e-ISSN:2146-409X

SAKARYA TIP DERGİSİ

MEDICAL JOURNAL

Cilt / *Vol*: 11

Sayı / *Issue*: 1

Mart / *March*: 2021

Dergimizin değerli okuyucuları,

Yeni bir sayı ile karşınızdayız. Bu sayı vesilesiyle tüm yazar ve okuyucularımızdan dergimiz ile ilgili yaşanan bazı gecikme ve aksaklıklardan dolayı özür dilemek istiyoruz. Malumunuz olduğu üzere pandemi sürecinden tüm sağlık çalışanları farklı düzeylerde olumsuz olarak etkilendi. Bu süreçte bizim editör kadromuz da aktif olarak pandemi ile ilgili hizmetlerde görev aldığından dolayı makale değerlendirme işlemlerinde gecikmeler yaşandı. Bu gecikmelerin ihmal kaynaklı olmadığından emin olmanızı istiyorum. Bu gecikmelerin önüne geçmek için yakın zamanda editör kadromuzu genişlettik. Sizlere daha iyi hizmet verebilmek umuduyla sağlıklı günler diliyorum.

Prof. Dr. Hasan Çetin EKERBİÇER
Editör

YAZIŞMA ADRESİ
Sakarya Tıp Dergisi
Sakarya Üniversitesi Tıp Fakültesi
Esentepe Kampüsü 54187 Serdivan - SAKARYA
Tel : 0 (264) 0 264 295 3134
Faks : 0 (264) 295 66 29
e-posta : hcekerbicer@gmail.com.tr

YAYINCI
Sakarya Üniversitesi
Sakarya üniversitesi Esentepe Kampüsü 54187 / SAKARYA

ULUSLARARASI BİLİMSEL DANIŞMA KURULU

GENEL BİLGİLER

Sakarya Tıp Dergisi, Acil Tıp, Adli Tıp, Aile Hekimliği, Algoloji, Anatomi, Aneztezi ve Reanimasyon, Beyin ve Sinir Cerrahisi, Çocuk Sağlığı ve Hastalıkları, Deri ve Zührevi Hastalıklar, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Fiziksel Tıp ve Rehabilitasyon, Fizyoloji, Genel Cerrahi, Göğüs Cerrahisi, Göğüs Hastalıkları, Göz Hastalıkları, Halk Sağlığı, Hava ve Uzay Hekimliği, Hematoloji, Histoloji ve Tıbbi Embriyoloji, İç Hastalıkları, Kadın Hastalıkları ve Doğum, Kalp ve Damar Cerrahisi, Kardiyoloji, Kulak Burun Boğaz Hastalıkları, Nöroloji, Nükleer Tıp, Ortopedi ve Travmatoloji, Plastik ve Rekonstriktif Cerrahi, Radyasyon Onkolojisi, Radyoloji, Ruh Sağlığı ve Hastalıkları, Spor Hekimliği, Sualti Hekimliği ve Hiperbarik Tıp, Tıbbi Biyokimya, Tıbbi Ekoloji ve Hidroklimatoloji, Tıbbi Farmakoloji, Tıbbi Genetik, Tıbbi Mikrobiyoloji, Patoloji, Üroloji Anabilim Dalları ve yukarıda adı geçen tüm bilim dallarının yan dallarıyla ile ilgili olabilecek retrospektif, prospektif veya deneysel araştırma, derleme, olgu sunumu, editöryal yorum/tartışma, editöre mektup, cerrahi teknik, ayırıcı tanı, tıbbi kitap değerlendirmeleri, soru- cevaplar ve tıp gündemini belirleyen güncel konuları yayınlayan, Ulusal ve Uluslararası tüm tıbbi kurum ve personele ulaşmayı hedefleyen bilimsel bir dergidir. 06/07/2019 tarihinden itibaren Diş Hekimliği, Beslenme ve Diyetetik, Sağlık Yönetimi Bilim Dallarından gönderilen çalışmalar koruyucu hekimlik konularını işlemek kaydıyla kabul edilecektir.

Dergi yılda dört sayı olarak Mart, Haziran, Eylül ve Aralık aylarında yayınlanmaktadır. Derginin resmi yayın dili Türkçe ve İngilizcedir. İngilizce yazım tercih sebebidir. Dergi ile ilgili her türlü işlem ve başvuru http://dergipark.gov.tr/smj adresinden yapılabilir. Geçmiş sayılarda yayınlanan çalışmalara bu adresten ulaşılabilir.

Bilimsel Politikalar ve Etik Sorumluluğu: Yazıların bilimsel sorumluluğu yazarlara aittir. Tüm yazarların çalışmaya aktif olarak katılmış olması gereklidir. Gönderilen yazıların dergide yayınlanabilmesi için daha önce başka bir bilimsel yayın organında yayınlanmamış olması gerekir. Gönderilen yazı daha önce herhangi bir toplantıda sunulmuş ise; toplantı adı, tarihi ve düzenlendiği şehir belirtilmelidir. Klinik araştırmaların protokolü ilgili kurumun etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. (Etik kurul tarih ve protokol numarası) Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvanhaklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Değerlendirme Süreci:

Dergiye gönderilen yazıların değerlendirilmesi üç aşamada yapılmaktadır. Birinci aşamada makaleler dergi standartları açısından incelenir, yazım kurallarına uymayan makaleler reddedilir. Makale yazım kurallarına göre düzenlendikten sonra aynı isimle yeniden dergiye yüklenebilir. İkinci aşamada makaleyi editör kurulu tarafından içerik ve yöntem açısından değerlendirmeye alınır. İlk iki aşamayı tamamlayan makaleler üçüncü aşamaya geçerek incelenmesi için hakemlere gönderilir.

Tüm yazılarda editöryel değerlendirme ve düzeltmeye başvurulur; gerektiğinde, yazarlardan bazı soruları yanıtlaması ve eksikleri tamamlaması istenebilir. Değerlendirme sonucu kabul, minör revizyon, major revizyon, yeniden yazılması gerekli ya da ret kararı çıkabilir. Dergide yayınlanmasına karar verilen makale basım sürecine alınır; bu aşamada tüm bilgilerin doğruluğu için ayrıntılı kontrol ve denetimden geçirilir; yayın öncesi şekline getirilerek yazarların kontrolüne ve onayına sunulur.

Yayın Hakkı:

1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı dergiyi yayımlayan kuruma aittir. Yazarlar, http://dergipark.gov.tr/smj internet adresinden ulaşacakları "Yayın Hakları Devir Formu"nu doldurup (mavi kalemle ve ıslak imzalı olacak şekilde tüm yazarlarca imzalanmış), DergiPark sitemi üzerinden göndermelidirler.

- Olgu sunumu/serisi ve derleme dışındaki bilimsel çalışmalarda etik kurul onay belgesi sisteme yüklenmelidir.
- Veri toplama süreci Aralık 2010 tarihinden önce tamamlanmış çalışmalar kabul edilmeyecektir.
- Bilimsel çalışmalar, çalışmadaki yazarların isim ve soy isimleri (çalışmaya dahil olan tüm yazar isimleri yazılmalı) ile çalışma başlığındaki tüm kelimelerin (bağlaçlar hariç) sadece ilk harfleri büyük harf olacak şekilde DergiPark sistemineyüklenmelidir.
- Yazarların aynı sayıda ilkisim oldukları yalnızca bir çalışmaları yayınlanacaktır.
- SCI, SSCI, SCIE, ESCI veya A&HCI'de
- indekslenen dergilerde yayınlanmış çalışmalarında Sakarya Tıp Dergisi'nde yayınlanmış herhangi bir çalışmaya atıfta bulunan yazarların çalışmalarına öncelik verilecektir. (Çalışma bilgilerinin ve varsa linkinin Editöre Sunum Sayfası'nda belirtilmesi gerekmektedir ve hckerbicer@gmail.com adresine mail atılarak hatırlatma yapılmalıdır).
- Yazım dili İngilizce olan bilimsel çalışmaların veya yazım dili Türkçe olan çalışmaların İngilizce özetlerinin yazımında akademik düzenleme hizmeti veren profesyonel kurum veya kuruluşlardan yardım alındığının belgelenmesi durumunda bu çalışmalara öncelik verilecektir.

Yazının Hazırlanması

- Derleme türündeki bilimsel çalışmalar için yazar sayısı üçü geçmemelidir.
- Olgusunumları için yazar sayısı altıyı geçmemelidir.
- Yazılar çift satır aralıklı ve 10 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2.5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Arial olmalıdır.
- Yazılar Microsoft Word formatında olmalıdır. (Tablolar dahilolacak şekilde)
- Kısaltmalar, özette ve ana metinde kelimenin ilk geçtiği yerde parantez içinde verilmeli ve tüm metin boyunca o kısaltma kullanılmalıdır. Küçük harflerle yapılan kısaltmalara getirilen eklerde ise kısaltmanın son harfinin okunuşu esas alınır: cm'yi, kg'dan, mm'den, kr.un. Büyük harflerle yapılan kısaltmalara getirilen eklerde ise kısaltmanın son harfinin okunuşu esas alınır: BDT'ye, TDK'den, THY'de, TRT'den, TL'nin vb. Ancak kısaltması büyük harflerle yapıldığı hâlde bir kelime gibi okunan kısaltmalara getirilen eklerde kısaltmanın okunuşu esas alınır: ASELSAN'da, BOTAŞ'ın, NATO'dan, UNESCO'ya vb.
- Editöre sunum sayfası ayrı bir Word dosyası olarak gönderilmelidir. Editöre sunum sayfasında gönderilen çalışmanın kategorisi, eş zamanlı olarak başka bir dergiye gönderilmemiş olduğu, daha önce başka bir dergide yayınlanmamış olduğu, varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ile varsa bu kuruluşların yazarlarla olan ilişkileri belirtilmelidir.
- Kapak sayfası ayrı bir Word dosyası olarak gönderilmelidir. Kapak sayfasında başlık basit ve anlaşılır şekilde olmalıdır (Türkçe ve İngilizce). Başlık 60karakterden daha uzun
- olduğu takdirde İngilizce ve Türkçe kısa başlık da kapak sayfasına eklenmelidir. Tüm yazarların adı, soyadı ve unvanları, ORCID numaraları, çalıştıkları kurumun adı ve şehri bu sayfada yer almalıdır. Bu sayfaya ayrıca "yazışmadan sorumlu" yazarın isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

İstatistik Bilgi Notu

- Kullanılan istatistiksel yöntem, orijinal veriye erişebilecek bilgili bir okuyucunun rapor edilen sonuçları onaylayabileceği bir ayrıntıda belirtilmelidir. İstatistiksel terimler, kısaltmalar ve semboller tanımlanmalıdır. Kullanılan bilgisayar programı, istatistiksel yönteme dair açıklama verilmelidir. Çalışma deseni ve istatistiksel yönteme dair kaynaklar mümkünse belirtilmelidir.
- Sonuçların sunumunda, özellikle ortalama ve yüzdelik verirken, ondalıklı hanelerin gösteriminde virgülden sonra sonra 2 hane kullanılmalıdır (112,2 yerine; 112,20 veya 112,21 gibi). P, t, Z değerleri istisnadır ve virgülden sonra 3 hane verilmelidir (p<0,05 yerine tam değer p=0,001). Tam sayı dışındaki gösterimlerde virgülden sonra iki hane, istatistiksel değerlerin (p,t,z,F,Ki-Kare gibi) virgülden sonra üç hane değerlerin sunulması, p değerlerinin sunumunda p<0,05 veya p>0,05 yerine test istatistiği ile birlikte tam p değerinin (bu değerin binde birden küçük olması durumunda p<0,001 biçiminde) gösterilmesi gerekmektedir.

Yazının Bölümleri

- Çalışmanın gönderildiği metin dosyasının içinde sırasıyla, Türkçe başlık, Türkçe özet, Türkçe anahtar kelimeler, İngilizce başlık, İngilizce özet, İngilizce anahtar kelimeler, çalışmanın ana metini, kaynaklar, her sayfaya bir tablo olmak üzere tablolar ve son sayfada şekillerin (varsa) alt yazıları şeklinde olmalıdır. Tablolar kaynaklardan sonra, her sayfaya bir tablo olmak üzere çalışmanın gönderildiği dosya içinde olmalı ancak çalışmaya ait şekil, grafik ve fotoğrafların her biri ayrı bir imaj dosyası (jpeg ya da gif) olarak gönderilmelidir.

Araştırma Makalesi:

Öz (Abstract): Türkçe ve İngilizce özetler çalışmanın başlığı ile birlikte verilmelidir. Özetler Amaç (Objective), Gereç ve Yöntemler (Materials and Methods), Bulgular (Results) ve Sonuç (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir.

Anahtar Kelimeler (Keywords): Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özetten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction): Giriş bölümünün son paragrafında çalışmanın amacını bildiren bir cümle yer almalıdır.

Gereç ve Yöntemler (Materials and Methods): Araştırmanın tipi, etik hususlar (etik onamının alındığı kurum, tarih ve no), kullanılan istatistiksel analiz yöntemleri belirtilmelidir.

Bulgular (Results) Tartışma (Discussion) Kaynaklar (References)

Makalenin son sayfasında etik onamının alındığı kurum, tarih ve no ayrıca belirtilmelidir.

Olgu Sunumu/Serisi:

Öz (Abstract): Türkçe ve İngilizce özetler makelenin başlığı ile birlikte verilmelidir. Özetler tek paragraflık olmalıdır. (100-150 kelime olmalıdır.)

Anahtar Kelimeler (Keywords): Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özetten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction)

Olgu Sunumu (Case Report) Tartışma (Discussion) Kaynaklar (References)

*Olgu sunumlarında, bilgilendirimiş gönüllü olur/onam formunun imzalatıldığına dair bilgiye makalede yer verilmesi gereklidir.

Derleme:

Öz (Abstract): Derleme özetleri kısa ve tek paragraflık olmalıdır (ortalama 100-150 kelime; bölümsüz, Türkçe ve İngilizce)

Anahtar Kelimeler (Keywords): Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özetten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction) Konu İle İlgili Başlıklar Sonuç (Conclusion) Kaynaklar (References)

Editöre Mektup:

Mektuplar, kaynaklar hariç 500 kelimeyi geçmemelidir. Türkçe ve İngilizce özete gerek yoktur. Kaynak sayısı 5 ile sınırlandırılmalıdır. Bir mektup en fazla 4 yazar tarafından yazılabilir. Editöre mektuplar hakem değerlendirme sürecine alınmaz, ancak editör tarafından gerekli durumlarda yazarlardan mektuba cevap vermeleri istenebilir.

Anahtar Kelimeler

- En az 3 en fazla 6 adet, Türkçe ve İngilizce yazılmalıdır.
- Kelimeler birbirlerinden noktalı virgül (;) ile ayrılmalıdır.
- İngilizce anahtar kelimeler "Medical Subject Headings (MESH)"e uygun olarak verilmelidir (www.nlm.nih.gov/mesh/MBrowser.html).
- Türkçe anahtar kelimeler Türkiye Bilim Terimleri'ne uygun olarak verilmelidir (www.bilimterimleri.com).

Kaynaklar

- Yazarlar yalnızca doğrudan yararlandıkları kaynakları yazılarında gösterebilirler.
- Kaynaklar yazıda geliş sırasına göre yazılmalı ve metinde cümle sonunda noktalama işaretlerinden hemen sonra "Üst Simge" olarak belirtilmelidir.
- Çalışmada bulunan yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 6 isim yazılıp "et al" eklenmelidir.
- Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org).
- Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır.
- Kaynak sayısının araştırmalarda 50 ve derlemelerde 100, olgu sunumlarında da
- 10 ile sınırlandırılmasına özen gösterilmelidir.
- Kaynakların dizilme şekli ve noktalamalar aşağıdaki örneklere uygun olmalıdır (Noktalamaişaretlerine lütfen dikkat ediniz):

Makale için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, makale ismi, dergi ismi, yıl, cilt, sayı, sayfa no'su belirtilmelidir.

Örnek: Dilek ON, Yilmaz S, Degirmenci B, Ali Sahin D, Akbulut G, Dilek FH. The use of a vessel sealing system in thyroid surgery. Acta Chir Belg 2005;105:369-372.

Kitap için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, bölüm başlığı, editörün(lerin) ismi, kitap ismi, kaçıncı baskı olduğu, şehir, yayınevi, yıl ve sayfalar belirtilmelidir.

Örnek:

- Yabancı dilde yayımlanan kitaplar için;
- Vissers RJ, Abu-Laban RB. Acute and Chronic Pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency Medicine: A comprehensive Study Guide. 6 st ed. New York: McGraw-Hill Co; 2005. p.573-577.
- Türkçe kitaplar için; Gökçe Ö. Peptik ülser. Dilek ON, editör. Mide ve Duedonum.
- 1. Baskı. Ankara: Anıt Matbaası; 2001. s:265- 276.
- On-line yayınlar için format; DOI tek kabul edilebilir on-line referanstır.

Şekil, Resim, Tablo ve Grafikler

- Şekil, resim, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmelidir.
- Şekil, resim, tablo ve grafiklerin açıklamaları ana metnin sonuna eklenmelidir.
- Tablolar her sayfaya bir tablo olmak üzere yazının gönderildiği dosya içinde olmalı ancak yazıya ait şekil, grafik ve fotoğrafların her biri ayrı bir imaj dosyası (jpeg ya da gif) olarak gönderilmelidir.
- Kullanılan kısaltmalar şekil, resim, tablo ve grafiklerin altındaki açıklamada belirtilmelidir.
- Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir.
- Resimler/fotoğraflar renkli, ayrıntıları görülecek derecede kontrast ve net olmalıdır.

Çıkar ilişkisi: Yazarların herhangi bir çıkar dayalı bir ilişkisi varsa bu açıklanmalıdır.

