.22 [1.14-1.35]
MONO %	3.75 [2.22-5.30]	Prothrombin Time (Coagulometer) sec	12.60 [11.80-13.80]
MONO	0.34 [0.18-0.52]	Fibrinogen g/L	4.76 [4.14-6.34]
EOS %	0.10 [0.00-0.30]	Albumin g/L	31.41±4.32 (14.90-43.50)
EOS K/uL	0.01 [0.00-0.02]	Lactate	1.80 [1.30-2.67]
BASO %	0.10 [0.00-0.20]	Blood gas oxygen	51.00 [36.55-69.20]
BASO K/uL	0.00 [0.00-0.01)	Interleukin 6	49.68 [18.80-143.27]

DISCUSSION

One of the situations encountered at every stage of life is infectious diseases. Vaccines are the most important element in reducing or eradicating the effects of infectious diseases that began with the existence of humans and are tried to be cured by various methods. The COVID-19 pandemic, which emerged towards the end of 2019 and affected the whole world in a short time, is an infectious disease with high contagion and mortality, so society needs to be immunized by vaccination. Vaccination studies have started with COVID-19 vaccines that were approved after COVID-19 vaccine studies. Even though some people are fully vaccinated, they can still be infected with the COVID-19 virus and transmit the virus to people around them. The aim of our study is to evaluate patients with COVID-19 that developed after COVID-19 vaccination.

The median age of patients who developed post-vaccination infection was found to be 72 years, and the majority of patients were 65 years and above. Elderly individuals are a group prone to be infected with the SARS-CoV-2 virus. Due to aging-related comorbidities and reduced immunological competence, older individuals are at very high risk of adverse outcomes due to infectious diseases.[17] Decreased immune system functions in elderly individuals increase susceptibility to SARS-CoV-2 infection and also limit the effectiveness of COVID-19 vaccines. This may cause differences in vaccine effectiveness between young individuals (<55 years of age) and the elderly. Vaccines that

are effective in young individuals may not produce immunity in older individuals.[18] In a study conducted at Yale New Haven Hospital in the USA to measure the course of the disease as a result of COVID-19 cases despite vaccination, it was found that the majority of individuals who developed COVID-19 infection despite vaccination survived the infection asymptomatic or mild, but older individuals had a more severe infection and some even died.[19] However, the study reported that the mean age among those with severe or critical illness was 80.5 (IQR 76.5–85.0) years. The result of our study supports the literature.

In addition to elderly individuals, young people and people with various chronic diseases have a high risk of being infected with the virus again after receiving the COVID-19 vaccine.[20] Individuals with chronic diseases may experience a more severe disease and even death may occur.[21] People with pre-existing medical conditions such as kidney diseases, obesity, cardiovascular diseases, cancer, type 2 diabetes, and chronic obstructive pulmonary disease (COPD) may face more serious health problems with COVID-19 infection.[22] When the literature was examined, Hung et al. first stated that 13 of 41 confirmed patients (32%) had underlying diseases, and these diseases were diabetes (20%), hypertension (15%), and cardiovascular diseases (15%).[23] In the study conducted by Wang et al., 64 of 138 patients (46.4%) had one or more concomitant chronic diseases, and these diseases were respectively hypertension (31.2%), diabetes (10.1%) and cardiovascular disease (14.5%) and malignancy (7.2%).[24] In the study where the characteristics and clinical course of 1000 COVID-19 patients in the USA were examined, the common comorbidities were as follows; hypertension (60.1%), obesity (48.3%), diabetes mellitus (37.2%), lung disease (22.3%), kidney disease (13.7%), coronary artery disease (13%), asthma (11.3%), and congestive heart failure (10.2%).[25] In a study conducted in Italy, 709 (68%) of 1043 patients had at least one comorbidity, and the most common comorbid diseases were; hypertension, cardiovascular disease, hypercholesterolemia, and diabetes mellitus have been reported.[26] In a meta-analysis study, comorbid chronic diseases in COVID-19 patients included hypertension (21%), diabetes (9.7%), respiratory system disease (1.5%), and cardiovascular diseases (8.4%) has been reported.[27] In our study, it was found that 79.45% of the patients had at least one chronic disease, and these chronic diseases were hypertension, diabetes mellitus, heart failure, coronary artery disease, COPD, malignancy, asthma, and hypothyroidism, respectively. The results of our study were found to be similar to the literature.

For individuals who are considered immune-compromised or impaired, the CDC recommends receiving a third COVID-19 vaccine 28 days after receiving two doses of the COVID-19 vaccine. The CDC explains that reminder vaccines try to create an updated defense mechanism of the body against COVID-19 disease. In a long-term cohort study conducted in England, it was determined that the protection against infection decreased after six months in patients infected with COVID-19 and vaccinated in the research group. However, it has been reported that it is also important which COVID-19 vaccine the second and third doses of COVID-19 vaccines are given. Because if two doses of the same type of vaccine are administered and the third dose of a different type of COVID-19 vaccine is administered; it is estimated that vaccination will not have a positive effect and, as a result, vaccination will reduce the level of protection from the disease.[28,29] In another cohort study conducted in Sweden, a similar result was reached; It was determined that the effectiveness of the vaccine was gradually decreasing in all study groups and the necessity of the third dose of vaccination was highlighted. Also in the study; it has been reported that the effect of the vaccine decreases more quickly in older individuals than in younger individuals. It is stated that the most important reason for the decrease in the effectiveness of vaccines is the deterioration of antibody-producing cells and immune system functions in the elderly with advanced age.[30] In our study, it was found that the majority of patients received 2 doses of COVID-19 vaccine (CoronaVac (Inactive vaccine)) and infection developed after 2 doses of vaccine. Although the

results of our study support the literature, it is thought that this result is due to the high number of older age patients in the patient population and the lack of booster dose vaccinations.

Previous reports have described different mortality rates in COVID-19 patients, ranging from 16% to 38%, 62% to 67%, and 78%.[23,24,31-33] In our study, 38.64% of COVID-19 patients were discharged; it was determined that 61.36% of them died. Our study has shown that COVID-19 patients have higher mortality rates than cases in the epicenters of other countries so far. It is thought that these high rates may be due to the high average age of the patients, the high rate of comorbid diseases, and the lack of booster dose vaccinations.

The limitations of the present study include the fact that it was conducted on a small group of respondents. The data came from a single clinical research center, as opposed to multiple clinical research centers. The findings of this study may vary from those of other domestic and international researchers, and they should be tested in clinical settings.

CONCLUSION

In conclusion; In our study, the average age of post-vaccine COVID-19 patients, comorbidity, and mortality rates were high, the majority of the patients were vaccinated with CoronaVac, an inactive SARS-CoV-2 vaccine, they received two doses of vaccine at the highest rate and did not receive a reminder dose of vaccine, and COVID-19 after 2 doses of vaccine. It was determined that they had the infection. Our results demonstrated vaccine efficacy and ineffective immune response to vaccines in the oldest age group and those with comorbid chronic diseases. Mortality and morbidity can be reduced by creating successful vaccination programs as well as protective measures in the fight against COVID-19. Overall, although vaccines have undoubtedly provided widespread protection against COVID-19 infection worldwide, future studies are needed to identify and mitigate factors associated with suboptimal vaccine response in individuals with hyperreactive infections.

Ethics Committee Approval

Ethics committee approval for this study was received from Sakarya University Faculty of Medicine Ethics Committee with number E-71522473-050.01.04-39900-357.

Peer-review

Externally and internally peer-reviewed.

Author contributions

Concept: G.K., P.Ö.O., N.K.M., C.K., Ş.T., Z.E., H.E., O.K., Design: G.K., P.Ö.O., N.K.M., C.K., Ş.T., Data collection or Processing: G.K., P.Ö.O., N.K.M., Analysis or interpretation: G.K.,C.K., Ş.T. Literature Search: G.K., P.Ö.,O., N.K.M., C.K., Ş.T., Z.E., H.E., O.K., Writing: G.K., P.Ö.O., N.K.M., C.K., Ş.T., Z.E., H.E., O.K.

Conflicts of interest

The authors declared no conflict of interest.

Funding

No funding was used for the study.

References

1. Choy RKM, Bourgeois AL, Ockenhouse CF, et al. Controlled Human Infection Models To Accelerate Vaccine Development. Clin Microbiol Rev. 2022 Sep 21;35(3):e0000821. doi: 10.1128/cmr.00008-21. Epub 2022 Jul 6. PMID: 35862754; PMCID: PMC9491212.
2. WHO COVID-19 dashboard (Internet] Acces link: https://data.who.int/dashboards/covid19/cases Access date: 9.6.24
3. Firouzabadi N, Ghasemiyeh P, Moradishooli F, et al. Update on the effectiveness of COVID-19 vaccines on different variants of SARS-CoV-2. Int Immunopharmacol. 2023 Apr;117:109968. doi: 10.1016/j.intimp.2023.109968. Epub 2023 Mar 2. PMID: 37012880; PMCID: PMC9977625.
4. Rizk JG, Kalantar-Zadeh K, Mehra MR, et al. Pharmaco-Immunomodulatory Therapy in COVID-19. Drugs. 2020 Sep;80(13):1267-1292. doi: 10.1007/s40265-020-01367-z. PMID: 32696108; PMCID: PMC7372203.
5. Hadid T, Kafri Z, Al-Katib A. Coagulation and anticoagulation in COVID-19. Blood Rev. 2021 May;47:100761. doi: 10.1016/j.blre.2020.100761. Epub 2020 Oct 8. PMID: 33067035; PMCID: PMC7543932.
6. Ghasemiyeh P, Mohammadi-Samani S. The necessity of early anti-inflammatory therapy initiation in cases with mild-to-moderate COVID-19: A personal experience from an attending pharmacist and his resident The necessity of early anti-inflammatory therapy in mild-to-moderate COVID-19: A personal experience from an attending pharmacist and his resident. Published online 2024. doi:10.22541/au.170665690.06722778/v1
7. WHO CW. Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results. New England Journal of Medicine. 2021;384(6):497-511. doi:10.1056/NEJMoa2023184
8. Cámara M, Sánchez-Mata MC, Fernández-Ruiz V, et al. A Review of the Role of Micronutrients and Bioactive Compounds on Immune System Supporting to Fight against the COVID-19 Disease. Foods. 2021 May 14;10(5):1088. doi: 10.3390/foods10051088. PMID: 34068930; PMCID: PMC8155867.
9. Li Y, Tenchov R, Smoot J, et al. A Comprehensive Review of the Global Efforts on COVID-19 Vaccine Development. ACS Cent Sci. 2021 Apr 28;7(4):512-533. doi: 10.1021/acscentsci.1c00120. Epub 2021 Mar 29. PMID: 34056083; PMCID: PMC8029445.
10. Nagpal D, Nagpal S, Kaushik D, et al. Current clinical status of new COVID-19 vaccines and immunotherapy. Environ Sci Pollut Res Int. 2022 Oct;29(47):70772-70807. doi: 10.1007/s11356-022-22661-1. Epub 2022 Sep 5. PMID: 36063274; PMCID: PMC9442597.
11. Baltas I, Boshier FAT, Williams CA, et al. Post-Vaccination Coronavirus Disease 2019: A Case-Control Study and Genomic Analysis of 119 Breakthrough Infections in Partially Vaccinated Individuals. Clin Infect Dis. 2022 Aug 25;75(2):305-313. doi: 10.1093/cid/ciab714. PMID: 34410361; PMCID: PMC8513403.
12. Kalayci BN, Karahan D. Evaluation of local and systemic side effects of Turkovac vaccine in adults. Turk J Med Sci. 2023;53(4):934-940. doi:10.55730/1300-0144.5657
13. Haghpanah F, Lin G, Levin SA, et al. Analysis of the potential impact of durability, timing, and transmission blocking of COVID-19 vaccine on morbidity and mortality. EClinicalMedicine. 2021 May;35:100863. doi: 10.1016/j.eclinm.2021.100863. Epub 2021 Apr 26. PMID: 33937734; PMCID: PMC8072137.
14. Menni C, Klaser K, May A, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. Lancet Infect Dis. 2021 Jul;21(7):939-949. doi: 10.1016/S1473-3099(21)00224-3. Epub 2021 Apr 27. PMID: 33930320; PMCID: PMC8078878.
15. Antonelli M, Penfold RS, Merino J, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. Lancet Infect Dis. 2022 Jan;22(1):43-55. doi: 10.1016/S1473-3099(21)00460-6. Epub 2021 Sep 1. PMID: 34480857; PMCID: PMC8409907.
16. Egan C, Knight S, Baillie K, et al. Hospitalised Vaccinated Patients during the Second Wave, Update April '21.
17. Cox LS, Bellantuono I, Lord JM, et al. Tackling immunosenescence to improve COVID-19 outcomes and vaccine response in older adults. Lancet Healthy Longev. 2020 Nov;1(2):e55-e57. doi: 10.1016/S2666-7568(20)30011-8. Epub 2020 Nov 9. PMID: 33521768; PMCID: PMC7834195.
18. Lord JM. The effect of ageing of the immune system on vaccination responses. Hum Vaccin Immunother. 2013 Jun;9(6):1364-7. doi: 10.4161/hv.24696. Epub 2013 Apr 12. PMID: 23584248; PMCID: PMC3901832.
19. Juthani PV, Gupta A, Borges KA, et al. Hospitalisation among vaccine breakthrough COVID-19 infections. Lancet Infect Dis. 2021 Nov;21(11):1485-1486. doi: 10.1016/S1473-3099(21)00558-2. Epub 2021 Sep 7. Erratum in: Lancet Infect Dis. 2022 Jan;22(1):e1. doi: 10.1016/S1473-3099(21)00708-8. PMID: 34506735; PMCID: PMC8423430.
20. Lipsitch M, Krammer F, Regev-Yochay G, et al. SARS-CoV-2 breakthrough infections in vaccinated individuals: measurement, causes and impact. Nat Rev Immunol. 2022 Jan;22(1):57-65. doi: 10.1038/s41577-021-00662-4. Epub 2021 Dec 7. PMID: 34876702; PMCID: PMC8649989.
21. European Medicines Agency. (2022). COVID-19 vaccines: Key facts. Erişim adresi: https://www.ema.europa.eu/en/human-regulatory/overview/public-healththreats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid19-vaccines-key-facts#immunity-(protection)-section (Erişim tarihi: 11.09.2022).
22. Centers for Disease Control and Prevention, "People with certain medical conditions," Sep. 2020. [Online]. Available: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
23. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5. Epub 2020 Jan 24. Erratum in: Lancet. 2020 Feb 15;395(10223):496. doi: 10.1016/S0140-6736(20)30252-X. PMID: 31986264; PMCID: PMC7159299.
24. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069. doi: 10.1001/jama.2020.1585. Erratum in: JAMA. 2021 Mar 16;325(11):1113. doi: 10.1001/jama.2021.2336. PMID: 32031570; PMCID: PMC7042881.
25. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. BMJ. 2020 May 29;369:m1996. doi: 10.1136/bmj.m1996. PMID: 32471884; PMCID: PMC7256651.
26. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020 Apr 28;323(16):1574-1581. doi: 10.1001/jama.2020.5394. Erratum in: JAMA. 2021 May 25;325(20):2120. doi: 10.1001/jama.2021.5060. PMID: 32250385; PMCID: PMC7136855.
27. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020 May;94:91-95. doi: 10.1016/j.ijid.2020.03.017. Epub 2020 Mar 12. PMID: 32173574; PMCID: PMC7194638.
28. Centers For Disease Control and Prevention (CDC). (2022). COVID-19 vaccines for moderately or severely immunocompromised people. Erişim adresi: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html (Erişim tarihi: 22.04.2024)
29. Hall V, Foulkes S, Insalata F, et al. Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection. N Engl J Med. 2022 Mar 31;386(13):1207-1220. doi: 10.1056/NEJMoa2118691. Epub 2022 Feb 16. PMID: 35172051; PMCID: PMC8908850.
30. Nordström P, Ballin M, Nordström A. Risk of infection, hospitalisation, and death up to 9 months after a second dose of COVID-19 vaccine: a retrospective, total population cohort study in Sweden. Lancet. 2022 Feb 26;399(10327):814-823. doi: 10.1016/S0140-6736(22)00089-7. Epub 2022 Feb 4. PMID: 35131043; PMCID: PMC8816388.
31. 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 May;8(5):475-481. doi: 10.1016/S2213-2600(20)30079-5. Epub 2020 Feb 24. Erratum in: Lancet Respir Med. 2020 Apr;8(4):e26. doi: 10.1016/S2213-2600(20)30103-X. PMID: 32105632; PMCID: PMC7102538.
32. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020 Apr 28;323(16):1612-1614. doi: 10.1001/jama.2020.4326. PMID: 32191259; PMCID: PMC7082763.
33. 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 Mar 28;395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3. Epub 2020 Mar 11. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. doi: 10.1016/S0140-6736(20)30606-1. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. doi: 10.1016/S0140-6736(20)30638-3. PMID: 32171076; PMCID: PMC7270627.

DOI:10.34084/bshr.1512256 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

The Effects of Sonic Activation of the Irrigation Solution on Postoperative Pain

Sonik Olarak Aktive Edilmiş İrrigasyon Solusyonunun Postoperatif Ağrı Üzerine Etkileri

Duygu Bilgili

İstanbul Aydın University, Faculty of Dentistry, Department of Endodontics, İstanbul, Türkiye

ORCID ID: Duygu Bilgili: https://orcid.org/0000-0002-1900-543X

***Sorumlu Yazar / Corresponding Author:** Duygu Bilgili, **e-posta / e-mail:** dygbilgili@hotmail.com

Geliş Tarihi / Received : 08-07-2024 **Kabul Tarihi / Accepted:** 27-07-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Bilgili D. The Effects of Sonic Activation of the Irrigation Solution on Postoperative Pain. J Biotechnol and Strategic Health Res. 2024;8(1):125-132

Abstract

Aim The aim of this study was to assess and compare the Vibringe Sonic Irrigation System and conventional needle irrigation (bevel open-ended) in terms of postoperative pain.

Material and Method Ninety asymptomatic, non-vital, single-rooted, and single-canal teeth were evaluated for present clinical study. The included teeth were separated into two treatment groups [Group CNI: Conventional needle irrigation, control (pink card), Group V: Vibringe (blue card)] via cards selected by the patients. After treatment, all participants were given a verbal descriptor scale for the assessment of the pain and taken analgesics at the 6th, 12th, 24th, and 72nd hours.

Results Although there was no significant difference in the number of teeth with pain between the groups at the 6th, 24th, and 72nd hours, there was statistically more teeth with pain in group V in the 12th hour evaluation. However, in group CNI, pain severity was significantly less than group V at all time periods.

Conclusion The outcome of this study denotes that the use of the Vibringe may cause an increase in the postoperative pain in comparison to conventional needle irrigation for asymptomatic teeth.