Teşekkür: Bu bölümde yazar olarak ismi geçmeyen ancak teşekkür edilmesi gereken kişiler veya kurumlar yer almalıdır.

Yayımlanmak Üzere Gönderilen Çalışmalar İçin Kontrol Listesi

Çalışmalar tam olmalı ve şunları kapsamalıdır:

- Tüm yazarlarca imzalanmış "Telif Hakkı Formu" (mavi kalemle ve ıslak imzalı olacak şekilde)
- Etik kurul onayının PDF veya JPEG formatındaki görüntüsü(Olgu sunumu- serisi ve derleme yazıları için gerekli değildir.)
- Editöre Sunum Sayfası
- Kapak Sayfası
- Yazının Bölümleri
- Türkçe ve İngilizce başlık
- Öz (Türkçe ve İngilizce)
- Anahtar sözcükler (en az3 ve en fazla 6Türkçe ve İngilizce)
- Uygun bölümlere ayrılmış ana metin
- Kaynaklar yazıda geliş sırasına göre yazılmalı ve metinde cümle sonunda noktalama işaretlerinden hemen sonra "Üst Simge" olarak belirtilmelidir.
- Dergi yazı kurallarına uygun olarak hazırlanmış kaynaklar listesi
- Bütün şekil, tablo ve grafikler
- Çalışmalar, çalışmadaki yazarların isim ve soy isimleri(çalışmaya dahil olan tüm yazar isimleri yazılmalı) ile çalışma başlığındaki tüm kelimelerin(bağlaçlar hariç) sadece ilk harfleri büyük harf olacak şekilde DergiPark sistemine yüklenmelidir.

Kontrol listesinde belirtilen koşulları sağlamayan çalışmalar için değerlendirme süreci başlatılamayacaktır.

Information to Authors

General Information:
Sakarya Medical Journal is a scientific journal that publishes retrospective, prospective or experimental research articles, review articles, case reports, editorial comment/discussion, letter to the editor, surgical technique, differential diagnosis, medical book reviews, questions-answers and also current issues of medical agenda from all fields of medicine and aims to reach all national/international institutions and individuals.
The manuscripts may be related to Emergency Medicine, Forensic Medicine, Family Medicine, Algology, Anatomy, Anesthesiology and Reanimation, Neurosurgery, Pediatrics, Dermatology, Infectious Diseases and Clinical Microbiology, Physical Medicine and Rehabilitation, Medical Physiology, General Surgery, Thoracic Surgery, Pulmonary Medicine, Ophthalmology, Public Health, Aviation and Space Medicine, Hematology, Histology and Medical Embryology, Internal Medicine, Obstetrics and Gynecology,

Cardiovascular Surgery, Cardiology, Otorhinolaryngology, Neurology, Nuclear Medicine, Orthopedics and Traumatology, Plastic and Reconstructive Surgery, Radiation Oncology, Radiology, Psychiatry, Sports Medicine, Underwater Medicine and Hyperbaric Medicine, Medical Biochemistry, Medical Ecology and Hydroclimatology, Medical Pharmacology, Medical Genetics, Medical Microbiology, Pathology, Urology disciplines and the subdisciplines of all the above mentioned disciplines. The studies related to the disciplines of Dentistry, Nutrition and Dietetics, Health Care Management will be accepted only if they are related to the Preventive Medicine topics.

The journal is published four times in a year and in March, June, September and December. The official languages of the journal are Turkish and English, but english manuscripts are preferred. Any processes and submissions about the journal can be made from the website: http://dergipark.gov.tr/smj Past issues of the journal are also available at this website.

ScientificPolicies and Ethics Responsibility:
The author(s) undertake(s) all scientific responsibility for themanuscript. All the authors must actively participate in the study. The author(s) guarantee(s) that the manuscript itself or any substantially similar content of the manuscript has not been published or is being considered for publication elsewhere. If the manuscript had been presented in a meeting before; the name, date and the province of the meeting should benoted.
The protocol of the clinical investigations must be approved by the appropriate ethical committee of the related institution. All manuscripts dealing with human subjects must contain, in the Materials and Methods section, a statement indicating that the study has been approved by the committee or there should be a statement that the research was performed following the Declaration of Helsinki principles (http://www. wma.net/e/policy/b3.htm). In research work which includes humans,

informed consent must be obtained prior to the study and this should be stated in the text. All papers reporting experiments using animals must include a statement in the Material and Methods section giving assurance that all animals have received humane care in compliance with the Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) and indicating approval by the institutional ethical review board.

Review Process:
The evaluation of the articles submitted to the journal is done in three stages. In the first stage, articles are assessed in terms of the journal publication standards and the articles that do not comply with the writing rules of journal are rejected. After the article is edited according to writing rules of journal, it can be uploaded to the journal with the same name again. In the second stage, the article is evaluated by the editorial board in terms of content and method. The articles that complete the first two stages are sent to the journalrefereesfor the peer reviewprocess. If needed, some questions can be asked to the authors to answer; or some defaults may have to be corrected by the authors. The result can be acceptance, minor revision, major revision, rejection in the current form, or rejection. Accepted manuscripts are forwarded for publication; in this stage, all information and data are checked and controlled properly; the proof of the article to be published by the journal are forwarded to the writers for proof reading and corrections.

Copyright Statement:
In accordance with the Copyright Act of 1976, the publisher owns the copyright of all published articles. All manuscripts submitted must be accompanied by the "Copyright Transfer and Author Declaration Statement form"(with a blue pen and wet signature by all authors) that is available in http://dergipark.gov.tr/smj and send it through the DergiPark website.

- Ethics committee approval certificate should be uploaded to the system for scientific studies except case report / series and review articles.
- Studies for which data collection process is completed before December 2010 will not beaccepted.
- Scientific studies should be uploaded to the DergiPark system including the names and surnames of the authors (all author names should be written and only the first letters of all the words (except connectors) in the title of the study.
- An author can only have one article published in an issue where she/he is the first author.
- Priority will be given to the works of the authors, who refer to any study published in the Sakarya Medical Journal in their studies published in the journals indexed in SCI, SSCI, SCIE, ESCI or A & HCI, (information about the study and the link, if any, should be stated on the Presentation to the Editor Page and e-mail to hcekerbicer@gmail.com).
- Priority will be given to studies where it is documented that an assistance has been obtained from professional institutions or organizations providing academic editing services in the writing of scientific studies in English, or in English abstracts of Turkish studies. Manuscript Preparation
- Author number for review articles should not exceed three.
- Author number for case report presentationsshouldnotexceedsix.
- Articles should be written with double line space in 10 font size and right, left, upper and lower margins should all be 2.5 cm. Writing style should be Arial.
- Manuscripts should be written with Microsoft Word (including tables)
- Abbrevations that are used should be defined in parenthesis where the full word is first mentioned.
- Cover Letter: Cover letter should be written with Microsoft Word and should include statements about manuscript category designation, single-journal submission affirmation, conflict of interest statement, sources of outside funding, equipments (if so), approval for language for articles in English and approval for statistical analysis for original research articles.
- Title Page: Title should be written with Microsoft Word. Title also should be concise and informative (in Turkish and English). The title page should include a list of all contributing authors and all of their affiliations. Positions of authors and names of departments and institutions to which they are attached and the province should be written. Supply full correspondence details for the corresponding author, including phone, mobile phone, ORCID number and e-mail address.

Statistical Note:
- The statistical method that used should be stated in detail that a knowledgeable reader can confirm the reported results.
- Statistical terms, abbreviations and symbols must be defined. The computer program and statistical method that used should be described completely.
- References to the study design and statistical method should be indicated if possible.
- In the presentation of the results, especially when giving the average and the percentage, 2 digits should be used after the comma in the display of the decimal places (insteadof 112,2, such as112,20 or 112,21).
- The values of p, t and z are exceptions and 3 digits should be given after the comma (insteadofp<0.05,exactvaluelikep=0.001).
- Two digits after comma in non- integer representations, three digits after comma in the presentation of statistical values (p, t, z, F, chi- square) and in the presentation of p values, it is necessary to show the exact p value with the test statistic instead of p <0.05 or p> 0.05 (if this value is less than one thousandth, like p
<0.001 format).

Article Sections:
- The text file should include the title, keywords and abstract both in Turkish and English, the text of the article, references, tables (onlyone tablefor one page) andfigure legends (if any), respectively.
- Within the text file, the names of the authors, any information about the institutions, the figures and images (jpeg or gif) should be excluded.

Original ResearchArticles:
Abstract: Turkish and English abstracts should be given with the title of the study.
Abstracts should be divided into Objective, Materials and Methods, Results and Conclusion and should not exceed 250 words.
Keywords: Turkish keywords should be indicated after the Turkish abstract and English keywords should be indicated after the English abstract.
Introduction: In the last paragraph of the introductory section, there should be a specific sentence that states the purpose of the study.
Materials and Methods: The type of research, ethical issues (the institution, date and number from which the ethical approval was obtained) , statistical analysis methods used should be specified.
Results Discussion References
On the last page of the article, the institution, date and number of which the ethical consent was obtained should also be specified.

Case Report/SeriesArticles:
Abstract: Turkish and English abstracts should be given with the title of the article. Abstracts
should be single-paragraph and must be 100- 150 words.
Keywords: Turkish keywords should be indicated after the Turkish abstract and English keywords should be indicated after the English abstract.
Introduction Case report Discussion References
*In case reports, informative volunteer / consent form should be included in the article.

Review Articles:
Abstract: Review abstracts should be short and single paragraph, 100-150 words on average, non- sectioned and Turkish (and English) or English only.
Keywords: Turkish keywords should be indicated after the Turkish abstract and English keywords should be indicated after the English abstract.
Introduction
Topic related titles Conclusion References

Letter to the Editor:
Letters should not exceed 500 words, excluding references. There is no need to Turkish and English abstracts. The number of references should be limited to 5. A letter can be written by up to 4 authors. Letters to the editor are excluded from the peer review process. However, the editor may ask the authors to respond to the letter when necessary.

Keywords:
- They should be minimally 3 and maximally 6 and should be written in Turkish and English.
- The words should be separated by semicolon (;), from each other.
- English key words should be appropriate to "Medical Subject
- Headings (MESH)" (www.nlm.nih.gov/mesh/MBrowser.html).
- Turkish key words should be appropriate to "Turkey Science Terms" (www.bilimterimleri.com)

References:
The authors are required to cite only those references that they can submit to the Journal in the event they are requested to do so. References in the text should be numbered as superscript numbers and listed serially according to the order of mentioning on a separate page, double- spaced, at the end of the paper in numerical order. All authors should be listed if six or fewer, otherwise list the first six and add the et al. Journal abbreviations should conform to the style used in the Cumulated Index Medicus (www.icmje.org). Onlylist the literaturethat is published, in press (with the name of the publication known) or with a doi number in references. It is preferred that number of references do not exceed 50 for research articles, 100 for reviews and 10 for case reports.

Follow the styles shown in examples below (please give attention to punctuation): Format for journal articles; initials of author's names and surnames, titles of article, journal name, date, volume, number, and inclusive pages, must be indicated.
Example: Dilek ON, Yilmaz S, Degirmenci B, Ali Sahin D, Akbulut G, Dilek FH. The use of a vessel sealing system in thyroid surgery. Acta Chir Belg 2005;105(4):369-72.

Format for books; initials of author's names and surnames, chapter title, editor's name, book title, edition, city, publisher, date and pages. Example: Vissers RJ, Abu-Laban RB. Acute and Chronic Pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency Medicine: A comprehensive Study Guide. 6 st ed. New York: McGraw- Hill Co; 2005. p.573-77.
Format for on-line-only publications; DOI is the only acceptable on-line reference.

Figures, Pictures, Tables and Graphics:
- All figures, pictures, tables and graphics should be cited at the end of the relevant sentence.
- Explanations about figures, pictures, tables and graphics must be placed at the end of the article.
- Figures, pictures/photographs must be added to the system as separate .jpg or .gif files.
- The manuscripts containing color figures/pictures/tables would be published, if accepted by the Journal. In case of publishing colorful artwork, the authors will be asked to pay extra printingcosts.
- All abbrevations used, must be listed in explanation which will be placed at the bottom of each figure, picture, table and graphic.
- For figures, pictures, tables and graphics to be reproduced relevant permissions need to be provided. This permission must be mentioned in the explanation.
- Pictures/photographs must be in color, clear and with appropriate contrast to separate details.

Conflict of İnterest:
If any of the writers have a relationship based on self-interest, this should be explained.

Acknowledgment:
Only acknowledge persons and institutions who have made substantial contributions to the study, but was not a writer of the paper.

Checklist for Submitted Articles:
- Articles must be complete.
- They must include the following:
- Cover Letter
- Title Page
- Article sections
- Turkish and Englishtitles
- Abstract (250 words) (Turkish and English)
- Keywords (minimum 3; maximum 6)
- Article divided into sections appropriate
- Complete and accurate references and citations
- List of references styled according to "journal requirements"
- All figures (with legends) and tables (with titles) cited.
- "Copyright Form" signed by the responsible author (with a blue pen and wet signature)

Manuscripts lacking any of the above elements will be rejected from the review process.

DERGİ HAKEM HEYETİ

İÇİNDEKİLER / CONTENTS

ARAŞTIRMA MAKALESİ / RESEARCH ARTICLES (1-200)

RESEARCH ARTICLE / *Araştırma Makalesi*

Laparoscopy Versus Open Appendectomy for Elderly Patients: A Single-Center Experience

Yaşlı Hastalarda Laparoskopik ve Açık Apendektominin Karşılaştırılması: Tek Merkez Deneyimi

Enis Dikicier[1], Barış Mantoğlu[2], Kayhan Özdemir[2], Muhammed Burak Kamburoğlu[2], Emre Gönüllü[2]

[1] Sakarya University Faculty of Medicine, Department of General Surgery, Sakarya, TURKEY
[2] Sakarya Research and Education Hospital, Department of General Surgery, Sakarya, TURKEY

Yazışma Adresi / *Correspondence:*
Enis Dikicier
Sakarya University Faculty of Medicine, Department of General Surgery, Sakarya / TURKEY
T: **+90 505 252 08 02** E-mail **: enisdikicier@gmail.com**

Geliş Tarihi / Received : **05.08.2020** Kabul Tarihi / Accepted : **13.12.2020**

Orcid :
Enis Dikicier, https://orcid.org/0000-0002-5074-0299
Barış Mantoğlu, https://orcid.org/0000-0002-2161-3629
Kayhan Özdemir, https://orcid.org/0000-0002-8041-198X
Muhammed Burak Kamburoğlu, https://orcid.org/0000-0003-2242-5723
Emre Gönüllü, https://orcid.org/0000-0001-6391-4414

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):1-8) DOI: 10.31832/smj.777166**

Abstract

Objective — Acute appendicitis rates are gradually increasing in the elderly people population with prolonged life expectancy. This study aims to compare applicability of laparo-scopic and open surgical methods in patients treated surgically for acute appendi-citis over 65 years of age.

Materials and Methods — Patients over 65 years old who underwent surgical treatment for acute appendicitis at the Sakarya University Hospital between 2011-2018 were included in the study. The patients were clas-sified according to the surgical method applied as laparo-scopic or open appendectomy and complicated or non-complicated appendicitis. All groups were evaluated in terms of mean age, gender, white blood cell (WBC) levels, presence of comorbid disease, ASA score, operation time, the onset of oral intake, duration of hospital stay, postoperative intensive care requirement, pres-ence of complications and mortality.

Results — Of the 161 patients who underwent appendectomy over 65, 98 were male (% 60,80) and 63 were female (% 39,20). It was determined that open appendectomy was performed in 109 (% 67,70) of the cases, and laparoscopic appendectomy in 52 (% 32,29). It was determined that 61 (% 55,91) of 109 cases undergoing open surgery and 22 (% 42,32) of 52 cases undergoing laparoscopic appendectomy were complicated acute appendicitis. Complications were observed in 24 (% 14,94) of one hundred and fifty patients. In terms of complications, no significant differ-ence was found between laparoscopically operated groups and open appendec-tomy groups (P=0,873).

Conclusion — Laparoscopic appendectomy is considered as a safely feasible method in the population of elderly and high comorbid patients.

Keywords — Appendicitis; Laparoscopy; Elderly.