Keywords Disinfection, postoperative pain, root canal therapy

Özet

Amaç *Bu çalışmanın amacı, Vibringe Sonik İrrigasyon Sistemi ile geleneksel iğne irrigasyonu (açılı ucu açık) postoperatif ağrı bakımından değerlendirmek ve karşılaştırmaktır.*

Gereç ve Yöntem *Asemptomatik, nonvital, tek köklü ve tek kanallı olan doksan diş bu klinik çalışma için değerlendirmeye alınmıştır. Dahil edilen dişler, hastalara seçtirilen kartlar aracılığı ile iki tedavi grubuna [Grup Gİİ: Geleneksel iğne irrigasyonu (pembe kart), Grup V: Vibringe (mavi kart)] ayrılmıştır. Endodontik tedaviler tek seansta, tek bir klinisyen tarafından yapılmıştır. Tedaviden sonra, 6., 12., 24. ve 72. saatteki ağrıyı ve alınan analjeziği değerlendirmek için bütün katılımcılara sözel tarif skalası verilmiştir.*

Bulgular *Gruplar arasında ağrılı diş sayısı bakımından 6., 24. ve 72. saatlerde anlamlı fark bulunmaz iken; 12. saat değerlendirmesinde ağrılı diş sayısı grup V'de istatistiksel olarak daha fazla olmuştur. Bununla birlikte; tüm zaman dilimlerinde ağrı şiddeti, grup Gİİ'de, grup V'ye göre anlamlı derecede daha düşük çıkmıştır.*

Sonuç *Bu çalışmanın sonucu; asemptomatik dişlerde Vibringe'in kullanımının geleneksel iğne irrigasyonu ile kıyaslandığında postoperatif ağrıda artışa neden olabileceğini göstermektedir.*

Anahtar Kelimeler *Dezenfeksiyon, postoperatif ağrı, kök kanal tedavisi*

INTRODUCTION

After endodontic treatment postoperative pain may be observed in the range of 3% to 58 %.[1] Depending on the severity of pain, the use of analgesics may also varies.[2] The possibility of pain occurring during or after root canal treatment is really scary for many patients, so this fear may cause the extraction to be preferred to root canal treatment.[3] Postoperative pain is caused by microbiological, chemical or mechanical factors which injure periapical region and provoke an inflammation.[4,5]

One of the most important procedures is the chemomechanical debridement of all canal systems for the successful root canal treatment.[6] Using an effective irrigating protocol is required for the most effective chemomechanical preparation.[7] However, extrusion of debris and the irrigation solutions and into the periradicular tissues may occur, which causes pain, swelling, and damaging of the vital tissue.[8-10] The balance between safety and effectiveness of the irrigation solution is specially important for the periradicular area.[11] Devices have been improved to enhance the irrigation efficacy and inhibit damage to the vital tissue, and lessen postoperative pain.[5,12] The activation of solutions (e.g., manual-dynamic activation, ultrasonic, sonic, and laser system) benefits more than conventional needle irrigation for cleaning canal systems.[13-16] However, the irrigation method may be related with the extrusion of the solution beyond the working length, affects pain.[9]

The Vibringe (Vibringe, Amsterdam, Netherlands) consist of cordless handpiece that fits into a disposable 10-mL Luer-Lock syringe. It includes both sonic activation (frequency: 2–3 kHz) and manual delivery of the irrigation solution.[15,17,18] Although there have been many studies comparing conventional needle irrigation and the Vibringe in terms of apical extrusion of debris[19] and debris removal efficacy[14,15,17], there is limited literature[20,21] regarding postoperative pain. Consequently, in present study, we aimed to assess and contrast the postoperative pain between Vibringe and conventional needle irrigation for non-vital, asymptomatic, teeth with one canal.

MATERIALS and METHODS

The present study was produced from the "thesis" which is registered to the "National The sis Center" in Türkiye (https://tez.yok.gov.tr/UlusalTezMerkezi/) with the thesis number 408462 [Name of the thesis: The effects of sonic activation of the solution on postoperatif pain (in Turkish with an abstract in English)]. Thi s prospective single-blind, controlled clinical study was conducted with the permission of the Republic of Türkiye Ministry of Health Turkish Medicines and Medical Devices Acency (protocol number 71146310 [2013-AC-CE-49]) and approval of Ethics Committee of Çukurova University for Clinical Research. All participants were treated in Çukurova University, Faculty of Dentistry, Department of Endodontics. Patients were informed about the study and informed consent form signed by the participants.

Patient Selection

All teeth were thoroughly examined radiologically and clinically. Pulp vitality was assessed through an electric pulp-testing device. Participants who were aged 18-60 years and having asymptomatic (no preoperative pain), non-vital, single-rooted teeth with one canal were incorporated into the study. The presence of periapical lesions in the teeth was not evaluated as a criterion. Exclusion criteria included patients with cardiac problems, diabetics, psychological and neurological problems who need to take medication, having allergy to local anesthetic agents. Participants who were breastfeeding, pregnant and had taken analgesic, anti-infla mmatory or antibiotic drugs at least one week before the treatment were excluded from the study. Teeth which needed retreatment were not included in this study. However, teeth which had only initiation treatment long before were included in the study as it was thought not to affect the result. Ninety teeth were incorporated into the inferential statistical analysis. Root canal treatment was performed in a single-visit by a single clinician.

Definition of Irrigation Systems

There were two groups with 45 samples in each one. There were pink and blue cards assigned for the groups. The pink card indicated group CNI (conventional needle irrigation, control), the blue card indicated group V (Vibringe). Before the treatments of the teeth, patients were asked to choose one of the cards. The number of men and women was statistically balanced for two groups because of eliminating the effect of the card color representing the groups. None of the patients knew which irrigation technique would be used during their treatments.

Endodontic Protocol

Patients were given local anesthetics (Maxicaine, İdol Medicine Refill, İstanbul, Türkiye). Coronal part of the root canal was instrumented with #25/.04 taper rotary system (Twisted-file, SybronEndo, Orange, CA, USA). When there was a large entrance of the canal, procedure of the coronal expansion was not applied. The root canals were irrigated according to the chosen card with a 0.5 mL saline solution and an electronic apex locater (Raypex 6, VDW, Munich, Germany) was used. The canals were mainly instrumented with the rotary system, while manual files were also used for shaping large root canals. Although the final instrumentation size was generally determined as three times larger than the first file which was binded at the working length, the final instrumentation size was sometimes increased since the needle tip reached up to 2 mm from the working length. The canals were irrigated with 2 % NaOCl solution during instrumentation up to 6 mL in total. Conventional needle (bevel open-ended) (Ayset Medical Products, Adana, Türkiye) and side-vented needle (I-tip, Medicinos, Linija UAB, Lithuania) were used in group CNI and group V, respectively. Since the flow rate of the solution in the Vibringe was stable, group CNI was adapted to group V to ensure equality (approximate 4.6 mL/min). An appropriate gutta percha (Diadent Group International Inc., Burnaby, BC, Canada) was placed into the canal, after a periapical radiograph was taken to verify working length. Afterwards, 3 mL NaOCl (2 %) and 3 mL saline solutions were performed as the final irrigation.

After the canals dried, they were filled using gutta percha plus 2Seal (VDW, Munich, Germany). Radiograph was taken to check the canal filling and the teeth were restored with composite (Premise, Kerr Corporation, Orange, CA, USA) filling in one visit.

Evaluation of Pain

A verbal descriptor scale[22,23] [0: not pain feel, 1: slight pain (not requiring analgesic), 2: medium pain, (relieved by analgesic), 3: serious pain (analgesics are not effective for reducing the pain)] was given to all patients for the assessment of the pain and analgesics were taken at the 6th, 12th, 24th, and 72nd hrs (hours) after the endodontic treatment. All participants were recommended to use analgesics [200 mg (milligram) ibuprofen] if required. All the patients took the clinician's telephone number to contact in case of an emergency. After the patients completed the questionaire forms, they came back to check and deliver the forms.

Statistical Analysis

The findings were analyzed by SPSS; Version 20.0 (IBM SPSS Inc., Chicago, IL, USA). For comparing categorical measurements between groups, Chi-square test was performed. For comparing age measurement between groups, independent samples t test was used. In all test, the significance level was considered to be 0.05.

RESULTS

Statistical difference has not detected between the groups in terms of age and sex. Table 1. shows the distribution of the demographic data ($p<0.05$).

Table 1. Distribution of the demographic			
	Group CNI	Group V	p
The average age	33.69	35.89	0.349
Standard deviation	±11.375	±10.760	
Female	24	17	0.204
Male	21	28	

Patients who marked "0" in the questionaire form were included in the "no pain" group and patients who marked "1, 2 or 3" in the form were included in the "pain" group to determine the presence of the pain (Table 2.). When all the time periods were evaluated, less tooth pain was observed in group CNI than group V. However, statistical difference has not detected in terms of the number of teeth with pain between the groups at at the 6th, 24th, and 72nd hrs, while there was statistically more teeth with pain in group V in the 12th hour.

Table 2. Descriptive analysis of the teeth distribution according to presence of pain			
PRESENCE OF THE PAIN			
Hours	Group CNI	Group V	p
6th	6 (13.3 %)	13 (28.9 %)	0.120
12th	2 (4.4 %)	10 (22.2 %)	0.027
24th	2 (4.4 %)	7 (15.6 %)	0.157
72nd	0 (0.0 %)	5 (11.1 %)	0.056

To determine the degree of the pain, pain intensities represented by "0, 1, 2, 3" were evaluated separately for the 6th, 24th, and 72nd hrs (Table 3.) after the treatment. Accordingly, postoperatif pain intensity in group CNI was less than it was in group V, statistically ($p<0.05$ significant over the 0.060 limit). However, pain severity could not be interpreted since there were few patients with severe (3) and moderate (2) pain. Furthermore, as the analgesic intake of the patients was low, it was not statistically significant.

Two patients (one of them was a female in group CNI, the other was a male in group V) had a mild pain in the gum area in the assessments at the 6th and 12th hrs, although there was no tooth pain. Furthermore, another patient (male, group V) had experienced pain in the injected site and took diclofenac potassium instead of ibuprofen 2 hrs after the treatment despite the absence of tooth pain. Another patient (female, group V) took a drug only at the 14th hour. One patient (male, group V) received a 400 mg drug instead of 200 mg at the 6th and 24th hrs. These patients were not excluded from the study. Besides, postoperative flare-up reaction developed in the teeth of three patients (one of them was in group CNI). Although one of them (in group V) did not contact the clinician about this reaction, the others came to the endodontic department and antibiotics were prescribed. One of the patients (group V) had a swelling at the gingiva one day after the treatment and the swelling was drained by the clinician.

Statistical difference has not detected between the number of teeth located in the maxilla or mandible. When the presence of postoperative pain was examined according to the jaws, in group V, postoperatif pain of the teeth in the maxilla was statistically higher than group CNI at the 6th and 12th hrs. However, statistical difference has not detected between the two groups in the way of the teeth in the mandible (Table 4).

Table 3. Pain intensity distribution at the 6th, 12th, 24th, and 72nd hrs					
FREQUENCIES and VALID PERCENT					
Groups	**Intensity**	**6th hrs**	**12th hrs**	**24th hrs**	**72nd hrs**
Group CNI	0	39 (86.7 %)	43 (95.6 %)	43 (95.6 %)	45 (100 %)
	1	6 (13.3 %)	2 (4.4 %)	2 (4.4 %)	0 (0.0 %)
	2	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
	3	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Group V	0	32 (71.1 %)	35 (77.8 %)	38 (84.4 %)	40 (88.9 %)
	1	11 (24.4 %)	8 (17.8 %)	5 (11.1 %)	3 (6.7 %)
	2	1 (2.2 %)	1 (2.2 %)	2 (4.4 %)	2 (4.4 %)
	3	1 (2.2 %)	1 (2.2 %)	0 (0.0 %)	0 (0.0 %)
	p Value	0.045	0.016	0.060	0.031

Table 4. Pain asssessments of the teeth according to the included maxilla or mandibula						
FREQUENCIES and VALID PERCENT						
Jaws	**Groups**	**6th hrs**	**12th hrs**	**24th hrs**	**72nd hrs**	**Count**
Maxilla	**Group CNI**	1 (4.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	25 (100 %)
	Group V	8 (27.6 %)	6 (20.7 %)	4 (13.8 %)	2 (6.9 %)	29 (100 %)
	p Value	0.028	0.025	0.115	0.493	
Mandibula	**Group CNI**	5 (25.0 %)	2 (10.0 %)	2 (10.0 %)	0 (0.0%)	20(100 %)
	Group V	5 (31.2 %)	4 (25.0 %)	3 (18.8 %)	3 (18.8%)	16 (100 %)
	p Value	0.722	0.374	0.637	0.078	

DISCUSSION

There are many studies[2,5,24-26] in the literature about pain after root canal treatment and it is important to assess the currently used irrigation systems regarding postoperative pain. The aim of present study was to determine whether there was a difference postoperative pain after using the Vibringe against conventional needle irrigation for asymptomatic teeth. The findings showed that there was statistically more teeth with pain in group V only at the 12th hour evaluation. It is thought that the sonic vibration in group V increased the apical extrusion and postoperative pain since vibration increased the activation of the solution. However, in a systematic review[27] (included another type of sonic device, EndoActivator) concluded that mechanical activation of the irrigation solution reduced postoperative pain. In this systematic review; it was stated that more postoperative pain occured due to the fact that positive pressure of the conventional needle (open-ended or side-vented needle) produces more hydraulic pressure. Furthermore, it has been reported that the remaining pulp residues may cause pain since the full working length can not be reached with the conventional needle.[27] Nevertheless, EndoActivator and Vibringe can also give different results in studies, though both are sonic systems. Although a study[28] with EndoActivator showed that the amount of irrigant extrusion was statistically lower than the side-vented needle, in another study[19] on the Vibringe and side-vented needle, statistical difference has not detect in the way of extruded debris.

In the present study, postoperative pain intensity was statistically lower in group CNI than in group V at all evaluation times after treatment. This result demonstrated that irrigation system may have a greater impact on intensity than the presence of postoperative pain. However, according to a meta-analysis study[29] machine-assisted agitation (included ultrasonic or sonic devices and negative apical pressure devices) reduces postoperative pain contrasted with conventional needle irrigation at both 24 hrs and 48 hrs. In a study[30] comparing EndoActivator and conventional open ended needle irrigation, statistically more pain intensity occurred in the group using the conventional needle at all time periods (8, 24, 48h). In this study,[30] it was stated that the inequality of the irrigation solution extrusion treated with conventional needle or agitation technique may cause this difference in postoperative pain. It has also been mentioned that direct comparison of the conventional needle irrigation and agitation techniques may be a limitation.[30] Moreover in a study[2] comparing Eddy, another sonic irrigation system, and a side-port needle irrigation; statistical difference has not detect in postoperative pain level among the irrigation procedures. For this reasons, using a device with both syringe delivery and agitation techniques, such as the Vibringe, may be more useful to contrast the influence of the conventional needle irrigation and sonic system.

Nevertheless, two different studies[20,21] comparing Vibringe and the conventional needle irrigation has not detected statistically significant difference between the groups in the way of postoperative pain. However, symptomatic vital teeth were used in these studies, contrary to our study. Furthermore, the preoperative pain severity was generally high in these studies. In addition, although the verbal descriptor scale was used for pain assessment in our study, these two studies employed the numerical rating scale. Because of these differences, the postoperative pain results may have been different from our study.

The bone structures of the maxilla and mandible are different from each other. Therefore, in our study, the mandible group CNI may have been affected more than the maxilla group. For this reason, in our study, while statistically significant has not detected between the two groups in the way of postoperative pain in the mandibular teeth, there was a difference at the 6th and 12th hrs in the maxillary teeth. This result related to the mandibular teeth in our study is similar to the study[21] evaluating the Vibringe and conventional needle irrigation in terms of postoperative pain, in which only mandibular premolars and molars

were used.

Apart from the irrigation system, there are many factors affecting postoperative pain.[31] Some studies suggested that the presence of preoperative pain,[32,33] the type of tooth, sex,[34] age of patients,[22] vitality of pulp, treatment visit,[35] and medical situation[36] affect postoperative pain. The inclusion criteria were determined by considering these factors. In addition to these factors, increased pressure in the irrigation solution may increase the risk of irrigation extrusion which may also affect postoperative pain.[37] The increase of the apical pressure in the irrigation solution is affected by the flow rate of the irrigant.[38] For this reason, the flow rate of the irrigant in group CNI was determined according to the constant flow rate of group V.

In this study, the difference in the types of needle tips used between the two groups may be a limitation. To minimize the effect of confounding variables, patients were assigned to groups by choosing cards and blinding. Attaching the needle to the Vibringe and applying with and without activating may be suggested for future studies. Nonetheless, there are a lot of factors that affect postoperative pain which is not eliminated. For example, postoperative pain may be related to periapical trauma because of the material's apical extrusion, missed root canal, injuring soft tissue because of the rubber dam or injection application, and maxillo-facial pain unrelated from teeth, as Gondim et al.[5] cited. Dorner et al.[39] reported; in addition to tissue damage, the feeling of damage is also defined as pain. Furthermore, pain caused by root canal treatment can be affected by previous experiences, conversations with others, and the media.[4] In other words, pain is a subjective pheno-menon and it would be beneficial to evaluate it considering the biopsychosocial model[40] suggested for the assessment of diseases. For this reason, it would be wise to be careful in generalizing the results of the this study.

CONCLUSION

Using of the Vibringe can increase the presence and severity of postoperative pain in comparison to conventional needle irrigation for asymptomatic non-vital teeth. It may also affect the severity of pain more than the presence of pain in comparison to conventional needle irrigation. However, it is important to conduct more studies on the Vibringe in terms of postoperative pain assessment.

Acknowledgment

This study was produced from the author's own thesis. The author thanks thesis advisor Assoc. Prof. Adile Şehnaz Yılmaz for their contributions to the thesis stages, from the ethical decision making stage of the thesis. Furthermore, the author thanks academic personnel of Çukurova University, Faculty of Dentistry, for the contributions of thesis stages.

This study has not been previously presented.

Ethical Committee Approval

This prospective single-blind, controlled clinical study was conducted with the permission of the Republic of Türkiye Ministry of Health Turkish Medicines and Medical Devices Acency [protocol number 71146310 (2013-AC-CE-49)] and approval of Ethics Committee of Çukurova University for Clinical Research.

Peer-review

Externally and internally peer-reviewed.

Conflict of Interest

The author has declared that there were no conflicts of interested related to this study. This literature was produced from the author's own thesis (https://tez.yok.gov.tr/UlusalTezMerkezi/ Name of thesis: The effects of sonic activation of the solution on postoperative pain).

Funding

This research was supported by Çukurova University Scientific Research Projects Unit (DHF2013LTP1).