Öz

Amaç — *Akut apandisit acil cerrahide sık görülen patolojilerdendir. Genellikle genç yaşta görülen bir hastalıktır. Ortalama yaşam süresinin uzaması ile yaşlı hasta popu-lasyonunda akut apandisit görülme oranları giderek artmaktadır. Bu çalışmanın amacı, 65 yaş üstü akut apandisit nedeni ile cerrahi olarak tedavi edilen hastalar-da laparoskopik ve açık cerrahi yöntemlerin sonuç-larını karşılaştırmaktır.*

Gereç ve Yöntemler — *2011-2018 yılları arasında Sakarya Üniversitesi Tıp Fakültesi Eğitim ve Araştırma Hastanesi'nde akut apandisit nedeni ile cerrahi tedavi uygulanan 65 yaş üstündeki olgular çalışmaya dahil edildi. Olgular uygulanan cerrahi yönteme göre lapara-skopik veya açık apendektomi ve komplike veya nonkomplike apandisit olarak değerlendirilerek sınıflandırıldı. Tüm gruplar yaş ortalaması, cinsiyet, beyaz küre (WBC) düzeyleri, komorbid hastalık varlığı, ASA skoru, operasyon süresi, oral alımın başlama zamanı, hastanede kalış süresi, postoperatif yoğun bakım ger-eksinimi, komplikasyon varlığı ve mortalite açısından değerlendirildi*

Bulgular — *65 yaş üstü apendektomi yapılan 161 olgunun 98'i erkek (% 60,80), 63'ü kadındı (% 39,20). Olguların 109'una (% 67,70) açık apendektomi, 52'sine (% 32,29) lapa-roskopik apendektomi uygulandığı belirlendi. Açık operasyon uygulanan 109 ol-gunun 61'inin (% 55,91), laparoskopik apendektomi uygulanan 52 olgunun 22'sinin (% 42,32) komplike akut apandisit olduğu sap-tandı. Opere edilen olguların 24'ünde (% 14,94), komplikasyon geliştiği gözlendi. Komplikasyonlar açısından laparoskopik opere edilen gruplarla açık apendektomi grupları arasında anlamlı farklılık saptanmadı (P=0,873). Gruplar yaş, cinsiyet, yandaş hastalık, ASA skoru ve preoperatif laboratuvar değerleri açısından benzer özellikler göstermekteydi*

Sonuç — *Laparoskopik apendektomi yaşlı ve komorbiditesi yüksek hasta populasyonunda güvenle uygulanabilir bir yöntemdir.*

Anahtar Kelimeler — *Apandisit; Laparoskopi; Yaşlı hasta*

INTRODUCTION

Acute appendicitis is one of the most common pathologies in emergency surgery.[1] It more frequently affects the younger age groups, with 70% of diagnosed cases under the age of 30. With the increase seen in the average life span, incidences of acute appendicitis have been increasing in the elderly.[2] According to the literature, the incidence of acute appendicitis is 8.6% in men and 6.7% in women in the general population, while incidences of acute appendicitis in patients over the age of 60 are 5–10%.[3]

The increase in life expectancy seen over the last few decades has brought the use of minimally invasive surgical interventions in the elderly patients into question. Currently, appendectomy is the standard treatment for acute appendicitis, while for surgical treatments of acute appendicitis, laparoscopic appendectomy is preferred over open surgical methods due to the shorter hospital stay, the shorter time to return to daily life and the fewer wound site complications.[4]

Despite the advantages offered by laparoscopic surgery, the use of the laparoscopic method for the surgical treatment of acute appendicitis in the elderly population is controversial due to the greater rate of comorbidities and the more complicated course of acute appendicitis in this group.5 The present study compares the applicability of laparoscopic and open surgery in patients aged 65 and over who were operated for acute appendicitis.

MATERIALS and METHODS

This is a descriptive, cross sectional and retrospective study. The data of patients who were operated for acute appendicitis at Sakarya University Medical Faculty Training and Research Hospital between 2011 and 2018 was screened and analyzed. Only cases aged 65 and over were included. Appendectomies under the age of 65, appendectomies performed as part of another operation, negative appendectomies and elective appendectomies were excluded from the study. The cases were classified as laparoscopic or open appendectomy, and as complicated or non-complicated appendicitis, in terms of the surgical method. Perforated ap-pendicitis according to perioperative evaluation, and gangrenous appendicitis with or without abscess formation were identified as complicated cases. The cases were classified into four groups, the complicated open appendectomy (COA) group, the non-complicated open appendectomy (NCOA) group, the complicated laparoscopic appendectomy (CLA) group and the non-complicated laparoscopic appendectomy (NCLA) group. All groups were assessed for mean age, gender, white blood cell (WBC) count, presence of comorbid diseases, American Society of Anesthesiology (ASA) score, duration of operation, onset of oral intake, length of hospital stay, need for postoperative intensive care (ICU), presence of complica-tions and mortality.

Acute appendicitis was diagnosed based on the findings of physical examination, laboratory data and abdominal tomography.

The laparoscopic appendectomies were performed with three trocars (10-mm umbilical, 10-mm left lower quadrant and 5-mm suprapubic) under general anesthesia. The maximum intraabdominal pressure applied was 12 mmHg. The mesoappendix was divided with a ligature and the radix was closed using two loop sutures or a hemostatic clip. The appendectomy specimen was removed from the abdomen using a plastic bag via the 10-mm trocar placed in the left lower quadrant. For gangrenous and perforated cases, the appendectomy location was irrigated with 2–3 L of 0.9% physiological saline and aspirated; and for complicated cases, an aspiration drainage tube was placed in the appendectomy location.

Statistical analysis

The Kolmogorov–Smirnov test was used to determine if the continuous and intermittent numerical variables showed normal distribution, and the homogeneity of variances were investigated with the Levene test. Descriptive

statistics of continu-ous and intermittent numerical variables are expressed as mean ± standard devia-tion or median (minimum–maximum), while categorical variables are expressed as number of cases and percent (%).

Among the groups, the parameters evaluated, the significance of the difference was evaluated by One-Way ANOVA and Kruskal Wallis test. If the Kruskal Wallis test statistics results were found to be significant, the situation(s) that caused the difference were determined using Dunn's multiple comparison test.

If at least one of the 2x2 cross tables had an expected frequency below 5, cate-gorical data were assessed using Fisher's Exact Test, while when the expected frequency was between 5 and 25, the Continuity Corrected Chi-Square test was used; otherwise, Pearson's Chi-Square test was conducted. Analyses of categorical data in cross-tabulations of RxC (if at least one of the categorical variables in the row or column were duplicate outcomes) were done using Pearson's ChiSquare test.

Analysis of the data was performed using IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). For $p < 0.05$, the results were considered statistically significant.
The study was approved by the Sakarya University Ethics Committee with the date of 29.05.2020 and the number E-8722. The study was conducted in accordance with the Helsinki declaration.

RESULTS

Of the 4,761 surgical treatments for acute appendicitis at the Sakarya University Medical Faculty Training and Research Hospital between 2011 and 2018, 161 (% 3,38) cases aged over 65 were included in this study. Of those who underwent an appendectomy, 98 (% 60,80) were male and 63 (% 39,20) were female. One hundred and nine (% 67,70) of the cases had open, and 52 (% 32,29) had laparo-scopic appendectomies. A traditional left lower quadrant Mc Burney incision was preferred in 103 (% 94,41), while a midline incision was preferred in six (% 5,62) cases who underwent an open appendectomy. Complicated acute appendicitis was the case in 61 (% 55.96) of the 109 open appendectomies and in 22 (42.30%) of the 52 laparoscopic appendectomies. The mean ages of the cases and the white blood cell counts were similar in all groups. Two (% 9.09) of the cases from the CLA group and one (% 1.60) case from the COA group were moni-tored in the intensive care unit postoperatively for one day. In two of the cases in the CLA group, the operation was switched to open surgery due to adhesion. All groups were similar in terms of age, gender, accompanying diseases, ASA score and preoperative laboratory values (Table 1).

All of the study cases were evaluated with a preoperative intravenous contrastenhanced abdominal computed tomography (CT). The parameters for an acute appendicitis diagnosis included increased appendiceal wall thickness, the pres-ence of perforation, periappendicular free air and the identification of a periappendicular/intraabdominal abscess on the abdominal CT. In the preoperative CT assessment, 78 (% 48,42) (NCLA: 30, NCOA: 48) of the cases were identified as non-complicated appendicitis, and 83 (% 51,58) (NCLA: 22, COA: 61) as complicated appendicitis due to the presence of perforation and periappendicular abscesses.

The comorbid diseases detected in all groups are summarized in Table 2, cardio-vascular disease and diabetes mellitus are the most common in both the laparo-scopic and open appendectomy groups. The other comorbid diseases identified were hypertension, bronchopulmonary disease, renal disease, cerebrovascular disease and anticoagulant use.
There were no mortalities within the first postoperative 30 days in any of the cases included in the study. Complications developed in 24 (% 14,90) of the operated cases (Table 3), with the most common postoperative complication being wound site infection, with 10 (% 6,20) cases. A postoperative intraabdominal abscess occurred in a total

Table 1: Clinical and operational parameters of the appendectomy groups

Patients Charesteristics (n=161)	Complicated Open Appendectomy (COA) (n= 61)	Noncomplicated Open Appendectomy (NCOA) (n=48)	Complicated Laparoscopic Appendectomy (CLA) (n= 22)	Noncomplicated Laparoscopic Appendectomy (NCLA) (n= 30)	p Value
Age (Year)	72,12±6.14	71,20±5.92	73,24±6.37	70,07±5.57	0,091†
Sex(M/F)	40/21	30/18	12/10	16/14	0,422‡
ASA SCORE					0,823‡
ASA 1	13	10	9	11	
ASA 2	44	35	10	18	
ASA 3	4	3	3	1	
WBC	14,7±4,1	13,7±3,5	15,1±4,5	13,1±3,2	0,820‡
Operation Time (minute)	65,82±24,26	54,12±20,14	90,17±29,2	60,21±22,65	0,520$
Use of drain	58 (% 95)a	9 (% 18,75)a	19 (% 86,3)b	5 (% 16,6)b	0,009a†
					0,016b†
Oral intake time	1,9±0,56	1,2 ±0,39	1,6±0,62	1,15±0,48	0,640†
Length of stay (days)	6,98 ±4,21	4,88± 3,47	5,28 ±3,93	3,72±2,89	0,110†
ICU admission	1	-	2	-	0,999‡
Mortality	-	-	-	-	-

† One-Way ANOVA, ‡ Pearson's Chi-Square test, $ Kruskal Wallis test, a: The difference between complicated and non-complicated open appendectomy groups in terms of drain usage was statistical-ly significant (p=0,009). b: The difference between complicated and non-complicated laparoscopic appendectomy groups in terms of drain usage is statistically significant (p=0,016). COA: Complicated Open Appendectomy, NCOA: Non-complicated Open Appendec-tomy, CLA: Complicated Laparoscopic Appendectomy, NCLA: Non-complicated Laparoscopic Appendectomy, M: Male, F: Female, ASA: American Society of Anesthesiologists, WBC: White Blood Cell, ICU: Intensive Care Unit

Table 2: Comorbid conditions in the all appendectomy groups

Comorbidities	Complicated Open Appendectomy (COA) (n= 61)	Noncomplicated Open Appendectomy (NCOA) (n=48)	Complicated Laparoscopic Appendectomy (CLA) (n= 22)	Noncomplicated Laparoscopic Appendectomy (NCLA) (n= 30)	p Value
Cardiac disease	28(%17,39)	21(%13,04)	9(%5,59)	11(%6,83)	0,592‡
Hypertension	18(%11,18)	17(%10,55)	8(%4,96)	7(%4,34)	0,589‡
Broncopulmoner disease	4(%2,48)	3(%1,86)	3(%1,86)	2(%1,24)	0,091‡
Renal failure	2(%1,24)	1(%0,62)	-	1(%0,62)	0,854‡
Diabetes Mellitus	24(%14,90)	20(%12,42)	12(%7,45)	10(6,21)	0,127‡
Cerebrovascular disease	7(%4,34)	6(%3,72)	3(%1,86)	4(%2,48)	0,154‡
Anticoagulan use	20(%12,42)	17(%10,55)	8(%4,96)	7(%4,34)	0,645‡

‡ Pearson's Chi-Square test, COA: Complicated Open Appendec-tomy, NCOA: Non-complicated Open Appendectomy, CLA: Compli-cated Laparoscopic Appendectomy, NCLA: Non-complicated Lapa-roscopic Appendectomy,

of four (% 2,41) (CLA: 2, COA: 2) cases, who were treated with percutaneous drainage and intravenous antibiotics. None of the cases required reoperation. A postoperative ileus was identified in two (% 1,20) (COA: 1, CLA: 1) cases, and postoperative atelectasis in four (% 2,4) (COA: 3, NCOA: 1) openly operated cases and three (% 1,86) (CLA: 2, NCLA: 1) laparoscopically operated cases. A single (% 0.60) case from the NCLA group experienced port-site bleed-ing. Furthermore, one (% 0.60) case from the CLA group suffered a postoperative pulmonary embolism and medical treatment was initiated. No statistically signifi-cance detected between the groups in terms of postoperative complications: Surgical site infection (p=0.885), intraabdominal abscess (p=0,253), atelectasis (p=0,234) (Table 3).

When the groups were evaluated in terms of length of hospital stay, the NCLA group had a shorter hospital stay than the other groups, although the difference was not statistically significant (p=0.110) (Table 1).

DISCUSSION

Several recent studies about the use of minimally invasive surgical methods have demonstrated the superiority of laparoscopic surgical methods over open surgery.[6] The use of laparoscopic methods over open surgery is currently increasing due to reasons such as reduced postoperative pain, shorter hospital stays, shorter time to return to daily life and fewer surgical site infections.[7]

Acute appendicitis is a condition that usually affects the young population. The possibility of acute appendicitis in the second and third decades is reported to be 9% and 7% in men and women, respectively.[8] Literature reports the prevalence of acute appendicitis to be 5–10% in the elderly population.[9] The prolonged average lifespan and the associated increase in elderly population have resulted in an increased incidence of acute appendicitis in the geriatric age group.[10]

In elderly patients, the most distinctive clinical symptom of acute appendicitis is pain in the lower abdomen. As the most distinct symptom of acute appendicitis, pain in the right lower quadrant is more subtle in elderly people than in younger patients. The classic triad of appendicitis, being right lower quadrant tenderness, fever and leukocytosis, is detected in only 26% of patients in the elderly population treated for acute appendicitis.[11] The use of laparoscopy in the surgical treatment of acute appendicitis has increased in parallel with technological and anesthetic developments.[12]

Laparoscopic surgery is preferred more for the geriatric patient group in terms of being less invasive and allowing

Table 3: Complications by operative approach

Comorbidities	Complicated Open Appendectomy (COA) (n= 61)	Noncomplicated Open Appendectomy (NCOA) (n=48)	Complicated Laparoscopic Appendectomy (CLA) (n= 22)	Noncomplicated Laparoscopic Appendectomy (NCLA) (n= 30)	p Value
Surgical site infections	5 (% 8,19)	2 (% 4,16)	1 (% 4,45)	2 (% 6,66)	0,885‡
İntraabdominal abscess	2 (% 3,22)	-	2 (% 9,09)	-	0,253‡
İleus	1 (% 1,63)	-	1 (% 4,54)	-	0.257‡
Atelectasis	3 (% 4,91)	1(% 2,08)	2 (% 9,09)	1 (% 3,33)	0,234‡
Pulmonary embolism	1 (% 1,63)	-	-	-	-
Port site bleeding	-	-	-	1(% 3,33)	-

‡ Pearson's Ki-Kare test, COA:Complicated Open Appendectomy, NCOA:Non-complicated Open Appendectomy, CLA:Complicated Laparoscopic Appendectomy, NCLA:Non-complicated Laparoscop-ic Appendectomy,

to make a proper differential diagnosis and also treating most of them, even; diagnosing acute appendicitis is already a challeng-ing procedure itself.[13]

There are numerous studies supporting the safety of the laparoscopic technique for the surgical treatment of acute appendicitis.[14] The use of the laparoscopic technique for complicated acute appendicitis, such as perforation, abscess and gangrene which are rather common in elderly patients, is somewhat controversial. Several authors argue that the laparoscopic technique increases the formation of postoperative intraabdominal abscesses in complicated appendicitis, due to longer operation duration with laparoscopy than with the open method and the CO2 insufflation.[15] Other authors argue that the formation of postoperative in-traabdominal abscesses is reduced by the irrigation and aspiration in complicated cases treated laparoscopically.[16] The present study identified postoperative abscess in two cases in the CLA group and two cases in the COA group, all of whom were evaluated as perforated and complicated appendicitis in preoperative imaging. When the laparoscopic and open methods were compared in terms of postoperative abscess frequency, however, no statistically difference was apparent between the groups (p=0.253).

Irrespective of the surgical method chosen, the most common postappendectomy complication is wound site infection. Literature reports fewer wound site infections with the laparoscopic surgery when compared to open surgical methods, due to the fact that the appendectomy specimen is usually removed from the abdomen in a plastic bag.[17] Gupta et al found that the CO2 insufflation used in laparoscopic appendectomy is likely to cause a bacterial increase in the peritoneal cavity, leading to an increase in surgical site infections, while many other authors assert that the laparoscopic surgery provides a better surgical view, and that intraabdominal drainage is easier with the laparoscopic method.[18-19] In the present study, wound site infections occurred in three (1.86%) (NCLA: 2 and CLA: 1) laparoscopically operated cases and in seven (4.34%) (COA: 5 and NCOA: 2) openly operated cases. Despite the greater frequency of wound site infections in the open method group, there was no statistically significant difference between the two groups in this regard (p=0,885).

Surgical experience is the most important parameter determining the duration of the operation in minimally invasive interventions. Numerous studies have found laparoscopic appendectomy to require more time than an open operation. A study by Galli et al, however, found that shorter operation durations can be achieved as laparoscopic experience increases when compared to the open method.[20] The prolonged duration of the laparoscopic method can be explained by the longer installation time of the laparoscopic system, the aspirationirrigation process in complicated cases and the longer time required to release secondary adhesions when compared to the open method. Although the present study identified distinctively longer operation durations in CLA cases than in the other groups, no statisti-cally significant difference was detected (p=0,520) and mortality was not the case in any of the patients.

The distinct advantage of laparoscopic appendectomy over open appendectomy is the shorter hospital stay, and there have been several studies reporting shorter hospital stays for patients treated with laparoscopic appendectomy.[21] In the present study, the length of hospital stay was shorter in the NCLA group than in the other groups, while there was no notable difference in the length of stay for the other groups (p=0,110) (Table 1).

The acid-base equilibrium changes, and cardiac and pulmonary effects of the pneumoperitoneum produced during laparoscopic procedures usually have an impact on the selection of the surgical procedure in the elderly, and makes the laparoscopic choice difficult. On the other hand, recent developments in anesthe-sia and postoperative care conditions have led to an increase in the feasibility of more complicated laparoscopic operations in the elderly.[22] In the

present study, an intraabdominal CO2 insufflation was performed with a pressure of 12 mm Hg in the laparoscopic appendectomy technique, with the patients in the left lateral position with the head down during the operation. Considering the postoperative complications, the present study identified no notable statistical difference between the laparoscopically and openly operated elderly patients (Table 3). There were fewer wound site infections in the laparoscopy group than the open surgery group, and operation duration was prolonged in the laparoscopic complicated appendicitis group; both findings did not achieve statistically significance. In conclusion, laparoscopic appendectomy seems to be safe and appropriate for elderly, with similar postoperative outcomes of the open surgery.