References

1. Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single- and multiple-visit endodontic treatment: a systematic review. Int Endod J. 2008; 41(2): 91–99. doi: 10.1111/j.1365-2591.2007.01316.x.
2. Kaplan T, Kaplan SS, Sezgin GP. The effect of different irrigation and disinfection methods on post-operative pain in mandibular molars: a randomised clinical trial. BMC Oral Health. 2022; 22(1): 601. doi: 10.1186/s12903-022-02651-y.
3. Harrison JW, Baumgartner JC, Svec TA. Incidence of pain associated with clinical factors during and after root canal therapy. part 1. Interappointment pain. J Endod. 1983; 9(9): 384-387. doi: 10.1016/s0099-2399(83)80190-3.
4. Seltzer S, Naidorf IJ. Flare-ups in endodontics: 1. etiological factors. J Endod. 1985; 11(11): 472–478. doi: 10.1016/S0099-2399(85)80220-X.
5. Gondim Jr E, Setzer FC, Dos Carmo CB, et al. Postoperative pain after the application of two different irrigation devices in a prospective randomized clinical trial. J Endod. 2010; 36(8): 1295-1301. doi: 10.1016/j.joen.2010.04.012.
6. Sabeti MA, Nekofar M, Motahhary P, et al. Healing of apical periodontitis after endodontic treatment with and without obturation in dogs. J Endod. 2006; 32(7): 628-633. doi: 10.1016/j.joen.2005.12.014.
7. De-Deus G, Garcia-Filho P. Influence of the NiTi rotary system on the debridement quality of the root canal space. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009; 108 (4): e71-76. doi: 10.1016/j.tripleo.2009.05.012.
8. Swanljung O, Vehkalahti MM. Root canal irrigants and medicaments in endodontic malpractice cases: a nationwide longitudinal observation. J Endod. 2018; 44(4): 559-564. doi: 10.1016/j.joen.2018.01.003.
9. Guivarc'h M, Ordioni U, Ahmed HMA, et al. Sodium hypochlorite accident: a systematic review. J Endod. 2017; 43(1): 16-24. doi: 10.1016/j.joen.2016.09.023.
10. Tanalp J, Gungor T. Apical Extrusion of Debris: A literature review of an inherent occurrence during root canal treatment. Int Endod J. 2014; 47(3): 211-221. doi: 10.1111/iej.12137.
11. Haapasalo M, Shen Y, Wang Z, et al. Irrigation in endodontics. Br Dent J. 2014; 216(6): 299-303. doi: 10.1038/sj.bdj.2014.204.
12. Alkahtani A, Al Khudhairi TD, Anil S. A comparative study of the debridement efficacy and apical extrusion of dynamic and passive root canal irrigation systems. BMC Oral Health. 2014; 14: 12. doi: 10.1186/1472-6831-14-12.
13. Caron G, Nham K, Bronnec F, et al. Effectiveness of different final irrigant activation protocols on smear layer removal in curved canals. J Endod. 2010; 36(8): 1361-1366. doi: 10.1016/j.joen.2010.03.037.
14. Dönmez Özkan H, Metin K, Bakir ZB, et al. A novel protein testing model to assay the efficacy of multiple irrigation activation techniques for removal of ex vivo biomolecular film. Photomed Laser Surg. 2018; 36(9): 493-498. doi: 10.1089/pho.2018.4452.
15. Rödig T, Bozkurt M, Konietschke F, et al. Comparison of the vibringe system with syringe and passive ultrasonic irrigation in removing debris from simulated root canal irregularities. J Endod. 2010; 36: 1410-1413. doi: 10.1016/j.joen.2010.04.023.
16. Blank-Gonçalves LM, Nabeshima CK, Martins GHR, et al. Qualitative analysis of the removal of the smear layer in the apical third of curved roots: conventional irrigation versus activation systems. J Endod. 2011; 37(9): 1268-1271. doi: 10.1016/j.joen.2011.06.009.
17. Johnson M, Sidow SJ, Looney SW, et al. Canal and isthmus debridement efficacy using a sonic irrigation technique in a closed-canal system. J Endod. 2012; 38(9): 1265-1268. doi: 10.1016/j.joen.2012.05.009.
18. Aksel H, Küçükkaya Eren S, Puralı N, et al. Efficacy of different irrigant protocols and application systems on sealer penetration using a stepwise CLSM analysis. Microsc Res Tech. 2017; 80(12): 1323-1327. doi: 10.1002/jemt.22944.
19. Karatas E, Ozsu D, Arslan H, et al. Comparison of the effect of nonactivated self-adjusting file system, Vibringe, Endovac, ultrasonic and needle irrigation on apical extrusion of debris. Int Endod J. 2015; 48(4): 317-322. doi: 10.1111/iej.12317.
20. Ahmed S, Elfar H, El Khodary S. Evaluation of postoperative pain after using sonic Vibringe irrigation system versus conventional syringe irrigation in single rooted teeth with symptomatic irreversible pulpitis: a randomized clinical controlled trial. Advanced Dental Journal. 2019; 1(3): 86-94. doi: 10.21608/ADJC.2019.17020.1031
21. Ali MEM, Magdy A, Hussien W. Evaluation of post-operative pain after irrigation using end-vented NaviTip tips versus Vibringe sonic irrigating system in teeth with acute pulpitis with apical periodontitis: a randomized clinical trial. Open Access Maced J Med Sci. 2020; 8:130-133.
22. Arias, A, de la Macorra JC, Hidalgo JJ, et al. Predictive models of pain following root canal treatment: a prospective clinical study. Int Endod J. 2013; 46(8): 784-793. doi: 10.1111/iej.12059. Epub 2013 Feb 12.
23. Attar S, Bowles WR, Baisden MK, et al. Evaluation of pretreatment analgesia and endodontic treatment for postoperative endodontic pain. J Endod. 2008; 34(6): 652-655. doi: 10.1016/j.joen.2008.02.017.
24. Gündoğar M, Sezgin GP, Kaplan SS, et al. Postoperative pain after different irrigation activation techniques: a randomized, clinical trial. Odontology. 2021; 109: 385-392. doi: 10.1007/s10266-020-00553-5.
25. Dagher J, El Feghali R, Parker S, et al. Postoperative quality of life following conventional endodontic intracanal irrigation compared with laser-activated irrigation: a randomized clinical study. Photobiomodul Photomed Laser Surg. 2019; 37(4): 248-253. doi: 10.1089/photob.2018.4558.
26. Erkan E, Gündoğar M, Uslu G, et al. Postoperative pain after SWEEPS, PIPS, sonic and ultrasonic-assisted irrigation activation techniques: a randomized clinical trial. Odontology. 2022; 110(4): 786-794. doi: 10.1007/s10266-022-00700-0.
27. Susila A, Minu J. Activated irrigation vs. conventional non-activated irrigation in endodontics–a systematic review. Eur Endod J. 2019; 4: 96-110. doi: 10.14744/eej.2019.80774.
28. Desai P, Himel V. Comparative safety of various intracanal irrigation systems. J Endod. 2009; 35: 545-549. doi: 10.1016/j.joen.2009.01.011.
29. Decurcio DA, Rossi-Fedele G, Estrela C, et al. Machine-assisted agitation reduces postoperative pain during root canal treatment: a systematic review and meta-analysis from randomized clinical trials. J Endod. 2019; 45(4): 387-393. doi: 10.1016/j.joen.2019.01.013.
30. Ramamoorthi S, Nivedhitha MS, Divyanand MJ. Comparative evaluation of postoperative pain after using endodontic needle and Endoactivator during root canal irrigation: a randomised controlled trial. Aust Endod J. 2015; 41(2): 78-87. doi: 10.1111/aej.12076.
31. Genet JM, Hart AAM, Wesselink PR, et al. Preoperative and operative factors associated with pain after the first endodontic visit. Int Endod J. 1987; 20(2): 53-64. doi: 10.1111/j.1365-2591.1987.tb00590.x.
32. Bamini L, Sherwood A, Arias A, et al. Influence of tooth factors and procedural errors on the incidence and severity of post-endodontic pain: a prospective clinical study. Dent J. 2020; 8(3): 73. doi: 10.3390/dj8030073.
33. Ince B, Ercan E, Dalli M, et al. Incidence of postoperative pain after single-and multi-visit endodontic treatment in teeth with vital and non-vital pulp. Eur J Dent. 2009; 3(4): 273–379.
34. Ng YL, Glennon, JP, Setchell DJ, et al. Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. Int Endod J. 2004; 37(6): 381-391. doi: 10.1111/j.1365-2591.2004.00820.x.
35. Albashaireh ZSM, Alnegrish, AS. Postobturation pain after single-and multiple-visit endodontic therapy. a prospective study. J Dent. 1998; 26(3): 227-232. doi: 10.1016/s0300-5712(97)00006-7.
36. O'Keefe, E. M. Pain in endodontic therapy: preliminary study. J Endod. 1976; 2(10): 315-319. doi: 10.1016/S0099-2399(76)80047-7.
37. Guerreiro-Tanomaru, JM, Loiola LE, Morgental R, et al. Efficacy of four irrigation naedles in cleaning the apical third of root canals. Braz Dent J. 2013; 24(1): 21-24. doi: 10.1590/0103-6440201302153.
38. Snjaric D, Carija Z, Braut A, et al. Irrigation of human prepared root canal--ex vivo based computational fluid dynamics analysis. Croat Med J. 2012; 53(5): 470-479. doi: 10.3325/cmj.2012.53.470.
39. Dorner TE, Muckenhuber J, Stronegger WJ, et al. The impact of socio-economic status on pain and the perception of disability due to pain. Eur J Pain. 2011; 15(1): 103–119. doi: 10.1016/j.ejpain.2010.05.013.
40. Engel GL. The need for a new medical model: a challenge for biomedicine. Science. 1977; 196 (4286): 129–136. doi: 10.1126/science.847460.

DOI:10.34084/bshr.1527769 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

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

Distribution of HCV Genotypes in Patients with Chronic Hepatitis C Infection: A Three-Year Single-Center Retrospective Study

Kronik Hepatit C Enfeksiyonu Olan Hastaların HCV Genotiplerinin Dağılımı: Üç Yıllık Tek Merkezli Retrospektif Çalışma

Melahat Gürbüz, Cengiz Demir, Selahattin Ünlü, Betül Fatmanur Yıldırım, Yeliz Çetinkol

Afyonkarahisar Health Siences University, Faculty of Medicine, Department of Medical Microbiology, Afyonkarahisar, Türkiye

ORCID ID: Melahat Gürbüz: https://orcid.org/0000-0001-6290-1216, Cengiz Demir: https://orcid.org/0000-0002-5569-886X, Selahattin Ünlü: https://orcid.org/0009-0002-9185-0109, Betül Fatmanur Yıldırım: https://orcid.org/0000-0003-2459-5451, Yeliz Çetinkol: https://orcid.org/0000-0003-4940-4498

***Sorumlu Yazar / Corresponding Author:** Melahat Gürbüz , **e-posta / e-mail:** drmelahatgrbz@hotmail.com

Geliş Tarihi / Received : 04-08-2024 **Kabul Tarihi / Accepted:** 16-08-2024 **Yayın Tarihi / Online Published:** 31-08-2024

Gürbüz M., Demir C., Ünlü S, Yıldırım B.F., Çetinkol Y. Distribution of HCV Genotypes in Patients with Chronic Hepatitis C Infection: A Three-Year Single-Center Retrospective Study . J Biotechnol and Strategic Health Res. 2024;8(1):133-140

Abstract

Aim Hepatitis C virus (HCV) is a single-stranded, positive-sense RNA virus belonging to the genus Hepacivirus in the Flaviviridae family. It has eight known genotypes and 93 subtypes. HCV can be transmitted through various routes, including blood transfusion, surgical procedures, sexual contact, and intravenous drug use, leading to both acute and chronic hepatitis. Genotype (GT) determination and viral load assessment are essential for selecting an appropriate antiviral treatment regimen and duration, and for monitoring treatment efficacy. We aimed to ascertain the genotype distribution over a three-year period.

Material and Method In this study, patients diagnosed with chronic HCV infection and followed at Afyon Health Sciences University Health Practice and Research Hospital between July 1, 2020, and June 30, 2023, were retrospectively evaluated for their age, gender, and HCV genotype data.

Results A total of 91 patients' HCV genotype data were included in the study. The study revealed that 95.6% of the patients were Turkish citizens, while 4.4% were of foreign nationality. Among the 91 patients, 60 (65.9%) were found to have genotype 1b, 12 (13.2%) had genotype 1a, 10 (11%) had genotype 3, 6 (6.6%) had genotype 4, 2 (2.2%) had genotype 2, and one patient (1.1%) had a co-infection of genotypes 3 and 4.

Conclusion Genotype 1b was dominant in our region. Identifying HCV genotypes is important in guiding the prognosis and treatment of chronic HCV infections and monitoring the epidemiologic changes. This information will be of great value in the health policy that targets HCV and in elimination efforts.