Acknowledgment

The authors declare no conflict of interest.

Disclosure statement

The authors received no financial support for the research and/or authorship of this article.

The study was approved by the Sakarya University Ethics Committee with the date of 29.05.2020 and the number E-8722.

References

1. *Storm-Dickerson TL, Horattas MC. What have we learned over the past 20 years about appendicitis in the elderly?. Am J Surg 2003;185:198–201.*
2. *Cohen-Arazi O, Dabour K, Bala M, Haran A, Almogy G. Management, treatment and outcomes of acute appendicitis in an elderly population: a single-center expe-rience. Eur J Trauma Emerg Surg 2017 Oct;43(5):723-727. doi: 10.1007/s00068-016-0735-9. Epub 2016 Nov 2.*
3. *Guller U, Jain N, Peterson ED, Muhlbaier LH, Eubanks S, Pietrobon R. Laparo-scopic appendectomy in the elderly. Surgery 2004;135(5):479-488.*
4. *Kim MJ, Fleming FJ, Gunzler DD, Messing S, Salloum RM, Monson JRT. Lapa-roscopic appendectomy is safe and efficacious for the elderly: an analysis using the National Surgical Quality Improvement Project database. Surg Endosc 2011; 25(6):1802-1807.*
5. *Kirshtein B, Perry ZH, Mizrahi S, et al. Value of laparoscopic appendectomy in the elderly patient. World J Surg 2009; 33:918–922.*
6. *Dowgiałło-Wnukiewicz N, Kozera P, Wójcik W, Lech P, Rymkiewicz P, Michalik M. Surgical treatment of acute appendicitis in older patients. Pol Przegl Chir 2019 Feb 7;91(2):12-15. doi: 10.5604/01.3001.0012.8556. PMID: 31032807*
7. *Renteria O, Shahid Z, Huerta S. Outcomes of appendectomy in elderly veteran patients. Surgery 2018; pii: S0039-6060(18)30196-X.*
8. *Frantz MG, Norman J, Fabri PJ. Increased morbidity of appendicitis with advanc-ing age. Am Surg 1995; 61:40-4.*
9. *Addiss DG, Shaffer N, Fowler BS. The epidemiology of appendicitis and appen-dectomy in the United States. Am J Epidemiol 1990; 132:910-25.*
10. *Yeh CC, Wu SC, Liao CC, Su LT, Hsieh CH, Li TC. Laparoscopic appendec-tomy for acute appendicitis is more favorable for patients with comorbidities, the elderly, and those with complicated appendicitis: a nationwide population-based study. Surg Endosc 2011 Sep; 25(9):2932-42. Epub 2011 Mar 18.*
11. *Pooler BD, Lawrence EM, Pickhardt PJ. MDCT for suspected appendicitis in the elderly: diagnostic performance and patient outcome. Emerg Radio 2012; 19:27-33.*
12. *Southgate E, Vousden N, Karthikesalingam A, Markar SR, Black S, Zaidi A. Laparoscopic vs open appendectomy in older patients. Arch Surg 2012; 147: 557-562.*
13. *Jaschinski T, Mosch C, Eikermann M, Neugebauer EA. Laparoscopic versus open appendectomy in patients with suspected appendicitis: a systematic review of meta-analyses of randomised controlled trials. BMC Gastroenterol 2015; 15: 4*
14. *Markides G, Subar D, Riyad K. Laparoscopic Versus Open Appendectomy in Adults with Complicated Appendicitis: Systematic Review and Meta-analysis. World Journal of Surgery 2010; 34: 2026-2040.*
15. *Kirshtein B, Bayme M, Domchik S, Mizrahi S, Lantsberg L. Complicated ap-pendicitis: laparoscopic or conventional surgery? World J Surg 2007; 31: 744-749.*
16. *Asarias JR, Schlussel AT, Cafasso DE, Carlson TL, Kasprenski MC, Washing-ton EN, Lustik MB, Yamamura MS, Matayoshi EZ, Zagorski SM. Incidence of postoperative intra-abdominal abscesses in open versus laparoscopic appendec-tomies. Surg Endosc 2011; 25: 2678-2683.*
17. *Taguchi Y, Komatsu S, Sakamoto E, Norimizu S, Shingu Y, Hasegawa H. Laparoscopic versus open surgery for complicated appendicitis in adults: a ran-domized controlled trial. Surg Endosc 2016 May;30(5):1705-12. doi: 10.1007/s00464-015-4453-x. Epub 2015 Aug 15.*
18. *Gupta R, Sample C, Bamehriz F, Birch DW. Infectious complications following laparoscopic appendectomy. Can J Surg 2006; 49: 397-400.*
19. *Moore CB, Smith RS, Herbertson R, Toevs C. Does use of intraoperative irriga-tion with open or laparoscopic appendectomy reduce post-operative in-traabdominal abscess? Am Surg 2011;77:78–80.*
20. *R. Galli • V. Banz • H. Fenner • J. Metzger. Laparoscopic approach in perfo-rated appendicitis: increased incidence of surgical site infection? Surg Endosc 2013; 27:2928–2933 DOI 10.1007/s00464-013-2858-y*
21. *Lin YM, Hsieh CH, Cheng CI, BL Tan, HT Liu. Laparoscopic appendectomy for complicated acute appendicitis does not result in increased surgical complications. Asian J Surg 2012;35: 113–116.*
22. *Liu L, Lv N, Hou C. Effects of a multifaceted individualized pneumoperitoneum strategy in elderly patients undergoing laparoscopic colorectal surgery: A retro-spective study. Medicine (Baltimore). 2019 Apr;98(14):e15112. doi: 10.1097/MD.0000000000015112. PMID: 30946379*

ARAŞTIRMA MAKALESİ / *Research Article*

Acil Serviste Spontan Pnömotoraks Tanısı Alan Hastaların Demografik Verilerinin Retrospektif Olarak Değerlendirilmesi

A Retrospective Evaluation of the Demographic Characteristics of Patients Diagnosed with Spontaneous Pneumothorax

Canan Akman[1], Murat Çetin[2]

[1] Çanakkale Onsekiz Mart Üniversitesi, Tıp Fakültesi, Acil Tıp Anabilim Dalı, Çanakkale, Türkiye
[2] İzmir Tınaztepe Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, İlk ve Acil Yardım Bölümü, İzmir, Türkiye

Yazışma Adresi / *Correspondence:*
Murat Çetin
İzmir Tınaztepe Üniversitesi Aydoğdu, 1267/1. Sk. No:4, 35400 Buca/İzmir
T: **+90 535 896 42 52** E-mail **: muratcetinn@gmail.com**

Geliş Tarihi / Received : **05.09.2020** Kabul Tarihi / Accepted : **27.12.2020**

Orcid :
Canan Akman https://orcid.org/0000-0002-3427-5649
Murat Çetin https://orcid.org/0000-0002-0667-7966

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):9-14) DOI: 10.31832/ smj.790812

Öz

Amaç Pnömotoraks, plevral boşlukta hava bulunmasıdır. Pnömotoraks tanılarının yarıdan fazlası herhangi bir travma durumu söz konusu olmadan ortaya çıkmaktadır. Bu durum spontan pnömotoraks (SP) adını almaktadır. Aynı zamanda pnömotoraks vakaları ile acil serviste sıkça karşılaşılmaktadır. Tanı ve tedavisinin acil olarak yapılması gereken bir plevra hastalığıdır. Bu çalışmada acil servise başvuran SP hastalarının demografik özellikleri, risk faktörleri, klinik özellikleri, tanı ve tedavi yaklaşımlarının farkındalığının ortaya konulması amaçlanmıştır.

Gereç ve Yöntem Ocak 2018-Haziran 2020 tarihleri arasında Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi acil servisine başvuran SP tanısı alan hastalar retrospektif olarak tek merkezli incelenmiştir. Hastalarda yaş, cinsiyet, acil servise geliş şekilleri, şikayetleri, altta yatan hastalık durumları, sigara öyküsü, daha önce pnömotoraks şikayeti varlığı, nüks ve sayısı, fizik muayene bulguları, eşlik eden durumlar, tansiyon pnömotoraks varlığı, tüp torakostomi tedavisi ve tedavinin sonuçları belirlenmiştir.

Bulgular Acil servise başvurup SP tanısı alan 53 hasta çalışmaya dahil edildi. Hastaların %92,5'i (n=49) erkektir. %92,5'ine (n=49) tüp torakostomi işlemi uygulanmıştır. Bu hastaların %84,9'u (n=45) göğüs cerrahi servisine, %11,3'ü (n=6) yoğun bakıma ve %2'si (n=3,8) dış merkeze sevk edilmiştir. Hastaların %88,7'si (n=47) şifa ile taburcu olmuştur.

Sonuç Spontan pnömotoraks zamanında müdahale edilmediğinde hayati tehlike oluşturabilecek bir klinik durumdur.

Anahtar Kelimeler Spontan pnömotoraks; Acil servis; Tüp torakostomi

Abstract

Objective *Pneumothorax is the presence of air in the pleural cavity. More than half of pneumothorax cases occur withou tany preceding trauma, and are referredto as spontaneous pneumothorax (SP). SP is also a commonly encountered clinical condition in emergency departments It is a pleural disease that requires urgent diagnosis and treatment. The purpose of this study is to determine the demographic features, risk factors, clinical features, as well as, awareness of approach to treatment in patients admitted to the emergency department with SP.*

Materials and methods *This retrospective, single-center study was conducted among patients diagnosed with SP in the Emergency department of Çanakkale Onsekiz Mart University between January 2018–June 2020. Age, gender, types of admission to the emergency room, complaints, underlying disease conditions, smoking history, presence of previous pneumothorax complaints, recurrence and number, physical examination findings, accompanying conditions, presence of tension pneumothorax, tube thoracostomy treatment and the results of the treatment were determined.*

Results *53 Patients diagnosed with SP after admittance to the emergency department were included in the study; with 92,5 % (n=49) male patients. 92,5 % (n=49) of these patients underwent tube thoracostomy. 84.9 % (n = 45) of these patients were referred to the chest surgery service, 11.3 % (n = 6) to intensive care and 2 % (n = 3.8) to an external center. 88.7% (n = 47) of the patients were discharged with recovery.*

Conclusion *Spontaneous pneumothorax is likely a life-threatening clinical condition if not treated in time.*

Keywords *Spontaneous pneumothorax; Emergency department; Tube thoracostomy*

GİRİŞ

Spontan pnömotoraks (SP), travma olmadan plevral boşlukta hava toplanması ve sonrasında buna eşlik eden akciğerin kollapsıdır.[1,2] Sağlıklı bir bireyde bu durumun oluşması primer spontan pnömotoraks, altta yatan akciğer hastalığı söz konusu ise sekonder pnömotoraks olarak ifade edilmektedir. Spontan pnömotoraks risk faktörleri arasında erkek cinsiyet, sigara kullanılması, uzun boy, düşük vücut ağırlığı, altta yatan akciğer hastalığı yer almaktadır.[3] Ani olarak görülen nefes darlığı, eşlik eden göğüs ağrısı, çarpıntı, prodüktif öksürük şikayeti görülebilmektedir.[4] Fizik muayenenin yapılması tanısal olarak anlamlıdır. Spontan pnömotoraks, hastalarının yönetimi yakın gözlem ve oksijen tedavisi yanında konservatif yaklaşım olduğu gibi aspirasyon, perkütan kateter ile drenaj, tüp torakostomi, video toraskopik cerrahi, aksiler veya lateral torakotomi tedavilerini de içermektedir.[5-8]

Çalışmamızda acil servise başvuran spontan pnömotoraks hastalarının demografik özellikleri, risk faktörleri, klinik özellikleri, tanı ve tedavi yaklaşımları açısından tecrübelerimizi paylaşmayı amaçladık.

GEREÇ ve YÖNTEMLER

Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi acil servisinde retrospektif olarak planlanan tek merkezli çalışmaya Çanakkale Onsekiz Mart Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu 01.07.2020 tarihli 2011-KAEK-27/2020-E.2000075170 nolu çalışma 2020-09 sayılı onay alındıktan sonra başlanmıştır. Elektronik kayıt sistemi üzerinden Ocak 2018-Haziran 2020 tarihleri arasında başvuran ve spontan pnömotoraks tanısı alan hastalar alınmıştır. Hastane otomasyon sisteminde dosyasına ulaşamadığımız ve 18 yaş altı hastalar çalışmaya alınmamıştır.

Verilerin istatistiksel olarak olarak değerlendirilmesinde SPSS 20.0 kullanılmıştır. Tanımlayıcı verilerin sunumunda sayı, yüzde, ortalama, standart sapma, ortanca, minimum, maksimum kullanılmıştır. Nominal verilerin karşılaştırılmasında ise Kikare Testi kullanılmıştır. $p<0.05$ istatistiksel olarak anlamlı kabul edilmiştir.

BULGULAR

Çalışmaya 53 hasta dahil edildi. Hastaların yaş ortalaması 50,5±24,7 yıl, ortancası 58,0 yıldı. (min:18,0-maks:90,0). Hastaların %92,5'i (n=49) erkek, %7,5'i (n=4) kadındı. Hastaların acil servise başvurusuna bakıldığında; 26'sı (%49,1) 112 Acil ambulansı ile 27'si (%50,9) ayaktan başvuru şeklindeydi. Hastaların 34'ü (%64,2) il merkezinden ve 19'u (%35,8) merkeze bağlı ilçelerden gelmişti.

Çalışmaya alınan hastaların 29'unda (%54,7) nefes darlığı en sık acil servis başvuru şikayeti olarak karşımıza çıkmaktaydı. Diğer şikayetler sırası ile göğüs ağrısı, çarpıntı ve öksürüktü. Fizik muayenede 34'ünde (%64,2) tek taraflı solunum seslerinin azaldığı tespit edildi. Hastaların acil servise başvurduğunda 49'unda (%92,5) eşlik eden patoloji yoktu. Üç hastada (%5,7) pnömomediastinum varken, 1 hastada (%1,8) akut böbrek yetmezliği tespit edildi.

Çalışmaya alınan hastaların 8'sinde (%15,1) daha önceden pnömotoraks öyküsü vardı. İki hastanın nüks sayısı 3 (%3,8) olarak tespit edildi. Otuz sekiz hasta (%71,7) sigara içicisiydi. Çalışmamızdaki hastaların 7'sinde (%28) kronik obstrüktif akciğer hastalığı (KOAH), 1'inde (%4) diabetes mellitus (DM) ve hipertansiyon, 1'inde (%4) hipertansiyon, 8'sinde (%32) pnömoni, 5'inde (%20) akciğer kanseri, 1'inde (%4) KOAH ve koroner arter hastalığı birlikteliği, 2'sinde (%8) KOAH ve pnömoni hikayesi mevcuttu.

Ayrıca hastaların 2'sinde (%3,8) tansiyon pnömotoraks varlığı görüldü. Hastaların 49'una (%92,5) tüp torakostomi uygulanırken, 6'sı (%11,3) yoğun bakıma, 45'i (%84,9) göğüs cerrahi servisine yatırıldı. Ancak 2 (%3,8) hasta başka bir hastaneye sevk edildi. Takiplerinde hastaların; 47'si (%88,7) taburcu, 6'sı (%11,3) eksitus olmuştur.

Tablo 1. Acil servise başvurup spontan pnömotoraks tanısı alan olguların başvuru bilgileri, geliş şikayetleri ve altta yatan hastalık varlığı			
Değişkenler		**n**	**%**
Hastaların geliş şekli	112 Ambulans	26	49,1
	Ayaktan gelen	27	50,9
Nereden geldiği	Merkez	34	64,2
	İlçe	19	35,8
Geliş şikayeti	Nefes darlığı	29	54,7
	Göğüs ağrısı	14	26,4
	Nefes darlığı ve göğüs ağrısı	8	15,1
	Nefes darlığı ve çarpıntı	1	1,9
	Çarpıntı	1	1,9
Altta yatan hastalık varlığı	Var	25	47,2
	Yok	28	52,8
Hastalıklar	KOAH	7	28,0
	DM ve Hipertansiyon	1	4,0
	Hipertansiyon	1	4,0
	Pnömoni	8	32,0
	Akciğer kanseri	5	20,0
	KOAH ve Koroner arter hastalığı	1	4,0
	KOAH ve Pnömoni	2	8,0

Tablo 2. Acil servise başvurup spontan pnömotoraks tanısı alan olguların muayene, tedavi ve son durum bilgileri			
Değişkenler		**n**	**%**
Fizik muayene	Tek taraflı solunum seslerinin azalması	34	64,2
	Tek taraflı solunum seslerinin yokluğu	19	35,8
Eşlik eden durumlar	Yok	49	92,5
	Pnömomediastinum	3	5,7
	Akut böbrek yetmezliği	1	1,8
Tansiyon pnömotoraks varlığı	Var	2	3,8
	Yok	51	96,2
Tüp torakostomi uygulanması	Var	49	92,5
	Yok	4	7,5
Acil servisten sonlanımı	Yoğun bakım	6	11,3
	Servis yatış	45	84,9
	Sevk	2	3,8
Hastaneden sonlanımı	Taburcu	47	88,7
	Eksitus	6	11,3

Tablo 2. Acil servise başvurup spontan pnömotoraks tanısı alan olguların muayene, tedavi ve son durum bilgileri				
Değişkenler		Nüks var n (%)	Nüks yok n (%)	p
Sigara kullanımı	**Var**	5 (13,2)	33 (86,8)	0,673
	Yok	3 (20,0)	12 (80,0)	
Kronik hastalık	**Var**	2 (8,0)	23 (92,0)	0,256
	Yok	6 (21,4)	22 (78,6)	

TARTIŞMA

Literatüre bakıldığında, Hallifax ve arkadaşlarının yaptığı bir çalışmada da spontan pnömotoraksın erkeklerde daha fazla olduğu görülmektedir.[9] Aynı şekilde başka bir çalışmada ise erkeklerde, kadın cinsiyete göre 6 kat daha sık olarak spontan pnömotoraks görüldüğü gösterilmiştir.[10] Çalışmamızda da hastaların 49 (%92,5)'u erkekti. Sigara içilmesinin spontan pnömotoraks için bir risk faktörü olduğu ifade edilmiştir.[1] Yapılan bir çalışmada sigara içen hasta grubunda, içmeyenlere göre spontan pnömotoraksın 20 kat daha fazla olduğu gösterilmiştir.[11] Göğüs cerrahlarının yaptığı bir çalışmada ise sigara içiminin yaygın olarak görüldüğü ülkelerde spontan pnömotoraksın sık görülen bir hastalık olduğu bildirilmiştir.[12] Çalışmamızda spontan pnömotoraksı olan hastalarımızın %71.7'sinde sigara içme öyküsü mevcuttur. Spontan pnömotoraks tanısı almış olgularımızın %52,8'inde herhangi bir hastalık mevcut değildir. Hastalığı olanların, %32'sinde akciğer enfeksiyonu, %28'inde kronik obstrüktif akciğer hastalığı, %20'sinde akciğer kanseri mevcuttur. Literatürde spontan pnömotoraksın akciğerde altta yatan bir nedenden kaynaklandığı ve kronik akciğer hastalıklarının bunun en sık nedenleri arasında olduğu belirtilmektedir.[6,11]

Nüks oranı ise spontan pnömotorakslarda %25-54 olarak literatürde verilmektedir.[1] Çelik ve arkadaşlarının yaptığı bir çalışmada ise nüks oranı %17 olarak verilmiştir.[3] Çalışmamızda ise nüks oranı %15,1 olarak bulunmuştur. Nüks sayısı olarak değerlendirildiğinde ise 2 nükse sahip hasta oranı %7,5'dur. Spontan pnömotoraks tanısında hastanın şikayetleri ve yapılan fizik muayene çok değerlidir. Hastaların başlıca şikayetleri göğüs ağrısı, nefes darlığı, çarpıntı, terleme, hipotansiyon ve siyanoz olabilmektedir.[6,13] Çelik ve arkadaşlarının yaptığı bir çalışmada hastaların en sık başvuru şikayeti nefes darlığı olarak verilmiştir.[3] Diğer bir çalışmada ise ani olan nefes darlığı ve göğüs ağrısı en sık hastaneye başvuru şikayeti olarak verilmiştir.[1] Hastalar sıklıkla göğüs ağrısı ve nefes darlığı gibi şikayetlerle başvuru yapmaktadır.[17]

Çalışmamızda hastaların acil servise başvurusunda en sık görülen iki şikayet %54,7 nefes darlığı, %26,4 göğüs ağrısıdır. Pnömotoraks hastalarında bir anda oluşan hipotansiyon, takipne, taşikardi ve siyanoz durumu tansiyon pnömotoraks açısından uyarıcı işaretlerdir. Ancak spontan pnömotoraks vakalarında tansiyon pnömotoraks görülmesi nadir olarak karşımıza çıkmakla birlikte bilinmelidir ki tansiyon pnömotoraks tanısı radyolojik değil, klinik bir tanıdır. Bu durum çok acil müdahaleyi gerektirmektedir.[1,16] Spontan pnömotoraksın tansiyon pnömotoraksa dönüşmesi %1-5 arasında bildirilmektedir.[17] Çalışmamızda tansiyon pnömotoraks varlığı %3,8 olarak bulunmuş, nadir olarak görüldüğü sonucuna katkı sağlamış ve bu olgularda intraplevral havayı boşaltmak ve mediastinal baskıyı azaltmak için acil tüp torakostomi uygulama yapılmıştır.[18,19] Spontan pnömotoraks fizik bulgusu bazen sinsi bir hava yaratsa da genelde karakteristiktir. Pnömotoraksın olduğu tarafta solunum seslerinin azalması ile kendini göstermektedir.[20] Hastalar solunum seslerinin azalmasından, solunum yetmezliğine kadar giden değişken bir klinik tablo ile karşımıza çıkabilmektedir. Spontan pnömotoraksın tedavisindeki esas amaç; plevral aralıktaki havayı boşaltmak, akciğerin ekspansiyonu sağlamak aynı zamanda nüksün önlenmesine de yardımcı olmaktır. Böylece nefes darlığı ve göğüs ağrısı semptomları da giderilebilmektedir.[16,21] Bu amaçla uygulanan yöntemler arasında gözlem ve oksijen verilmesi, aspirasyon, perkütan kateter ile drenaj, tüp torakostomi, video ile toraskopik cerrahi, torakotomi yer almaktadır.[22]

Çalışmamızda acil servise gelen hastalara tüp torakostomi tedavisi %92,5 oranında yapılmış ve diğer cerrahi tedavi yaklaşımlarına ihtiyaç duyulmamıştır. Yapılan çalışmalar göstermekte ki, sadece uygulanan tüp torakostomi işlemi büyük oranda tedaviye yeterli cevap verebilmektedir. Primer olarak tedavi yaklaşımı pnömotoraksın derecesine göre konservatif yaklaşım veya tüp torakostomidir. Çalışmamızda konservatif yaklaşım oranı %7,5'dur.[1,6] Acil serviste spontan pnömotoraks tanısı alan hastaların %84,9'u tüp torakostomi işlemi uygulandıktan sonra göğüs cerrahi

servisine yatırılmış, %11,3'ü ise yoğun bakıma yatılmıştır. Spontan pnömotoraksa eşlik eden durumlara bakıldığında %3 oranında pnömomediastinum görülmektedir. Spontan gelişen pnömomediastinum tablosu nadir olarak görülmekle birlikte, hastalarda göğüs ağrısı ve nefes darlığına neden olduğundan klinik tabloya eşlik edebileceği de düşünülmelidir.[23]

Sonuç olarak, Spontan pnömotoraks hastaları genellikle acil servise göğüs ağrısı, nefes darlığı şikayetleri ile başvurmaktadır. Fizik muayenede bu hastalarda solunum seslerinde azalma veya seslerin alınamaması en sık olarak görülmektedir. Bu hastaların yönetiminde tüp torakostomi altın standart olarak yerini hala korumaktadır. Bu hastaların ilk başvuru alanları olarak acil servisten başlayarak; takip ve tedavilerine devam edilmektedir.

Unutulmamalı ki zamanında acil müdahale edilmediğinde spontan pnömotoraks yaşamı tehdit eden klinik bir tablodur. Zamanında tanı konulması ile birlikte yapılan uygun tedavi ile mortalite ve morbidite azaltılabilmektedir.

Çalışma Çanakkale Onsekiz Mart Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu 01.07.2020 tarihli 2011-KAEK-27/2020-E.2000075170 sayılı onayı ile Helsinki Deklerasyonuna uyularak yapılmıştır.

Kaynaklar

1. *Özkan S, Yazıcı Ü,Erkmen SŞ, Taştepe Aİ, Karaarslan K, Aydın S, Şahin MF. Spontan Pnömotoraksta Tedavi Yaklaşımlarımız: 48 Olgunun Değerlendirilmesi. Türkiye Acil Tıp Dergisi - Turk J EmergMed 2011;11(1):20-24.*
2. *Durceylan E, İliklerden DM. Spontan Pnömotoraksta Klinik Deneyimlerimiz. Osmangazi Tıp Dergisi. 2019; 41(2): 147-152.*
3. *Çelik B, Furtun K, Demir H, Yılmaz MA. Spontan pnömotorakslı olgularımızın klinik özellikleri. Gülhane Tıp Dergisi 2009; 51: 71-74.*
4. *De Vries WC, Wolfe WG: The management of spontaneous pneumothorax in emphysema. Surg Clin North Am. 1981; 60:851.*
5. *Henry M, Arnold T, Harvey J. BTS guidelines for the management of spontaneous pneumothorax. Thorax 2003; 58: ii39–52.*
6. *Kuzucu A, Soysal Ö, Ulutaş H. Optimal timing for surgical treatment to prevent recurrence of spontaneous pneumothorax. Surg Today 2006; 36: 865–868.*
7. *Şengül AT, Büyükkarabacak BY, Yetim DT, Çelik B, Sürücü P, Başoğlu A. Spontan Pnömotoraksta Tedavi Seçenekleri. J Kartal TR 2014;25(1):27-33.*
8. *Yıldıran H, Şahinoğlu T. Devlet hizmet yükümlülüğü süresinde spontan pnömotorakslara yaklaşım. Ortadoğu Tıp Dergisi 2019; 1: 1-5.*
9. *Hallifax JR, McKeown E, Sivakumar P et al. Ambulatory management of primary spontaneous pneumothorax: an open-label, randomised controlled trial. Lancet 2020;396:39–49.*
10. *Soysal S, Topaçoğlu H, İtil O et al. Acil Serviste Erişkin Spontan Pnömotorakslı Hastaların Özellikleri. Türkiye Acil Tıp Dergisi 2005; 5(1): 14-17.*
11. *Eken KY, Güleç E, Atasoy S, Gücü A. Primer Spontan Pnömotoraksta Klinik Deneyimlerimiz. Akciğer Arşivi: 2003; 4: 138-140.*
12. *Karasu S, Tokat AO, Kısacık E, Çakmak H, Karakaya J, Aydın E, Gülhan E, Kaya S. Spontan Pnömotoraks: 260 Hastanın Analizi. J Clin Anal Med 2012;3(2): 174-7.*
13. *Tözüm H, Sarıtekin E, Hoşgün D, Kul C, Erdem Ş. Her pnömotoraks, primer spontan pnömotoraks değildir. İzmir Göğüs Hastanesi Dergisi, Cilt XXV, Sayı 3, 2011*
14. *Fry WA, Paape K. Pneumothorax. In: Shields TW, LoCicero III J, Ponn RB, Rusch VW (eds). General Thoracic Surgery. 6th ed. Philadelphia: Lippincott Williams &Wilkins, 2005: 794–805.*
15. *Beauchamp G, Ouellette D. Spontaneous pneumothorax and pneumomediastinum In: Pearson FG, Cooper JD, Deslauriers J (eds). Thoracic Surgery. 2nd ed. Philadelphia: Churchill Livingstone, 2002: 1195–1213.*
16. *Metin M. Pnömotoraks. Güncel Göğüs Hastalıkları Serisi 2018; 6 (2): 7-15.*
17. *Leigh-Smith S, Harris T. Tension pneumothorax-time for a re-think? EmergMed J 2005; 22: 8-16.*
18. *Kaneda H, Nakano T, Taniguchi Y, et al. Three-step management of pneumothorax: time for a re-think on initial management. Interact Cardiovasc Thorac Surg 2013; 16: 186-92*
19. *Chan SS. The role of simple aspiration in the management of primary spontaneous pneumothorax. J Emerg Med 2008; 34:131e8.*
20. *Miller A. Spontaneous pneumothorax. In: Light RW, Lee YCG, eds. Textbook of pleuraldiseases. 2nd edn. London: Arnold Press, 2008: 445-63.*
21. *De Leyn P, Lismonde M, Ninane V, Noppen M, Slabbynck H, Van Meerhaeghe A, et al. Guidelines Belgian Society of Pneumology. Guidelines on the management of spontaneous pneumothorax. ActaChirBelg 2005;105:265-7.*
22. *Tschopp JM, Rami-Porta R, Noppen M, Astoul P. Management of spontaneous pneumothorax: state of the art. Eur Respir J 2006;28:637-50.*
23. *Göktekin MÇ. Acil serviste spontan pnömomediastinum tanılı hastaların değerlendirilmesi. Cukurova Med J 2019;44(4):1155-1159.)*

RESEARCH ARTICLE / *Araştırma Makalesi*

Relationship between Perceived Social Support, Depressive Symptoms and Hopelessness Levels of Caregivers of Children with Disabilities

Engelli Çocuğu Olan Bireylerin Depresyon ve Umutsuzluk Düzeyleri ile Algılanan Sosyal Destek Arasındaki İlişki

Melek Aytekin[1], Nurgül Özdemir[2], Şengül Kocamer Şahin[3]

[1] Student of Psychiatric Nursing- Gaziantep Children and Obstetrics and Gynecology Hospital, Gaziantep, Turkey
[2] Gaziantep University, Faculty of Health Science, Department of Psychiatric Nursing, Gaziantep
[3] Gaziantep University, Faculty of Medicine, Department of Psychiatry, Gaziantep, Turkey

Yazışma Adresi / *Correspondence:*
Şengül Kocamer Şahin
Gaziantep University, Faculty of Medicine, Department of Psychiatry, Üniversite avenue- 27310 Şehitkamil, Gaziantep, Turkey
T: **+90 342 360 12 00** E-mail **: snglkcmr@hotmail.com**

Geliş Tarihi / Received : **20.08.2020** Kabul Tarihi / Accepted : **31.12.2020**

Orcid :
Melek Aytekin, https://orcid.org/0000-0003-4905-3149
Nurgül Özdemir https://orcid.org/0000-0002-9466-1357
Şengül Kocaman Şahin https://orcid.org/0000-0002-5371-3907

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):15-24) DOI: 10.31832/smj.779706**

Abstract

Objective Disability not only affects the disabled child. It also has psychological and social impacts on family members and caregivers. The purpose of the study was to determine the relationship between severity of depressive symptomes and hopelessness levels of caregivers of children with disabilities and their perceived social support.

Materials and Methods A total of 205 caregivers of disabled children were included in this cross-sectional study. A 'sociodemographic questionnaire', 'Beck Depression Scale', 'Beck Hopelessness Scale' and 'Multidimensional Perceived Social Support Scale' were used to assess the subjects in this cross-sectional study. Direct and indirect effects of a predictor in path models of mediation and moderation were calculated. The bootstrapping method has been used to calculate confidence intervals for indirect effects.

Results It was determined that the hopelessness levels were high (r = 0.594, p <.001) for individuals with high levels of depressive symptomes, the perceived social support was low for caregivers with high hopelessness levels (r = −0.149, p =.033), and that the perceived social support levels were low for caregivers with high levels of depressive symptomes (r=−0.128, p =.068). It was shown that hopelessness increases, and depression develops indirectly with decreasing psychosocial support.

Conclusion This study reveals the importance of perceived social support in the development of hopelessness and depression, which increase the burden of caregivers. Increasing the psychosocial support systems of caregivers of children with disabilities can reduce their levels of hopelessness and depression and increase their ability to care.

Keywords Depression; Disability; Caregiver; Hopelessness; Perceived social support

Öz

Amaç *Engellilik sadece engelli çocuğu etkilemez. Aynı zamanda aile üyeleri ve bakıcılar üzerinde psikolojik ve sosyal etkileri vardır. Bu çalışmada, engelli çocuğu olan bireylerin depresyon ve umutsuzluk düzeyleri ile algılanan sosyal destek arasındaki ilişkinin belirlenmesi amaçlanmıştır.*

Gereç ve Yöntemler *Kesitsel tipteki bu çalışmaya toplam 205 engelli çocuğu olan birey dahil edildi. Değerlendirme için "sosyodemografik anket", "Beck Depresyon Ölçeği", "Beck Umutsuzluk Ölçeği" ve "Çok Boyutlu Algılanan Sosyal Destek Ölçeği" kullanıldı. Mediasyon ve moderasyon yol modellerinde bir yordayıcının doğrudan ve dolaylı etkileri hesaplandı. Bootsrapping yöntemi, dolaylı etkiler için güven aralıklarını hesaplamak için kullanıldı.*

Bulgular *Engelli çocuğu olan bireylerde ölçek toplam puan ortalamaları; Beck Depresyon Ölçeği 21,53±12,82, Beck Umutsuzluk Ölçeği 9,21±4,75, Çok boyutlu algılanan sosyal destek ölçeği 44,72±15,72 olarak saptandı. Depresyon düzeyi yüksek olan bireylerin umutsuzluk düzeylerinin yüksek (r=0,594, p=0,000), umutsuzluk düzeyleri yüksek olan bireylerin algıladıkları sosyal desteğin düşük olduğu (r=-0,149, p=0,033), depresyon düzeyleri yüksek olan bireylerin algıladıkları sosyal destek düzeylerinin düşük olduğu (r=-0,128, p=0,068) saptandı. Bireylerin depresyon, umutsuzluk ve algıladıkları sosyal destek düzeyleri ile engelli çocuklarının bakımlarını karşılayabilme ve çocuklarıyla yeterince ilgilenebilme durumları arasında istatistiksel olarak anlamlı bir fark olduğu saptandı (p<0,05).*

Sonuç *Bu çalışma, bakım verenlerin yükünü artıran umutsuzluk ve depresyon gelişiminde algılanan sosyal desteğin önemini ortaya koymaktadır. Engelli çocukların bakım verenlerinin psikososyal destek sistemlerinin artırılması, umutsuzluk ve depresyon düzeylerini azaltabilir ve bakım yeteneklerini artırabilir.*

Anahtar Kelimeler *Depresyon; Engellilik, Bakımveren; Umutsuzluk; Algılanan sosyal destek*

INTRODUCTION

Disability is defined as the inability of an individual to continue his/her life naturally because of flaws in their mental, physical and psychological behaviours and their innate deficiencies and defects.[1,2] According to the World Health Organisation, disability is defined as an impairment or limitation in the healthy development of the bodily functions of an individual and the execution of these bodily functions.[3]

Social support is defined as psychological and instrumental resources provided by social networks for an individual to cope with stress.[4] It can be stated that the perceived social support is quite high for an individual who believes that he/she is loved and respected by others and that there are other people he/she can receive help from when necessary and who thinks that his/her relationships provide satisfaction.[5]

Hopelessness involves negative expectations for the future and negative assessments related to the future.[6] Severity of depressive symptomes symptoms and hopelessness are directly proportional.[7] Other symptoms that accompany hopelessness are symptoms observed in major depression, such as unhappiness, despair, guilt, inability to work, inability to make decisions and inaction.[8]

Disability not only affects the disabled child. It also has physiological, psychological and social impacts on family members and caregivers, and may cause various problems.[9] Studies which put forth this change indicate that there are breakdowns in the social lives, professional lives and family relations of families with disabled children.[10]

Cultural and ethnic differences in parenting styles in different countries[11] are also expected to manifest in the care of children with disabilities. Parents in Turkey have different hurdles to overcome when providing care to their children with intellectual disabilities that are different from those in other Western countries.[12] In the traditional culture of Turkey, where interdependence is emphasised, authoritarian parenting - which provides a high degree of control over children - is at the forefront.[13] This culture may cause individuals to be more dependent on their parents. However, from a more favourable perspective, individuals who grow up with responsibility and duty awareness, strive more to provide support for their families and relatives 13 if these efforts do not transform into oppression.[14] The emotions caused by disabled children in parents are also closely related to the reactions of people in their immediate circle, such as relatives and friends.[15,16] Things may get even more complicated as a result of these reactions.[16,17]

The purpose of the present study was to determine the relationship between severity of depressive symptomes, hopelessness levels and perceived social support in individuals with disabled children. A hypothese was developed to determine the directions of relationships: As psychosocial support decreases, hopelessness increases and depression develops indirectly.