Keywords Genotype, hepatitis C virus, viral load

Özet

Amaç *Hepatit C virüsü (HCV), Flaviviridae ailesindeki Hepacivirus cinsine ait tek sarmallı, pozitif anlamlı bir RNA virüsüdür. Bilinen sekiz genotipi ve 93 alt tipi vardır. HCV kan transfüzyonu, cerrahi prosedürler, cinsel temas ve damar içi uyuşturucu kullanımı gibi çeşitli yollarla bulaşabilir ve hem akut hem de kronik hepatite yol açabilir. Genotip (GT) belirleme ve viral yük değerlendirmesi, uygun bir antiviral tedavi rejimi ve süresinin seçilmesi ve tedavi etkinliğinin izlenmesi için esastır. Üç yıllık bir dönem boyunca genotip dağılımını tespit etmeyi amaçladık.*

Gereç ve Yöntem *Bu çalışmada, Afyon Sağlık Bilimleri Üniversitesi Sağlık Uygulama ve Araştırma Hastanesi'nde 1 Temmuz 2020 ile 30 Haziran 2023 tarihleri arasında kronik HCV enfeksiyonu tanısı alan ve takip edilen hastalar yaş, cinsiyet ve HCV genotip verileri açısından retrospektif olarak değerlendirilmiştir.*

Bulgular *Toplam 91 hastanın HCV genotip verileri çalışmaya dahil edilmiştir. Çalışma, hastaların %95,6'sının Türk vatandaşı olduğunu, %4,4'ünün ise yabancı uyruklu olduğunu ortaya koymuştur. 91 hastanın 60'ında (%65,9) genotip 1b, 12'sinde (%13,2) genotip 1a, 10'unda (%11) genotip 3, 6'sında (%6,6) genotip 4, 2'sinde (%2,2) genotip 2 ve bir hastada (%1,1) genotip 3 ve 4 ko-enfeksiyonu olduğu tespit edilmiştir.*

Sonuç *Bölgemizde genotip 1b baskın genotip olarak saptandı. HCV genotiplerinin belirlenmesi, kronik HCV enfeksiyonlarının prognoz ve tedavisinin yönlendirilmesinde ve epidemiyolojik değişikliklerin izlenmesinde önemlidir. Bu bilgiler HCV'yi hedef alan sağlık politikalarında ve eliminasyon çalışmalarında büyük değer taşıyacaktır.*

Anahtar Kelimeler *Genotip, hepatit C virüs, viral yük*

INTRODUCTION

The Hepatitis C virus (HCV) is a single-stranded RNA virus with a positive polarity. It is classified under the Hepacivirus genus within the Flaviviridae family. Hepatitis C virus (HCV) represents a significant global public health challenge, with a high mortality rate associated with a range of complications including liver failure and chronic hepatitis C infection, as well as acute hepatitis C infection and the development of liver cancer.[1]

The HCV genome is approximately 9.4 kbp in length and is initially translated into a large polyprotein. Subsequently, the polyprotein is processed by a viral protease, resulting in the generation of ten distinct proteins. These include three structural proteins (core, E1, and E2) and seven non-structural proteins (p7, NS2, NS3, NS4A, NS4B, NS5A, and NS5B). In particular, the NS3/4A protease and NS5B RNA polymerase have been determined to play a critical role in the pathogenesis of HCV.[2] Over the past decade, HCV strains have diversified, aided by advances in sequencing technologies, leading to variations in their geographical distribution. The number of recognized genotypes (GT) has risen from 6 to 8, with the number of subtypes increasing from 67 to 93.[3-7]

Global prevalence studies have shown that anti-HCV antibody prevalence ranges from 1% to 3.5% in the general population, whereas studies on individuals who inject drugs show a significantly higher average prevalence, ranging from 40% to 52%.[8] However, studies focusing solely on the presence of HCV antibodies require confirmation, as these data may include individuals who have spontaneously recovered or have been treated. Despite the widespread use of anti-HCV antibodies as a marker for HCV infection and their use in estimating prevalence and comparing global HCV infection levels, the classification of genetic variants remains the most critical indicator of HCV spread. Numerous studies have indicated that HCV genotype is a key determinant of both treatment outcome and disease pathogenesis.[9] It is important to understand the distribution, diversity, and patterns of HCV genotypes in order to eff e ctively control HCV infection. Genotype distribution can provide valuable insights into transmission routes and sources of infection. Moreover, HCV genotype is a determining factor in the effi cacy of direct-acting antiviral (DAA) therapy, and thus plays an essential role in the selection and duration of interferon-free DAA regimens.

Th e objective of this study was to ascertain the genotype distribution of chronic hepatitis C patients admitted to our hospital over a three-year period. Additionally, we sought to determine whether there were any changes in the distribution over the years and to investigate the relationship between genotypes and age and gender.

MATERIALS and METHODS

In this study, the age, gender, and HCV genotype data of patients diagnosed with chronic HCV infection and fol-lowed at Afyonkarahisar Health Sciences University Health Practice and Research Hospital between July 1, 2020, and June 30, 2023, were retrospectively evaluated using patient records and the hospital information system. The HCV genotype and HCV-RNA data of the patients included in the study were recorded at the time of their initial admission to our hospital. For genotype determination, samples collected until 2022 underwent extraction using the Cobas 4800 au-tomated system (Roche, USA), and testing was performed using the Roche Cobas HCV GT kit on the Cobas z 480 Real-Time PCR device. For samples collected after 2022, the Magnesia®2448 Extraction and PCR System (Anatolia Geneworks, Türkiye) was utilized. Quantitative detection of HCV-RNA was conducted using the Bosphore Ultra HCV Quantification Detection Kit, and HCV genotypes were identified using the Bosphore HCV Genotyping Kit v3 (Anatolia Geneworks, Türkiye). The PCR procedures were performed on the Montania 4896 Real-Time PCR device (Anatolia Geneworks, Türkiye). The results were interpreted according to the recommendations of the kit manufacturer. The Bosphore Ultra HCV Quantification

Detection Kit is sensitive to HCV-RNA levels as low as 8 IU/mL and can quantitatively detect HCV-RNA within a range of $1x10^1$ to $1x10^9$ IU/mL. Both systems used for HCV genotyping were capable of separately identifying genotypes 1a, 1b, 2, 3, 4, 5, and 6.

Th e study was conducted in accordance with the ethical standards set forth by the Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University (Decision No. 443-2023/10).

Statistical Analysis

The obtained data were statistically analyzed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). The mean age and gender distributions were assessed. The chi-square test and Fisher's Exact test were employed to compare categorical variables between groups. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 91 patients with identified HCV genotypes were included in the study. Of these, 38.5% were female, and 61.5% were male, with a mean age of 51 ± 19.2 years (range 7-83 years) across all patients. The age distribution by genotypes and demographic data of the patients are presented in Table 1 and Table 2.

Table 1. Age Distribution of HCV Genotypes

	Genotypes				
	1a	1b	2	3	4
Median Age (min-max)	36 (28-72)	58 (7-83)	28 (25-28)	69 (21-51)	66 (23-67)

Of the patients, 95.6% were Turkish citizens, while 4.4% were of foreign nationality (Table 2). When examining the distribution of HCV genotypes among foreign nationals identified in this study, three of the four foreign patients were found to have GT 1b, and one had GT 4. The GT 4-positive patient was a 23-year-old Somali woman, while the other foreign patients were from Afghanistan, Uzbekistan, and Azerbaijan.

In our study, when analyzing genotype positivity by age groups, the highest rate (31.8%) was found in the group aged over 65 years (Table 2). Only one patient under 18 years of age was identified, who was a 7-year-old Afghan patient.

Table 2. Demographic Data and HCV Genotype Distribution of HCV-Positive Patients

Demographic Variables		n	%
Nationality	Turkish	87	95.6
	Foreign	4	4.4
Gender	Female	35	38.5
	Male	56	61.5
Year	2020	29	31.9
	2021	24	26.4
	2022	38	41.7
Age Group	< 18	1	1.1
	18-35	25	27.5
	36-45	11	12.1
	46-65	25	27.5
		29	31.8

Among the 91 patients followed for chronic HCV infection over the three-year period, GT 1b was identified in 60 patients (65.9%), GT 1a in 12 patients (13.2%), GT 3 in 10 patients (11%), GT 4 in 6 patients (6.6%), GT 2 in 2 patients (2.2%), and a combination of GT 3 and GT 4 in 1 patient (1.1%) (Table 3).

When examining the distribution of genotypes by gender, the difference between female and male patients with positive genotype was found to be statistically significant (p=0.0018). GT 2 and GT 3 were not detected in female patients, while the only mixed genotype (GT 3+ GT 4) in our study was identified in a female patient (Table 3).

A comparison of the data by year revealed that GT 1a was significantly higher in 2022 than in other years (p=0.0008). In contrast, no significant difference was observed for GT 1b across the years (p=0.0623) (Table 4).

Table 4. Yearly Distribution of HCV Genotypes Identified in This Study

	2020		2021		2022		Total	
	n	%	n	%	n	%	n	%
Genotype 1a	1	3.4	2	8.3	9	23.7	12	13.2
Genotype 1b	27	93.2	17	70.9	16	42.1	60	65.9
Genotype 2	-	-	-	-	2	5.3	2	2.2
Genotype 3	-	-	3	12.5	7	18.4	10	11
Genotype 4	-	-	2	8.3	4	10.5	6	6.6
Genotype 3+4	1	3.4	-	-	-	-	1	1.1
Total	**29**	**100**	**24**	**100**	**38**	**100**	**91**	**100**

Table 5. Data from HCV Genotype Studies at Different Centers in Türkiye

Study	Year	Region	Number	Genotypes (%)								
				1	1a	1b	2	3	4	5	6	Mix Type
Gökahmetoğlu et al.[10]	2011	Kayseri	146	9	5.5	85.5	2.7	-	35.6	-	-	-
Çetin et al.[11]	2016	Adana	119	-	12.6	58.8	7.6	16.8	3.4	0.8	-	-
Akgün et al.[12]	2017	Adıyaman	71	4.2	8.5	71.8	11.3	4.2	-	-	-	-
Tiryaki et al.[13]	2018	Aydın	182	2.2	18.1	69.2	1.7	7.2	1.7	-	-	-
Öz et al.[14]	2019	Sakarya	235	2.1	5.5	77.4	0.8	8.5	2.9	-	-	2.5
Sari et al.[15]	2020	İstanbul	413	12.3	12.6	53.8	5.3	11.9	2.3	0.5	-	-
Ağca et al.[16]	2021	Bursa	740	5.8	6.1	72.8	2	9.2	2.5	0.1	-	1.5
Özkaya et al.[17]	2021	Trabzon	670	3.4	3.7	82.8	1.8	6.7	0.9	-	-	0.6
Alaçam et al.[18]	2022	İstanbul	546	2.6	13.2	56.2	6.7	14	8.8	1.3	0.2	8.6
Bulut et al.[19]	2023	Van	95	-	13.7	65.3	2.1	16.8	2.1	-	-	-