MATERIALS and METHODS

Study population

This was a cross-sectional descriptive study. Individuals who applied to pediatri outpatient or whose children hospitalized in pediatry clinic of the Ministry Of Health Gaziantep Obstetrics and Gynecology and Children Hospital during the dates of February 2017 to April 2018 for treatment of their disabled children comprised the study population. Parents of children with physical and/or intellectuel disabilities were included in the study. Physical disabled children are selected as who needs some form of mobility aid, such as walker, crutches and/or wheelchairs. The diagnosis of intellectual disability had been made according to the DSM 5, and a clinical examination was performed by a psychiatrist. Verbal communication barriers (hearing and speaking) in the individual with the disabled child were considered as exclusion criteria. Interviews were conducted individually with the parents of the disabled children, and those who agreed to participate in the study were in-

formed about the study by a psychiatric nurse.

Procedure

The purpose of the study was explained to the participants after which they were informed that participation was entirely voluntary and that they could opt-out whenever they wished to do so. In addition, they were asked to fill in the 'Informed Consent Form', 'Personal Information Form' as well as the 'Beck Depression Scale', 'Beck Hopelessness Scale' and 'Multidimensional Scale of Perceived Social Support'.

Data Acquisition Tools

Beck Depression Scale (BDS): Beck et al. (1961) developed the BDS for measuring the behavioural findings of depression in adolescents and adults.[18] It is a self-assessment scale comprising 21 multiple-choice questions used for measuring the risk, level and severity of depression in both healthy individuals and those with depression. Each item contains four options listed in the order of emotional severity and is scored between 0 and 3. Hisli et al. carried out the Turkish adaptation of the BDS as well as the required validity and reliability studies.[19] Cronbach's alpha was 0.91. Studies were conducted with polyclinic patients to determine the breakpoints of the BDS. It was observed as a result of the study that BDS scores of 17 and above can distinguish depression that requires treatment at an accuracy of above 90%.[20]

Beck Hopelessness Scale (BHS): This scale was developed by Beck et al. to measure the pessimism level of the individual related to the future as well as negative expectations.[21] Seber carried out the translation, validity and reliability studies for the BHS as a result of which an α value of 0.86 was determined.[22] Durak (1994) conducted studies on the scale afterwards and acquired more detailed information on its validity, reliability and factor structure.[23] It was reported that hopelessness was not the case for those with scores ranging between 0 and 3, a slight hopelessness existed for individuals with scores ranging between 4 and 8, a moderate level of hopelessness was present for those with scores ranging between 9 and 14 and individuals with scores ranging between 15 and 20 had high levels of hopelessness.[24]

Multidimensional Scale of Perceived Social Support (MSPSS): Eker et al. worked on the factor structure, validity and reliability of the revised scale.[25,26] Cronbach's alpha was 0.89 in total evaluation. The MSPSS is a scale comprised of 12 items. Each contains three groups of four items related to the source of the support. These are 'family', 'friends' and 'significant other'. Each item was scored with a 7-point Likert scale. The sub-scale score is obtained by summing the scores of the four items in each sub-scale, and the total scale score is calculated by adding up the scores for each of the sub-scales. High scores indicate that perceived social support is high.

Statistical Analysis

The compliance of the data with a normal distribution was tested via the Shapiro-Wilk test. The Student t-test was used for comparing the properties with a normal distribution in the two independent groups, and the Mann-Whitney U test was used for comparing the properties without normal distribution in the two independent groups. In addition, a one-way analysis of variance and Fisher's least significant difference multiple comparison tests were used for properties with normal distributions in the comparison of numerical data in more than two independent groups, whereas the Kruskal-Wallis test and all multiple pairwise comparison tests were used for properties without normal distribution. We calculated the direct and indirect effects of a predictor in path models of mediation and moderation. The bootstrapping method was used to calculate confidence intervals for the indirect effects. Mediation models are extended regression models that make the effect of particular covariates in the model explicit. Moderation was performed by multiplying the predictor variables. The relationships between the numerical variables were tested via the Spearman correlation coefficient. Cronbach alpha

coefficients were calculated for testing reliability. The average ± standard deviation was used for numerical variables as descriptive statistics, whereas the number and percentage values were presented for categorical variables. SPSS Windows version 24.0 package software was used for statistical analyses, and P <.05 was accepted as statistically significant.

Written approvals were obtained before the study from Gaziantep University Clinical Studies Ethics Council and Gaziantep University Union of Public Hospitals General Directorate (Ethical Code: 27.02.2017 / 65). Explanations were made to the individuals who participated in the study regarding the purpose of the study and the content of the forms after which their verbal consent was taken, and they were asked to sign a written voluntary consent form.

RESULTS

A total of 205 individuals with disabled children consisting of 167 mothers and 38 fathers participated in the study. It was determined that 28.8% of the participants were older than 40 years, 86.3% were married, and 34.1% were primary school graduates. It was observed that 68.8% of individuals did not have social security, 29.3% were relatives with their spouses, and 32.7% had a daughter, and 34.1% had a son. Table 1 presents the frequency and percentage values for the sociodemographic characteristics of individuals with disabled children.

Table 1. Socio-Demographic Characteristics of Individuals with Disabled Children

VARIABLES	**n**	**%**
Age		
18-24	26	12.6
25-29	34	16.6
30-34	43	21.0
35-39	43	21.0
40 and above	59	28.8
Gender		
Female	167	81.5
Male	38	18.5
Marital Status		
Married	177	86.3
Single	28	13.7
Education Status		
Not literate	54	26.3
Primary School	98	47.8
High School	37	18.
University	16	7.8
Kindredship Among Spouses		
Yes	60	29.3
No	145	70.7
Physical Disability		
Yes	7	3.4
No	198	96.6

Of the disabled children, 53.2% were male, 32.7% were in the 4 to 6 years age interval, 73.7% were receiving care from private rehabilitation centres (Table 2).

Table 2. Socio-Demographic Characteristics of Individuals with Disabled Children which are related to their Disabled Children

VARIABLES	n	%
Gender of the Disabled Child		
Female	96	46.8
Male	109	53.2
Age of the Disabled Child		
0-3	39	19.0
4-6	67	32.7
7-12	46	22.4
12-15	35	17.1
16-18	18	8.8
Disabled Child receiving care from private rehabilitation centres		
Yes	151	73.7
No	54	26.3

It was determined that 54.1% of parents received specialist support for their disabled children, 37.6% did not have sufficient knowledge on the status of their disabled children, 31.2% did not deal with the care of their children at a sufficient level, 47.3% could not meet the financial needs associated with the care of their disabled child, 61.5% did not receive state support for the care of their disabled child, 54.1% could not properly spare time for their other children because they have a disabled child, 84.4% had accepted the disability of their children as a family and that 71.2% felt guilty for the disability of their children. It was determined that the people in the immediate circle of 46.8% of the individuals distanced themselves because of the disability of the child, that 79.5% experienced feelings of shame because of the disability of their child since they go out to different social environments with their disabled child. Also, around 53.7% of the participants display negative attitudes and behaviours towards the disabled child, and 80.0% have concerns related to the future of their disabled child.

The average BDS total score for individuals with disabled children was determined as 21.53 ± 12.82, BHS was 9.21 ± 4.75 and MSPSS was 44.72 ± 15.72. Table 3 presents the average total scores and sub-scales scores of the BDS, BHS and MSPSS.

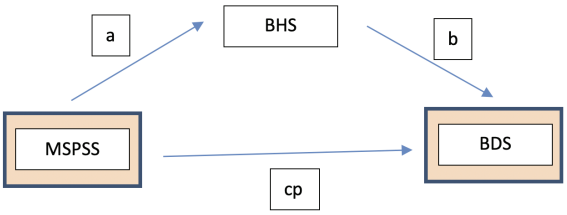
Table 3. Beck Depression Scale, Beck Hopelessness Scale and Sub-Scales, Multidimensional Perceived Social Support Scale and Sub-Scales Total Score Averages (s=205)

	x ±S.d.	Min.	Max.
Beck Depression Scale	21.53 ± 12.82	0.00	63.00
Beck Hopelessness Scale			
Hope	3.22 ± 2.09	0.00	7.00
Feelings and Expectations About the Future	2.01 ± 1.67	0.00	5.00
Loss of Motivation	3.98 ± 2.12	0.00	8.00
Total BHS Score Average	9.21 ± 4.75	0.00	20.00
MSPSS and Sub-Scales			
Family	17.19 ± 6.67	4.00	28.00
Friend	14.65 ± 6.75	4.00	28.00
Significant Other	12.89 ± 6.34	4.00	28.00
Total MSPSS Score Average	44.72 ± 15.72	12.00	84.00
x ±S.d.: Mean ± Standard deviation, MPSSS: Multidimensional Perceived Social Support Scale			

A positive and statistically significant relationship was determined between the BDS and BHS applied to individuals with disabled children ($r = 0.594$, $p = .000$). No correlation was determined between the BDS and MSPSS ($r = -0.128$, $p = .068$). A negative and statistically significant relationship was determined between the MSPSS and BHS ($r = -0.149$, $p = .033$).

We tested the hypothesis that BHS mediates the relationship between the MSPSS and BDS where decreases in the MSPSS improve the BHS, which in turn increases the BDS. In other words, increases in the MSPSS were associated with decreases in the BDS indirectly through decreases

in the BHS (Figure 1). Specifically, for every 0.055 (a = −0.055, Std. = 0.021) unit decrease in the association between the MSPSS and BHS, there was a 0.084 decrease in the BDS (a = −0.084, Std. = 0.033). (Exogenous variable: MSPSS, Mediator variable: BHS, Endogenous variable: BDS) (Table 4).



BDS: Beck Depression Scale, BHS: Beck Hopelessness Scale, MPSS: Multidimensional Perceived Social Support Scale, a: relationship direction from MSPSS to BDS b: relationship direction from BHS to BDS cp: relationship direction from MSPSS to BDS

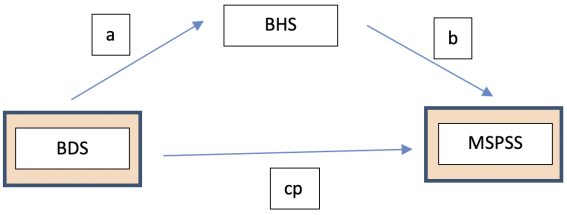
Figure 1: Mediation model between Beck Depression Scale, Beck Hopelessness Scale, Multidimensional Perceived Social Support Scale

Table 4 : Mediating role of hopelessness between social support and depressive symptoms

		Estimates	Std. Err.	Z	p-value
BDS	BHS (b)	1.527	0.157	9.751	<0.001
	MSPSS (cp)	-0.038	0.047	-0.793	0.428
BHS	MSPSS (a)	-0.055	0.021	-2.645	0.008
a*b	Indirect Effect (ab)	-0.084	0.033	-2.552	0.011*

BDS: Beck Depression Scale, BHS: Beck Hopelessness Scale, MPSS: Multidimensional Perceived Social Support Scale

On the other hand, we also tested another hypothesis that assumed the BHS still mediates the relationship between the MSPSS and BDS where increases in the BDS improve the BHS, which in turn increase the MSPSS (Figure 2). We were not able to prove that either the BDS has a direct or an indirect effect on the MSPSS (0.428 and 0.091, p-values of direct and indirect effects, respectively) (Exogenous variable: BDS, Mediator variable: BHS, Endogenous variable: MSPSS) (Table 5).



BDS: Beck Depression Scale, BHS: Beck Hopelessness Scale, MPSS: Multidimensional Perceived Social Support Scale a: relationship direction from BDS to BHS b: relationship direction from BHS to MSPSS cp: relationship direction from BDS to MSPSS

Figure: 2: Mediation model between Beck Depression Scale, Beck Hopelessness Scale, Multidimensional Perceived Social Support Scale

Table 5 : Mediating role of hopelessness between depressive symptoms and social support

		Estimates	Std. Err.	Z	p-value
MSPSS	BHS (b)	-0.474	0.277	-1.712	0.087
	BDS (cp)	-0.081	0.103	-0.793	0.428
BHS	BDS (a)	0.213	0.021	10.047	<0.001
a*b	Indirect Effect (ab)	-0.101	0.06	-1.688	0.091

BDS: Beck Depression Scale, BHS: Beck Hopelessness Scale, MPSS: Multidimensional Perceived Social Support Scale

It was determined that 68.8% of individuals with disabled children might take care of their children sufficiently. A statistically significant difference was determined between the average BDS, BHS and MSPSS total scores of individuals who are and are not able to take care of their children sufficiently (p <.05). Table 6 presents the comparison of the average BDS, BHS and MSPSS total scores for individ-

Table 6. Comparison of the Beck Depression Scale, Beck Hopelessness Scale and Multidimensional Perceived Social Support Scale Total Score Averages for Individuals with Disabled Children with regard to whether they are able to take care of their children sufficiently or not (s=205)

Taking Sufficient Care of Disabled Child	n	%	Beck Depression Scale x ±S.d.	Beck Hopelessness Scale x ±S.d.	Multidimensional Perceived Social Support Scale x ±S.d.
Yes	141	68.8	18.96 ± 12.59	8.57 ± 4.52	46.79 ± 15.95
No	64	31.2	27.17 ± 11.53	10.61 ± 5.00	40.16 ± 14.29
Total	205	100	21.53 ± 12.82	9.21 ± 4.75	44.72 ± 15.72
Statistical Values			z=-4.341 **p=0.001***	z=-2.815 **p=0.005***	t=2.805 **p=0.005***

***p<0.05 statistically significant; Z: Mann whitney u ; t: Student t test**
x ±S.d.: Mean ± Standard deviation

uals with disabled children regarding whether they can take care of their children sufficiently.

It was determined that 53.2% of disabled children are male. The average BDS total score was determined as 24.31 ± 12.74 for individuals with disabled male children, whereas their average BHS total score was determined as 10.16 ± 4.54, and the average MSPSS total score was 42.45 ± 15.15. A statistically significant difference was determined when the average BDS and BHS total scores, along with the male gender status of the disabled children were compared (p <.05). No statistically significant difference was determined between the average MSPSS total scores when comparisons were made regarding the genders of the disabled children (p >.05). Table 7 presents the comparison of the average BDS, BHS and MSPSS total scores regarding the gender of the disabled children.

No statistically significant difference was determined when the average BDS, BHS and MSPSS total scores were compared regarding the age groups of the disabled children (p >.05).

Table 7. Comparison of Beck Depression Scale, Beck Hopelessness Scale and Multidimensional Scale of Perceived Social Support in terms of Gender Status of Individuals with Disabled Children (N=205)

Gender of disabled child	n	%	Beck Depression Scale x ±S.d.	Beck Hopelessness Scale x ±S.d.	Multidimensional Perceived Social Support Scale x ±S.d.
Yes	96	46.8	24.31 ± 12.74	10.16 ± 4.54	42.45 ± 15.15
No	109	53.2	19.07 ± 12.44	8.38 ± 4.80	46.72 ± 16.00
Total	205	100	21.53 ± 12.82	9.21 ± 4.75	44.72 ± 15.72
Statistical Values			t=2.975 **p=0.003***	z=-2.2706 **p=0.007***	z=-1.844 p=0.065

***p<0.05 statistically significant; Z: Mann whitney u ; t: Student t test**
x ±S.d.: Mean ± Standard deviation

DISCUSSION

In this study, the relationships between severity of depressive symptomes and hopelessness symptom levels and their perceived social support levels were examined for individuals with disabled children in addition to the sociodemographic characteristics that have an impact on these relationships. The results suggest that hopelessness increases and depression develops indirectly with decreasing perceived psychosocial support.

The average BDS total score for individuals with disabled children who participated in the study was 21.53 ± 12, where 82 is the equivalent to moderate depression severity. This average score was determined at high values ranging between 14.2 ± 13 in similar studies carried out in parents of disabled children.[27,28] The average BHS total score was determined as 9.21 ± 4.75 for individuals with disabled children who participated in the study. Average BHS total score values ranging between 5.6 and 12.4 were determined in similar studies.[29,30] We found that hopelessness increases and depression develops indirectly with decreasing psychosocial support.

The average MSPSS total score was determined as 44.72 ± 15.72 for individuals with disabled children who participated in the study. It was determined that the perceived social support levels of individuals are at moderate levels. These values were determined to vary between 54.5 and 44.9 in similar studies.[29,31,32]

In different cultures, expectations of children with intellectual disabilities are varied.[33] In Turkey, better communication with the child is more important than academic skills, and social support is especially essential from family and friends for wellbeing.[34,35] A negative relationship was observed between hopelessness levels of individuals and their perceived social support. This negative relation was also apparent in previous studies.[29,31] With regard to sub-scales, a negative and statistically significant relationship was observed between feelings and expectations about the future and family and friends subscales. This result supports the opinion that the feelings and expectations about the future of individuals with disabled children increase negatively as perceived social support from families or friends decreases. Thus, parents and their children with intellectual disabilities reported having family-related and systemic barriers to developing plans.[36] Decreasing psychosocial support seems to decrease hope for the future.

Studies mostly indicated a positive relationship between the social support perceived by caregivers and depression.[37,38] A study in the UK reported that social support could increase resilience in parents of disabled individuals.[39] A positive parenting programme improves the resilience of caregivers.[40] It was reported as a result of a study conducted in Australia that high social support lowers parent-related stress.[41] Indeed, there is a statistically significant relationship between severity of depressive symptomes and providing care to disabled children. Children with intellectual disabilities were found to be at higher risk of experiencing unsupportive care than children with typical development.[42] Also, increased parent-child conflict was found to be associated with greater behavioural problems for children with intellectual disabilities.[43] This relationship between parental stress and children's behavioural problems was found to be bidirectional.[44] The BDS and BHS scores of individuals who can provide sufficient care to their disabled children are lower compared with those who are not able to provide sufficient care. Parents were found to show a strong sense of responsibility for their child's problematic behaviours.[45] Depressive parents may feel guilty because of their child's behaviours and attribute the source of the problems to themselves. These results lead us to think that an increase in severity of depressive symptomes and hopelessness levels prevents caregivers from providing adequate care to disabled children.

It was determined that severity of depressive symptomes and hopelessness levels of individuals with disabled female children were higher compared with those of individuals

with male disabled children, whereas no statistically significant difference was determined between their levels of perceived social support. It has been proposed in a similar study that hopelessness levels are higher for individuals with disabled female children than with those who are male.[46] However, another study reported that individuals with disabled male children have higher hopelessness levels.[47] Aydoğan and Akıncı (1999) conducted a study in which no statistically significant difference was determined between the hopelessness levels of the parents and the gender of their children.[1] Kaner carried out a study to determine the social support and life satisfaction and found that the gender variable causes no statistically significant difference in the perceived social support levels of parents.[48] The different results of various studies may be related to different expectations. When the social structure in our country is taken into consideration, it can be thought that parents have different levels of expectations and concerns for disabled female and male children.[49] It is thought that society is still sensitive regarding gender roles when it concerns disabled children. It might be considered natural for male children to receive care from others while the physical changes that occur in female children during their adolescence raise concerns of parents. Higher risks regarding sexual abuse towards disabled female children[50] might also be considered a factor that increases the depression and hopelessness of parents concerning the future of their disabled daughters. Data obtained from developed countries also indicate that families that provide care to disabled individuals are undoubtedly defenceless against certain types of stress. However, it has also been suggested that factors such as adaptive coping strategies, perceived social support and a positive evaluation of the disability of the child contribute to the individual.[51]

The fact that there is no control group, and that the disabled children do not have the same diagnoses was the most important limitation of the study. Causality relationships could not be discussed because of the cross-sectional nature of the study. The diagnosis of intellectual disability was made according to the DSM 5, and a clinical examination was performed by a psychiatrist. Moreover, structured psychiatric assessments, such as the SCID II were not performed. Thus, some accompanying diagnoses were likely to be missed. The lack of knowledge of the degree of intellectual disability is also an important limitation.

CONCLUSION

A positive relationship was determined between severity of depressive symptom levels and hopelessness levels, while a negative relationship was determined between perceived social support and severity of depressive symptom levels. The increase in severity of depressive symptomes and hopelessness levels may prevent caregivers from providing adequate care to disabled children. Individuals with disabled children should be evaluated psychologically, and they should receive psychological support when it is considered that they have high risks of depression and hopelessness.

Acknowledgement

The study was derived from Tuskish thesis. The authors would like to thank Enago (www.enago.com) for the English language review.

References

1. *Akıncı-Aydoğan A. Özürlü çocuğa sahip anne babaların umutsuzluk düzeylerinin belirlenmesi. 1999, Yayınlanmamış Doktora Tezi. Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü.*
2. *Cobb RB, Alwell M. Transition planning/coordinating interventions for youth with disabilities: A systematic review. Career Development for Exceptional Individuals 2009; 32:(2):70-81.*
3. *Organization, W.H. International classification of impairments, disabilities, and handicaps: a manual of classification relating to the consequences of disease, published in accordance with resolution WHA29. 35 of the Twenty-ninth World Health Assembly, May 1976. 1980.*
4. *Cohen, S. Social relationships and health. American psychologist 2004; 59:(8):676.*
5. *Ardahan, M. Sosyal destek ve hemşirelik. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi 2006; 9:(2):68-75.*
6. *Liu, R.T., E.M. Kleiman, B.A. Nestor, and S.M. Cheek. The hopelessness theory of depression: A quarter-century in review. Clinical Psychology: Science and Practice 2015; 22:(4):345-365.*
7. *Ribeiro, J.D., X. Huang, K.R. Fox, and J.C. Franklin. Depression and hopelessness as risk factors for suicide ideation, attempts and death: meta-analysis of longitudinal studies. The British Journal of Psychiatry 2018; 212:(5):279-286.*
8. *Rodríguez-Naranjo, C. and A. Caño. Daily stress and coping styles in adolescent hopelessness depression: Moderating effects of gender. Personality and Individual Differences 2016; 97:109-114.*
9. *Sen, E. and S. Yurtsever. Difficulties experienced by families with disabled children. Journal for Specialists in Pediatric Nursing 2007; 12:(4):238-252.*
10. *Lach, L.M., D.E. Kohen, R.E. Garner, J.C. Brehaut, A.R. Miller, A.F. Klassen, et al. The health and psychosocial functioning of caregivers of children with neurodevelopmental disorders. Disability and rehabilitation 2009; 31:(9):741-752.*
11. *Park, I.J., H. Du, L. Wang, D.R. Williams, and M. Alegría. The Role of Parents' Ethnic-Racial Socialization Practices in the Discrimination–Depression Link among Mexican-Origin Adolescents. Journal of Clinical Child & Adolescent Psychology 2019:1-14.*
12. *Prevoo, M.J. and C.S. Tamis-LeMonda. Parenting and globalization in western countries: Explaining differences in parent–child interactions. Current opinion in psychology 2017; 15:33-39.*
13. *Aksoy, A.B., U.P.Ş. Kılıç, and Ö.G. Kahraman. Asya kültürlerinde ebeveynlik stilleri ve uygulamalari. Çukurova Üniversitesi Sosyal Bilimler Enstitüsü Dergisi 2009; 18:(2):14-25.*
14. *Kaya, T. Gelin-Kaynana İletişiminin Niteliğini Belirleyen Kültürel Etmenler. 2019.*
15. *Taanila, A., L. Syrjälä, J. Kokkonen, and M.R. Järvelin. Coping of parents with physically and/or intellectually disabled children. Child: Care, Health and Development 2002; 28:(1):73-86.*
16. *Tokuç, F.Ö. Otistik çocuk ve aile özelliklerinin aile işlevlerine etkisi. TC Marmara Üniversitesi Sağlık Bilimleri Enstitüsü Yüksek Lisans Tezi. Ġstanbul 2009.*
17. *Canarslan, H., Engelli çocuğa sahip ailelerin yaşam kalitesinin incelenmesi. 2014, Trakya Üniversitesi Sosyal Bilimler Enstitüsü.*
18. *Beck, A.T., C. Ward, M. Mendelson, J. Mock, and J. Erbaugh. Beck depression inventory (BDI). Arch Gen Psychiatry 1961; 4:(6):561-571.*
19. *Hisli, N. The validity and reliability of the Beck Depression Inventory among university students. Turkish Journal of Psychology 1989; 7:(23):3-13.*
20. *Hisli, N. Beck Depresyon Envanteri'nin geçerligi üzerine bir çalısma [A study on the validity of Beck Depression Inventory, in Turkish]. Turkish Journal of Psychology 1988; 7:3-13.*
21. *Beck, A.T., A. Weissman, D. Lester, and L. Trexler. The measurement of pessimism: the hopelessness scale. Journal of consulting and clinical psychology 1974; 42:(6):861.*
22. *Seber, G., N. Dilbaz, C. Kaptanoğlu, and D. Tekin. UMUTSUZLUKÖLÇEĞİ: GEÇERLİLİK VEGÜVENİRLİĞİ. Kriz Dergisi 1993; 1:(3).*
23. *Durak, A. and R. PALABIYIKOĞLU. BECK UMUTSUZLUK ÖLÇEĞİ GEÇERLİLİK ÇALIŞMASI. Kriz Dergisi 1994; 2:(2):311-319.*
24. *Duman, S., Ö. Taşğın, and S. Özdağ. Beden eğitimi ve spor yüksekokulu spor yöneticiliği bölümünde okuyan öğrencilerin umutsuzluk düzeylerinin incelenmesi. Selçuk Üniversitesi Beden Eğitimi ve Spor Bilim Dergisi 2009; 11:(3):27-32.*
25. *Wilcox, S. Multidimensional Scale of Perceived Social Support. Psychological Trauma: Theory, Research, Practice, and Policy 2010; 2:(3):175-182.*
26. *Eker, D. Cok boyutlu algilanan sosyal destek olceginin gozden gecirilmis formunun faktor yapisi, gecerlik ve guvenirligi. Turk Psikiyatri Dergisi 2001; 12:17-25.*
27. *Bumin, G., A. Günal, and Ş. Tükel. Anxiety, depression and quality of life in mothers of disabled children. SDÜ Tıp Fakültesi Dergisi 2008; 15:(1):6-11.*
28. *Natan, K. Zihinsel engelli çocuğu olan ve zihinsel engelli çocuğu olmayan annelerin depresyon ve kaygı düzeyleri. Yayınlanmamış yüksek lisans tezi. İstanbul: Maltepe Üniversitesi Sosyal Bilimler Enstitüsü 2007.*
29. *Akmaniş, B. Otistik çocuğu olan annelerin algıladıkları sosyal desteğe göre umutsuzluk düzeylerinin incelenmesi. Yayımlanmamış Yüksek Lisans Tezi). Maltepe Üniversitesi, İstanbul 2010.*
30. *30. Ünlüer, E. 2-6 yaş arası otistik çocuğa sahip annelerin algıladıkları sosyal destek ve umutsuzluk düzeyleri arasındaki ilişkinin incelenmesi. 2009.*
31. *Görgü, E. 3-7 yaş arası otistik çocuğa sahip olan annelerin algıladıkları sosyal destek düzeyleri ile depresyon düzeyleri arasındaki ilişki. 2005.*
32. *Sungur-Bozdoğan, İ. Zihinsel engelli çocuğa sahip ebeveynlerin algıladıkları sosyal destek ve yalnızlık puanları arasındaki ilişkinin incelenmesi. Yayımlanmamış Yüksek Lisans Tezi, Atatürk Üniversitesi, Eğitim Bilimleri Enstitüsü, Erzurum 2011.*
33. *Wilt, C.L. and M.E. Morningstar. Parent Engagement in the Transition From School to Adult Life Through Culturally Sustaining Practices: A Scoping Review. Intellectual and developmental disabilities 2018; 56:(5):307-320.*
34. *Yalçın, İ. İyi oluş ve sosyal destek arasındaki ilişkiler: Türkiye'de yapılmış çalışmaların meta analizi. Türk Psikiyatri Dergisi 2015; 26:(1):21-32.*
35. *3ARICIOĞLU, A. and F. GÜLTEKİN. Zihinsel Engelli Çocuk Annelerinin Sosyal Destek ve Gelecek Algıları: Psikolojik Danışmanların Rolleri. 2017.*
36. *Lee, C.e., M.M. Burke, and C.R. Stelter. Exploring the Perspectives of Parents and Siblings Toward Future Planning for Individuals With Intellectual and Developmental Disabilities. Intellectual and developmental disabilities 2019; 57:(3):198-211.*
37. *Yüzer, S., R. Yiğit, R. YİĞİT, B. Taşdelen, and B. TAŞDELEN. ÇOCUĞU HASTANEDE YATAN ANNELERİN ALDIĞI SOSYAL DESTEK İLE DEPRESYON DÜZEYLERİ ARASINDAKİ İLİŞKİ. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi 2006; 9:(4):54-62.*
38. *Atagün, M.İ., Ö.D. Balaban, Z. Atagün, M. Elagöz, and A.Y. Özpolat. Kronik hastalıklarda bakım veren yükü. Psikiyatride Güncel Yaklaşımlar 2011; 3:(3):513-552.*
39. *Whiting, M., A. Nash, S. Kendall, and S. Roberts. Enhancing resilience and self-efficacy in the parents of children with disabilities and complex health needs. Primary Health Care Research & Development 2019; 20.*
40. *Egami, C. Triple P intervention support to improve caregiving resilience for caregivers with children with developmental problems. Impact 2018; 2018:(10):27-29.*
41. *Patton, K.A., R. Ware, L. McPherson, E. Emerson, and N. Lennox. Parent-related stress of male and female carers of adolescents with intellectual disabilities and carers of children within the general population: A cross-sectional comparison. Journal of Applied Research in Intellectual Disabilities 2018; 31:(1):51-61.*
42. *Rodas, N., S. Zeedyk, and B. Baker. Unsupportive parenting and internalising behaviour problems in children with or without intellectual disability. Journal of Intellectual Disability Research 2016; 60:(12):1200-1211.*
43. *Totsika, V., R.P. Hastings, D. Vagenas, and E. Emerson. Parenting and the behavior problems of young children with an intellectual disability: Concurrent and longitudinal relationships in a population-based study. American journal on intellectual and developmental disabilities 2014; 119:(5):422-435.*
44. *Neece, C.L., S.A. Green, and B.L. Baker. Parenting stress and child behavior problems: A transactional relationship across time. American journal on intellectual and developmental disabilities 2012; 117:(1):48-66.*
45. *Jacobs, M., L.M. Woolfson, and S.C. Hunter. Attributions of stability, control and responsibility: how parents of children with intellectual disabilities view their child's problematic behaviour and its causes. Journal of Applied Research in Intellectual Disabilities 2016; 29:(1):58-70.*
46. *Firat, S., R.S. Diler, A. Avci, and G. Seydaoglu. Comparison of psychopathology in the mothers of autistic and mentally retarded children. Journal of Korean medical science 2002; 17:(5):679.*
47. *YILDIRIM, A., R.H. AŞILAR, P. KARAKURT, A. Yıldırım, R.H. Aşılar, and P. Karakurt. Engelli çocukların annelerinin ruhsal durumlarının belirlenmesi. Florence Nightingale Hemşirelik Dergisi 2013; 20:(3):200-209.*
48. *Kaner, S. Engelli Çocuğu olan Anababaların Algıladıkları Stres, Sosyal Destek ve Yaşam Doyumlarının İncelenmesi. Ankara Üniversitesi: Bilimsel Araştırma Projesi Kesin Raporu 2004:7-67.*
49. *Dedeoğlu, S. Toplumsal cinsiyet rolleri açısından Türkiye'de aile ve kadın emeği. Toplum ve Bilim 2000; 86:139-170.*
50. *İMREN, S.G., A. Ayşe, C. YusufoĞlu, and A.R. ARMAN. Cinsel istismara uğrayan çocuk ve ergenlerde klinik özellikler ve intihar girişimi ile ilişkili risk etmenleri. Marmara Medical Journal 2013; 26:(1):11-16.*
51. *John, A. and M. Zapata Roblyer. Mothers parenting a child with intellectual disability in urban India: An application of the stress and resilience framework. Intellectual and developmental disabilities 2017; 55:(5):325-337.*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Relationship Between Neutrophil-Lymphocyte Ratio and Empirical Antibiotic Therapy in Patients with Fever of Unknown Origin

Nedeni Bilinmeyen Ateşli Hastalarda Nötrofil-Lenfosit Oranı ile Ampirik Antibiyotik Tedavisi Arasındaki İlişki

Cengiz Karacaer[1], Oğuz Karabay[2], Ali Tamer[1]

[1] *Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi, İç Hastalıkları Anabilim Dalı, Sakarya*

[2] *Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Hast. Anabilim Dalı, Sakarya*

Yazışma Adresi / *Correspondence:*
Cengiz Karacaer

Sakarya Eğitim ve Araştırma Hastanesi, İç Hastalıkları Anabilim Dalı, Sakarya
T: **+90 505 740 01 68** E-mail **: karacaerc@yahoo.com**

Geliş Tarihi / Received : **20.10.2020** Kabul Tarihi / Accepted : **06.12.2020**

Orcid :
Cengiz Karacaer , https://orcid.org/0000-0002-7164-4810
Oğuz Karabay https://orcid.org/0000-0003-1514-1685
Ali Tamer https://orcid.org/0000-0003-2005-0737

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):25-31) DOI: 10.31832/smj.813151**

Abstract

Objective	Empirical antibiotic therapy is usually applied by physicians to patients with fever when the origin of the infection can not yet be determined.The aim of this study is to determine the cost-effectiveinflammatoryparametersin empirical antibiotic therapy in patients with fever of unknown origin(FUO).
Materials and Methods	A total of 577 patients, whose blood cultures were taken and followed up by the NBA, were divided into two groups as fever group due to infection(IRFG) and fever group not related to infection(NIRFG), and their five-year data were analyzed retrospectively from the patient information registry system. From the complete blood count test results, the neutrophil count was proportioned to the lymphocyte count parameter, and the neutrophil lymphocyte ratio and thrombocyte lymphocyte ratio values were calculated.
Results	Total of 577 patients were divided into two groups as infection related fever group (IRFG) and non-infection related fever group (NIRFG), and were included in the study. The durations of first antibiotic usages were 4.54 ± 3.08(1–14) days and 5.35 ± 3.8(1–21) days in IRFG and NIRFG, respectively. Neutrophil-to-lymphocyte ratio (NLR) was 8.00 (3.00-15.00) in the IRFG, whereas it was 5.00 (3.00-9) in the NIRFG (p = 0.001). Platelet-to-lymphocyte ratio (PLR) was 21.00 (9.00-41.00) in the IRFG, whereas it was 16.00 (7.25-27.75) in the NIRFG and was not significant (p = 0.165).
Conclusion	Since neutrophil-lymphocyte ratio can be checked from routine blood tests and is not an expensive method, it can be used as an advantageous diagnostic method in patients with fever of unknown origin(FUO).