DISCUSSION

Hepatitis C virus (HCV) is an infectious agent that infects approximately 3-4 million individuals annually, resulting in over 350.000 deaths. As reported by the World Health Organization (WHO), more than 71 million individuals residing in the Eastern Mediterranean and European regions, including Türkiye, are afflicted with a chronic hepatitis C infection.[20] In an effort to address the public health threat posed by HCV, the WHO has launched several global initiatives and proposed a strategy for HCV elimination in 2016. This strategy outlines principal objectives, including a reduction in the incidence of new hepatitis infections, an enhancement of access to testing and treatment, and an improvement in surveillance and monitoring systems. The objective is to achieve a reduction of 90% in chronic hepatitis C incidence and a 65% reduction in hepatitis C-related mortality by the year 2030. Despite notable progress in HCV treatment, access to care remains a challenge for many individuals, primarily due to high costs and limited healthcare resources.[21]

To date, eight HCV genotypes and 93 subtypes have been

identified, each showing around 30% genetic variability across the viral genome.[3] The considerable genetic diversity presents a significant challenge for both vaccine development and the development of effective antiviral treatments. The success and duration of therapy can be significantly influenced by the specific viral strains involved. Understanding of the HCV genotype is of significant clinical importance, as the efficacy of treatment, as measured by the sustained virologic response (SVR) rate, is heavily influenced by the distribution of genotypes and subtypes. The SVR rate is defined as the proportion of patients with persistent viremia 24 weeks after the completion of antiviral therapy.[22] Historically, the standard treatment for HCV infections was based on PEG-IFNα/RBV, which was observed to positively impact SVR rates compared to other antiviral therapies.[23] However, IFNα/RBV treatment was associated with suboptimal efficacy, extended treatment durations, and various adverse outcomes, particularly when compared to the newer and more costly direct-acting antivirals (DAAs).[24] DAAs, which inhibit viral proteins crucial for viral replication, have been reported to enhance SVR rates.[25] As a result, a deeper understanding of HCV epidemiology, particularly the global distribution of various genotypes, could assist in mitigating the impact of this serious disease.[26]

The geographical distribution of HCV genotypes exhibits considerable heterogeneity. In developed nations, "epidemic subtypes" (1a, 1b, 2a, and 3a) are common, whereas "endemic" strains are generally found in regions such as West Africa, South Asia, Central Africa, and Southeast Asia.[20] Globally, GT 1 is the most frequently identified genotype at 49.1%, followed by GT 3 (17.9%), GT 4 (16.8%), GT 2 (2%), and GT 6 (1.4%).[27] Genotypes 5, 7, and 8 together account for less than 1% of global HCV infections.[28] Genotype GT 4 is most prevalent in the Middle East, Central, and Eastern Africa, whereas GT 1 is predominantly found in North and South America, Europe, and Australia. The most common genotype in the Indian subcontinent is GT 3, while GT 2 is widespread in West Africa. GT 5 is prevalent in South Africa, and GT 6 is prevalent in Southeast Asia. The recently identified genotypes 7 and 8 are more prevalent in Central Africa and the Indian subcontinent, respectively.[29]

The phenomenon of rising human migration has contributed to the gradual shifting of the distribution of HCV genotypes, although this pattern of change has yet to be fully elucidated. The presence of distinct HCV GT1 strains has been documented in Germany and Cyprus.[30,31] In Canada, multiple distinct HCV GT 2 strains have been identified, particularly among patients of African descent.[32] Concerning HCV GT 4, Ethiopian data indicate the presence of four distinct sub-genotypes (4d, 4r, 4l, and 4v).[33] Although Simmonds et al. reported that the HCV 5a sub-genotype is the most prevalent in South Africa, they also suggested that other sub-genotypes and recombinant viruses might exist, and that recombination events play a crucial role in the evolution of RNA viruses.[34] Furthermore, studies have shown that the epidemiology of HCV GT 4 is evolving. This strain has begun to emerge in numerous Western European countries, largely as a consequence of demographic shifts, migration, and alterations in the patterns of injection drug use.[35]

Understanding the various HCV genotypes and subtypes is of paramount importance, as they can have a significant impact on the efficacy of treatment and the clinical outcomes in patients with HCV infections. For instance, interferon-based therapy has exhibited superior efficacy for genotypes 2 and 3, whereas first-generation HCV protease inhibitors demonstrated greater effectiveness for genotype 1. Fortunately, second-generation DAAs provide broader coverage across genotypes. Nevertheless, despite the considerable impact of pangenotypic treatment regimens, they are costly and frequently challenging to obtain in low- and middle-income countries.[29]

In Türkiye, recent data indicate that GT 1b remains the dominant genotype, with prevalence rates ranging from

53.8% to 85.8% (Table 5). While some studies suggest a proportional decline in GT 1b over time, others have reported no significant changes.[18,36,37] In our study, GT 1b was the most frequently detected genotype at 65.9%, and although there was a proportional decrease over the years, no statistically significant difference was observed.

Research has shown that the frequency of GT 1a in Türkiye ranges between 3.7% and 18.1% (Table 5). In our study, the GT 1a rate was 13.2%, which is consistent with the aforementioned findings. Furthermore, it was found to be significantly higher in 2022 in comparison to other years (p=0.0008). (Table 4). The results of epidemiological studies conducted in Europe indicate a decrease in genotypes 1b and 2 and an increase in genotypes 1a, 3, and 4, with a notable prevalence among younger patients and intravenous drug users. The observed increase in GT 1a in our study is consistent with these findings. However, in light of the data from our study, it is not possible to conclude that this group of patients, who are in a wide age range, are especially young or that the transmission is caused by drug use.[38]

Globally, GT 3, which typically ranks second in HCV genotype distribution, is more common in low- and middle-income countries and accounts for 25% of all HCV infections. GT 3 is also notably prevalent among intravenous drug users worldwide.[39] Studies conducted in Türkiye have reported GT 3 prevalence rates ranging from 4.2% to 16.8% (Table 5). Additionally, numerous studies have noted an increase in the number and proportion of GT 3 cases over time. This rise has been attributed to factors such as the influx of foreign patients and a notable increase in intravenous drug use.[36,37] In our study, GT 3 was detected at a rate of 11%, with a proportional increase observed over the years, aligning with the literature (Table 3).

HCV GT 4 is most prevalent in the Middle East, Central, and Eastern Africa.[29] Studies conducted in Türkiye indicate that the prevalence of GT 4 ranges from 0.9% to 35.6% (Table 5). These studies suggest that GT 4 has increased over the years, particularly in regions with a high concentration of people from the Middle East, often due to post-war migration.[40] In our study, the GT 4 rate was 6.6%, consistent with Turkish data. Among the six GT 4 cases, only one patient (a Somali national) was foreign (Table 3). Additionally, while no GT 4 cases were detected in 2020, a proportional increase was observed in 2021 and 2022, though this was not statistically significant (Table 4).

Kuru et al. emphasized the importance of detecting mixed genotype infections, as they can lead to treatment failures.[41] Recent studies from various regions of Türkiye have reported mixed genotype rates ranging from 0.6% to 8.6% (Table 5). In our study, mixed genotypes were identified at a rate of 1.1%, with a combination of genotypes 3 and 4 detected.

In a study conducted in our country, when genotypes were analyzed in terms of gender distribution, no significant difference was observed among patients with GT 1 and GT 4, whereas a statistically significant male predominance was noted in the GT 2 and GT 3 groups.[42] In the study conducted by Tezcan et al., it was determined that GT 1b is more common in women, while other subtypes apart from GT 1b are more frequently observed in men.[43] In a study conducted in Istanbul, GT 1a and GT 3 were found to be more prevalent in men, while GT 1b was more common in women.[44] In the study conducted by Selek et al., no statistically significant difference was found between gender and age groups in terms of HCV genotype distribution.[45] In another study, GT 1 was found to be more prevalent in elderly patients, while GT 3 was more common in younger patients.[46] In our study, the highest rate (31.8%) was observed in the age group over 65 years (Table 2), with GT 1b being the most frequently detected in this group. Additionally, when the distribution of genotypes by gender was analyzed, GT 1b was found to be more common in women, while other subtypes, particularly GT 1a, were more frequently observed in men. Our findings were found to be

consistent with the literature. The difference between male and female patients who tested positive for the genotype was statistically significant (p=0.0018).

Özkaya et al.'s study found that the origins of foreign patients were similar to those in our study, with an overall genotype positivity rate of 4.5%, and GT 1b being the most frequently detected genotype.[17] Consistent with these findings, our study found that three of the four foreign patients, who made up 4.4% of the total patient population, had GT 1b, and one had GT 4. The GT 4 case was a Somali female patient, while the other foreign patients were from Afghanistan, Uzbekistan, and Azerbaijan.

Guntipalli et al. reported that the most common genotypes in the Turkic republics, Russia, and surrounding countries were 1, 3, and 2, respectively. In Russia, GT 1b was prevalent at rates of 55% to 80%, but the frequency of GT 3 has increased among younger individuals due to the rise in intravenous drug use.[27]

CONCLUSION

The findings of our study indicate that GT 1b, the most prevalent genotype in Türkiye, was the predominant genotype among patients who sought care at our hospital over the three-year period. It is, however, a matter of concern that the prevalence of less common genotypes and mixed-type HCV infections is on the rise in Türkiye. In the absence of treatment for foreign patients and without the assurance of effective migrant control, there is a risk of significant shifts in the epidemiology of HCV genotypes in the coming years.

The detection of HCV genotypes is of paramount importance for the guidance of prognosis and treatment of chronic HCV infections, as well as for the surveillance of shifts in HCV epidemiology. The use of direct-acting antivirals (DAAs), particularly in regions where new variants are being identified, reinforces the confidence in achieving the strategic objective of global HCV elimination by 2030. However, continued public health eff forts are essential to ascertain further instances of novel subtypes and to observe the advent or circulation of variants that may exhibit resistance to DAA therapy.

Ethical Approval

The study was conducted in accordance with the ethical standards set forth by the Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University (Decision No. 443-2023/10).

Peer-review

Externally and internally peer-reviewed.

Author Contributions

Concept: M.G., S.Ü., Y.Ç. Design: M.G., C.D., S.Ü., B.F.Y., Y.Ç., Data collection or Processing: M.G., C.D., B.F.Y., Analysis or interpretation: M.G., C.D., S.Ü., B.F.Y., Y.Ç., Literature Search: M.G., C.D., S.Ü., B.F.Y., Y.Ç., Writing: M.G., C.D., S.Ü., B.F.Y., Y.Ç.

Confli ct of Interest

The authors declare that they have no conflict of interest.

Funding

This study received no financial support.

References

1. Vos T, Barber RM, Bell B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386:743-800.
2. Taherkhani R, Farshadpour F. Epidemiology of hepatitis C virus in Iran. World J Gastroenterol. 2015;21(38):10790.
3. Smith DB, Bukh J, Kuiken C, et al. Expanded classification of hepatitis C virus into 7 genotypes and 67 subtypes: updated criteria and genotype assignment web resource. Hepatology. 2014; 59: 318–27.
4. Borgia SM, Hedskog C, Parhy B, et al. Identification of a novel hepatitis C virus genotype from Punjab, India: expanding classification of hepatitis C virus into 8 genotypes. J Infect Dis. 2018; 218:1722–9.
5. Murphy DG, Sablon E, Chamberland J, et al. Hepatitis C virus genotype 7, a new genotype originating from Central Africa. J Clin Microbiol. 2015; 53: 967–72.
6. Bukh J, Purcell RH, Miller RH. At least 12 genotypes of hepatitis C virus predicted by sequence analysis of the putative E1 gene of isolates collected worldwide. Proc Natl Acad Sci U S A. 1993; 90: 8234–8.
7. Simmonds P, Holmes EC, Cha TA, et al. Classification of hepatitis C virus into six major genotypes and a series of subtypes by phylogenetic analysis of the NS-5 region. J Gen Virol. 1993; 74: 2391–9.
8. Larney S, Peacock A, Leung J, et al. Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. Lancet Glob Health. 2017;5:e1208-e1220.
9. Maunye TK, Gededzha MP, Blackard JT, Rakgole JN, Selabe SG. Hepatitis C Virus Genotype 5 Variability in Treatment-Naïve Patients in South Africa. Intervirology. 2023;66(1):77-87.
10. Gökahmetoğlu S, Atalay MA, Kılınç A. Hepatit C virüs genotiplerinin pirosekanslama yöntemi ile belirlenmesi. Erciyes Tıp Derg 2011; 33: 99-102.
11. Cetin AD, Kibar F, Cetiner S, et al. Determination of hepatitis C virus genotype and HCV infection transmission routes in Cukurova University Medical Faculty Hospital. Turk Hij Den Biyol Derg. 2017;74(3):201-10.
12. Akgün S, Tarhan G, Sayıner H. S, et al. Adıyaman ilinde hepatit C virüsü genotip dağılımının belirlenmesi. Ortadoğu Tıp Dergisi. 2017; 9(1): 1-5.
13. Tiryaki Y, Çetin-Duran A, Özçolpan OO. Distribution of hepatitis C virus genotypes in Aydın Province. Viral Hepat J. 2018;24(3):70-4.
14. Öz S, Köroğlu M, Özbek A, et al. Sakarya ilinde hepatit C virüs genotip dağılımı; üç yıllık retrospektif çalışma. OTSBD. 2019;4(4):444-53.
15. Sari ND, Karataş A, İncı A, et al. Yerli ve Yabancı Hastalarda Hepatit C Virüs Genotip Dağılımının Değerlendirilmesi. Türkiye Klinikleri. Tip Bilimleri Dergisi. 2020; 40(2):148-53.
16. Ağca H, Ener B, Sağlık İ, et al. Hepatit C virüsü genotiplerinin retrospektif incelenmesi. Turk Mikrobiyol Cem Derg. 2021;51(3):303-8.
17. Özkaya E, Buruk CK, Aydın F, et al. Distribution of hepatitis C virus genotypes: 18-year experience in an academic center. Viral Hepat J. 2021;27(3):118-23.
18. Alacam S, Bakir A, Karatas A. Hepatitis C virus genotypes and viremia in a tertiary hospital in Istanbul, Türkiye. J Infect Dev Ctries. 2022;16: 668-74.
19. Bulut, D, Sayar M. S. Van İlindeki Hepatit C Genotip Dağılımı ve Bulaş için Öngörülen Risklerin Değerlendirilmesi. Van Tip Dergisi. 2023;30(4):332-8.
20. World Health Organization. Global Hepatitis Report 2017. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
21. World Health Organization Global Health Sector Strategy on Viral Hepatitis 2016–2021. Available online: https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf;jsessionid=60A93ADD1A191FF6A0FA823314D24C43?sequence=1.
22. Gower E, Estes C, Blach S, et al. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014; 61: S45-57.
23. Hauser G, Awad T, Brok J, et al. Peginterferon plus ribavirin versus interferon plus ribavirin for chronic hepatitis C. Cochrane Database Syst Rev. 2014;(2):CD005441.
24. Ermis F, Senocak TE. New treatment strategies for hepatitis C infection. World J Hepatol. 2015; 7(17): 2100-2109.
25. Jakobsen JC, Nielsen EE, Feinberg J, et al. Direct-acting antivirals for chronic hepatitis C. Cochrane Database Syst Rev. 2017; 18(9): CD012143.
26. Schietroma I, Corano Scheri G, Pinacchio C, et al. HCV and hepatocellular carcinoma: pathogenetic mechanisms and impact of DAA's. Open Virol J. 2018; 12(Suppl 1, M3): 16-25.
27. Guntipalli P, Pakala R, Kumari Gara S, et al. Worldwide prevalence, genotype distribution and management of hepatitis C. Acta Gastroenterol Belg. 2021;84(4): 637-56.
28. Spearman CW, Dusheiko GM, Hellard M, et al. Hepatitis C. Lancet. 2019;394:1451-66.
29. Di Stefano M, Ismail MH, Leitner T, et al. A novel candidate hepatitis C virus genotype 4 subtype identified by next generation sequencing full-genome characterization in a patient from Saudi Arabia. Frontiers in Microbiology. 2023;14: 1285367.
30. Wang B, Krüger L, Machnowska P, et al. Characterization of a hepatitis C virus genotype 1 divergent isolate from an HIV-1 coinfected individual in Germany assigned to a new subtype 1o. Virol J. 2019;16(1):28.
31. Oikonomopoulou M, Demetriou V L, Kostrikis L G, et al. Re-analysis of unassigned hepatitis C virus (HCV) strain CYHCV025: evidence of a highly divergent lineage within genotype 1. Mol. Phylogenet. Evol. 2017; 109: 362–6.
32. Li C, Cao H, Lu L, et al. Full-length sequences of 11 hepatitis C virus genotype 2 isolates representing five subtypes and six unclassified lineages with unique geographical distributions and genetic variation patterns. J. Gen. Virol. 2012; 93: 1173–84.
33. Hundie GB, Raj VS, GebreMichael D, Pas SD, Haagmans BL. Genetic diversity of hepatitis C virus in Ethiopia. PLoS One. 2017;12(6):e0179064.
34. Simmonds P, Bukh J, Combet C, et al. Consensus proposals for a unified system of nomenclature of hepatitis C virus genotypes. Hepatology.2005; 42: 962–73.
35. Ciccozzi M, Equestre M, Costantino A, et al. Hepatitis C virus genotype 4d in southern Italy: reconstruction of its origin and spread by a phylodynamic analysis. J. Med. Virol. 2012; 84: 1613–9.
36. Erman Daloğlu A, Parkan ÖM, Erdoğan A, et al. Damar içi madde bağımlılığı olan ve madde bağımlısı olmayan hastalar arasında hepatit C virus (HCV) genotiplerinin dağılımı. Mikrobiyol Bul. 2021;55(1):30-40.
37. Çabalak M, Bal T, Demir M, et al. Genotype distribution of hepatitis C virus in Hatay province of Türkiye. Viral Hepat J. 2020;26(2):56-60.
38. Kırdar S, Yaşa MH, Aydin N, et al. The distribution of hepatitis C virus genotypes in patients with chronic hepatitis C infection. Meandros Medical And Dental Journal. 2015;16(3):108-13.
39. Petruzziello A, Marigliano S, Loquercio G, Cacciapuoti C. Hepatitis C virus (HCV) genotypes distribution: an epidemiological up-date in Europe. Infect Agent Cancer. 2016;11:53.
40. Altindis M, Dal T, Akyar I, et al. Six-year distribution pattern of hepatitis C virus in Türkiye: A multicentre study. Biotechnol Biotec Eq. 2015;30(2):335-40.
41. Kuru C, Hamidi AA. Genotype distribution of hepatitis C virus and demographic features of the patients in the province of Karabük. Viral Hepat J. 2020;26(3):163-6.
42. Kuşcu F, Kömür S, İnal AS. Changing epidemiology of chronic hepatitis C in Adana. Viral Hepat J. 2014;20(1):15-8.
43. Tezcan S, Ulger M, Aslan G, et al. Determination of hepatitis C virus genotype distribution in Mersin province, Türkiye. Mikrobiyol Bul. 2013;47(2):332-8.
44. Bulut ME, Topalca US, Murat A, et al. HCV Genotype Distribution of Patients with Chronic Hepatitis C in Istanbul. Sisli Etfal Hastan Tip Bul. 2021;55(1):86-92.
45. Selek MB, Baylan O, Karagöz E, Özyurt M. Changes in hepatitis C virus genotype distribution in chronic hepatitis C infection patients. Indian J Med Microbiol. 2018;36(3):416-21.
46. Karabulut N, Alacam S, Yolcu A, Onel M, Agacfidan A. Distribution of hepatitis C virus genotypes in Istanbul, Türkiye. Indian J Med Microbiol. 2018;36(2):192-6.