Keywords Empirical antibiotic therapy; Fever of unknown origin; Neutrophil to lymphocyte ratio; Platelet-to-lymphocyte ratio.

Öz

Amaç	*Ampirik antibiyotik tedavisi, enfeksiyon kaynağının henüz belirlenemediği durumlarda hekimlerin ateşi olan hastalara yaygın olarak uyguladıkları bir yöntemdir. Bu çalışmanın amacı, nedeni bilinmeyen ateşi olan hastalarda (NBA) ampirik antibiyotik tedavisinde maliyet-etkinin flamatuar parametreleri belirlemektir.*
Gereç ve Yöntemler	*Kan kültürleri alınmış olan NBA ile takip edilen toplam 577 hasta enfeksiyona bağlı ateş grubu (EBAG,n:203) ve enfeksiyona bağlı olmayan ateş grubu (EBOAG,n:374) olarak iki gruba ayrıldı ve beş yıllık verileri hasta bilgi kayıt sisteminden geriye dönük olarak incelendi. Tam kan test sonuçlarından nötrofil sayısı, lenfosit sayısı parametresine oranlanarak nötrofil lenfosit oranı ve trombosit lenfosit oranı değerleri hesaplandı.*
Bulgular	*Toplam 577 hasta enfeksiyona bağlı ateş grubu (EBAG) ve enfeksiyona bağlı olmayan ateş grubu (EBOAG) olarak iki gruba ayrıldı. İlk antibiyotik kullanım süreleri EBAG veEBOAG'da sırasıyla 4.54 ± 3.08 (1-14) gün ve 5.35 ± 3.8 (1–21)gündü(p = 0.023). Nötrofil-lenfositoranı (NLO) EBAG'da 8.00 (3.00-15.00)iken, EBOAG'da 5.00 (3.00-9.00)idi (p = 0.001). Trombosit-lenfositoranı (TLO) EBAG'da 21.00(9.00-41.00)iken, EBOAG'da 16.00 (7.25-27.75)idiveanlamlıdeğildi (p = 0.165).*
Sonuç	*Nötrofil lenfosit oranı rutin kan testlerinden bakılabilen ve pahalı bir yöntem olmaması nedeniyle, nedeni belirlenemeyen ateşli (NBA)hastalarda avantajlı bir tanı metodu olarak kullanılabilir.*

Anahtar Kelimeler *Ampirik Antibiyotik Tedavisi; Nedeni Bilinmeyen Ateş; Nötrofil Lenfosit Oranı; Trombosit Lenfosit Oranı.*

INTRODUCTION

Fever of unknown origin (FUO) was initially described by Petersdorf and Beason as body temperature above 38.3 °C. It is defined as fever that is not diagnosed despite on week of research on patients who had fever for at least three weeks and were eventually hospitalized.[1] Although laboratory and diagnostic imaging tests contribute to advanced technology, challenges remain for FUO diagnosis and treatment.[2] FUO consists of four general categories: infectious, neoplastic, non-infectious and others.[3] In most previous studies, infections are indicated as the leading causes of FUO, in which abscess, endocarditis, tuberculosis and complicated urinary tract infections are the main ones.[4] Adult-onset Still's disease (AOSD) and systemic lupus erythematosus are the most common reasons in young individuals of the Non-infectious inflammatory disease (NIID) group. Temporal arteritis and polymyalgia rheumatica are mostly defined in the elderly individuals of NIID group.[5]

It is challenging to differentiate infectious fever from non-infectious on, which in turn makes it difficult to decide starting an antibiotic therapy in patients with non-infectious fever. In those cases, C-reactive protein (CRP) and procalcitonin(PCT) are important biomarkers to conclude whether an empirical antibiotic therapy should be initiated.[6] Also, it has been suggested that the neutrophil: lymphocyte ratio (NLR) in peripheral blood is useful for distinguishing between types of infection and also useful for predicting the outcome of the infection.[7]

Proper empirical antibiotic treatment reduces mortality, along with the duration of intensive care unit and hospitalization.[8] In some cases, antibiotic usage is not applicable. Unnecessary use of antibiotics should be avoided by considering appropriate antibiotic selection and antibiotic resistance on both patient and cost basis. Empirical antibiotic therapy should not be applied if the fever persists over a long time period. Antibiotic application might mask the disease, delay diagnosis and prevent appropriate treatment. One of the most common mistakes in antimicrobial usage is adding or changing antibiotics, although there is no clear evidence of an infectious disease.[9,10]

In this study, we aimed to investigate the distribution of antibiotic treatments applied to patients with FUO, who were admitted to our clinic due to fever and were hospitalized.

MATERIAL and METHODS

Study site and study period

This study was conducted between January 1, 2015 and January 1, 2020 at Sakarya Training and Research Hospital (SUTRH) Internal Medicine Clinic. SUTRH has total of 935 beds, in which 120 of them are in the intensive care unit (ICU). This study was performed in the internal medicine clinic of third step hospital, which has 36 beds. Patients who applied to the hospital with fever and received inpatient treatment at the internal medicine clinic were included in the study. Patients were evaluated in two groups as infection related fever group (IRFG) and non-infection related fever group (NIRFG), based on their fever etiologies.

Infection Related Fever Group (IRFG)

In this groups, the culture of patients, who applied to the clinic with fever, demonstrated reproduction, which is an indicative of an infectious disease.

Non-Infection Related Fever Group (NIRFG)

In this groups, the culture results of patients, who had fever and were followed up in the clinic turned out negative. Infections were excluded from the source of fever and this group is designated as non-infectious.

Inclusion and exclusion criteria

All patients being followed up at least one day at SUTRH Internal Medicine Clinic were included in the study. The study group consisted of patients who were admitted with fever. Patients who were followed up in the clinic for less

than 1 day and whose medical records were missing were excluded from the study. Patients under 17 were not included from the study as well.

Data collection

The medical records of patients who were hospitalized at SUTRH Internal Medicine Clinic and admitted with fever were investigated retrospectively. The culture information of patients, antibiotics received, number of antibiotics administered, as well as initiation and duration of antibiotic usage were recorded on the patient registration form along with additional information regarding hospitalization.

Patient demographics, as well as PCT, CRP, erythrocyte-sedimentation rate (ESR), alanineaminotransferase (ALT), aspartate aminotransferase (AST), creatinine, thyroid stimulant hormone (TSH), lactatedehydrogenase (LDH), white blood cell (WBC), lymphocytes (Lym), neutrophil (Neu), mean platelet volume (MPV) and platelet levels were recorded.

Laboratory parameters

Blood samples were obtained in the morning, after eight hours of fasting during diagnosis and follow-up, and were sent to the laboratory immediately to be centrifuged at 2000 rpm for 15 minutes. For biochemical parameters, the samples were placed into a dry tube and investigated using a Beckman Coulter AU680® with Beckman Coulter kits. Blood was collected into an EDTA coated tube for hemogram examination using a WIC-LYSE for CELL DYN 3700 Kits on the Abbott Cell-Dyn 3700® Device.

ESR was performed using Rapida ESR100® in capillary tubes. The CRP parameter was studied with SIEMENS BN II®with Cardio Phase CRP WN®kits. Blood samples for PCT were obtained from the tubes with decomposed serum. PCT was measured with a timely-mannered reinforced cryptate emission technology by measuring the signal sent by time lagged immunocomplex (BIOMERIEUX/mini IDAS). TSH parameter was studied with Abbott Architect I 2000 SR®. The data was automatically uploaded to the hospital database system and screened consequently. MPV (N: 7.5- 11.5 femtoliter) values were recorded from the measured value in the hemogram.

Statistical Analysis

Data analysis was performed using IBM SPSS 21 (IBM Corp., Armonk, NY, USA®Z). All results are presented as frequencies, percentages, mean ± S.D and median [IQR]. Chi-square test was used to compare categorical variables. Kolmogorov-Smirnov test was used to determine whether continuous data were normally distributed. All normally distributed data were analyzed using Student's t-test, while non-normally distributed data were analyzed using the Mann-Whitney U test.The statistically significant two tailed p-value was considered as <0.05 unless otherwise noted.

Ethics approval

Ethics approval for this study was obtained from Sakarya University Faculty of Medicine Non-Interventional Ethics Committee (Number: 71522473 / 050.01.04/47).

RESULTS

Throughout the study period, 203 (36%) of 577 patients, who were followed in the clinic for fever, were considered as IRFG and 374 (64%) were NIRFG. In the IRFG, 133 (65.5%) of patients were male, and the mean age was 66.42 ± 16.58 years. Total of 206 (55.1%) patients in the NIRFG were male, and the mean age was 65.41 ± 18.03 years. There was no significant difference between ages (p> 0.05). The length of hospitalization was similar in both groups, in which the average length of stay in NIRFG was 7.97 ± 6.59 days and 8.85 ± 7.6 days in IRFG (p = 0.145, Table 1).

While the mean ESR in IRFG was found 71.47 ± 34.28 mm / h; it was 62.68 ± 39.29 mm / h (N: <50 years; <20 mm/h, >50years;<30 mm/h) in NIFRG (p= 0.013). Mean CRP values were 141.82±107.19 mg / L and 97.49±88.77 mg / L (N: (N:0-5) in IRFG and NIFRG, respectively (p= 0.001).

Mean Alb levels were 2.91±0.60 in IRFG and NIFRG was 3.06±0.65mg/dL (N:3,2-4,6) mg/dL in NIFRG (p= 0,006). Median PCT in IRFG was 1.03(0.22-8.41) ng/ml, whereas it was 0.36 (0.09-1.11) ng/ml (N:< 0.5) in NIFRG. Median neutrophil-to-lymphocyte ratio (NLR) was 8.00 (3.00-15.00) in the IRFG, whereas it was 5.00 (3.00-9) in the NIFRG (p = 0.001). Median platelet-to-lymphocyte ratio (PLR) was 21.00 (9.00-41.00) in the IRFG, whereas it was 16.00 (7.25-27.75) in the NIRFG and was not significant (p= 0.001) (Table 2).

The distribution of hospitalization clinic was shown in table-1. The classification of diagnosis was extensively evaluated. Patients diagnosed with anemia and gastrointestinal bleeding were significantly higher in NIRFG (p<0.05). However, patients suffering from gastroenteritis, cellulitis, cholangitis, abscess, upper respiratory tract infection, sepsis, urinary tract infection, central venous catheter infection, diabetes mellitus and pneumonia were significantly higher in IRFG (p<0.05, Table 1).

Red blood distribution width, monocytes (%), lymphocytes (%), basophils (%), albumin, iron, and folate levels significantly elevated in NIRFG compared to IRFG. Among laboratory parameters of IRFG, WBC, MCV, Hgb, neutrophil count, creatinine, CRP, PCT, and ESR levels were significantly higher than that of NIRFG. Other laboratory parameters were comparable in both groups (Table 2).

The time to initiate the first antibiotic was 2.12 ± 1.98 days in IRFG and 2.70 ± 2.78 days in NIRFG (p = 0.021). The duration of first antibiotic usage was 4.54 ± 3.08 and 5.35 ± 3.8 days in IRFG and NIRFG, respectively, and there was a statistically significant difference between groups (p = 0.023). Average number of antibiotics administered was 1.77 ± 0.99 in IRFG patients and 1.47 ± 0.77 in NIRFG patients, along with a significant difference between the groups (p = 0.001) (Table 3). The first empirical antibiotic was ceftriaxone, which was used by 82 (40.1%) IRFG patients and 120 (32.1%) NIRFG patients (p = 0.024). Secondly,moxifloxacin was administered to 36 (17.7%) IRFG patients and 42 (11.2%) NIRFG patients (p = 0.001). The final antibiotic was ampicillin- sulbactam and it was used by 17 (8.4%) and 34 (9.1%) patients od IRFG and NIRFG, respectively (p = 0.155).

Table 1. Demographic data and diagnostic distribution of patients in non-infectious fever and infectious fever groups

Features	Non-infectious Fever Group (n:374)	Infectious Fever Group (n:203	P
Age	65.41±18.03	66.42 ±16.58	0.509
Gender(male)	206 (55.1)	133 (65.5)	**0.015**
Thyroid disease	119 (31.8)	63 (31.0)	0.847
Gastroenteritis	0	8 (3.9)	**0.001**
Cellulitis	0	4 (2.0)	**0.006**
Cholangitis	0	10 (5.0)	**0.001**
Abscess	0	3 (1.5)	**0.018**
URTD	0	6 (3.0)	**0.001**
Sepsis	0	4 (2.0)	**0.006**
USI	1 (0.3)	35 (17.2)	**0.001**
CRI	2 (0.5)	9 (4.4)	**0.001**
DM	128 (34.2)	92 (45.3)	**0.009**
Anemia	71 (19.0)	16 (7.9)	**0.001**

Abbreviations: COPD; Chronic obstructive pulmonary disease, FMF; Familial Mediterranean Fever, CCHF; Crimean-Congo hemorrhagic fever, ITP; Immune thrombocytopenic purpura, URTD; Upper respiratory tract diseases, USI; Urinary sytems infectious, IBD; Imphlamotory boweel disease, CRI; catheter-related infection, CVD; Cerebrovasular disease, DM; Diabetes Mellitus, CRF; Chronic renal failure, CHF; Congestive heart failure, GI: Gastrointestinal, HM; Hematologic malignancy, DCA; Diabetic ketoacidosis

Table 2. Laboratory parameters of patients in non-infectious and infectious fever groups

Parameters	Non-infectious Fever Group (n:374)	Infectious Fever Group (n:203)	P
White blood cell count, $10^3/mm^3$	10.30±8.83	12.30±10.20	**0.014**
Platelet count, $10^3/mm^3$	232.26±123.96	231.71±150.80	0.963
Neutrophil count, $10^3/mm^3$	7.94±7.07	9.65±6.40	**0.004**
MCV	85.37±13.74	88.38±7.84	**0.004**
Lymphocyte count, $10^3/mm^3$	1.58±3.04	1.73±8.13	0.743
Hemoglobin, g/dl	9.63±2.66	10.17±2.36	**0.017**
Hematocrit, %	29.22±7.97	30.48±7.40	0.064
Albumin, gr/L	3.06±0.65	2.91±0.60	**0.006**
ALT, IU/L	19.00 [11.00-39.00]	16.50 [10.00-38.00]	0.195
AST, IU/L	71.16±270.44	54.13±113.7	0.394
C-reactive protein (CRP), mg/L	97.49±88.77	141.82±107.19	**0.001**
Sedimentation, mm/h	62.68±39.29	71.47±34.28	**0.013**
LDH, U/L	460.80±876.02	334.76±413.0	0.094
Procalcitonin, ng/mL	0.36 [0.09-1.11]	1.03 [0.22-8.41]	**0.001**
NLR	5[3.00-9]	8[3.00-15.00]	**0.001**
PLR	21.00 (9.00-41.00)	16.00 (7.25-27.75)	**0.001**
TSH	0,93 [0.45-1.69]	0.77 [0.35-1.48]	0.139

Abbreviations: MCV; Mean corpusculer volume, Alb; Albumine, ALT; Alanine aminotransferase, AST; aspartat aminotransferaz, CRP; C-reactive protein, LDH; Lactate dehydrogenase, ESR; Erythrocyte Sedimentation Rate, TSH; Thyroid-stimulating hormone, NLR; Neutrophil/Lymphocyte

Table 3. Comparison of antibiotherapy in infectious and non-infectious patients with fever

Parameters	Non-infectious Fever Group (n:374)	Infectious Fever Group (n:203)	P
First Antibiotic Start Time (Day)	2.70±2.78	2.12±1.98	0.021
First Antibiotic Usage Time (Day)	5.35±3.8	4.54±3.08	0.023
Mean antibiotic count	1.47±0.77	1.77±0.99	0.001
Frequently Used Antibiotics Respectively			
Seftriakson	120 (%32.1)	82 (%40.1)	0.024
Moksifloksasin	42 (%11.2)	36 (%17.7)	0.001
Ampisilin/Sulbaktam	34 (%9.1)	17 (%8.4)	0.155
Piperasilin-Tazobaktam	14 (%3.7)	9(%4.4)	0.094

DISCUSSION

In this study, it was observed that the time to start empirical antibiotics was delayed in NIRFG compared to IRFG. In addition, we observed that the number of antibiotics used in IRFG patients was significantly higher than that of NIRFG. The duration of empirical antibiotic usage was significantly longer in NIRFG with respect to IRFG. The reason behind his might be the fact that fever in NIFRG patients did not alleviate in spite of the antibiotics and the inflammatory markers did not improve. The most commonly used antibiotic was ceftriaxone since broad-spectrum antibiotics are prescribed with the approval of an infection disease specialist, and additionally third generation cephalosporins are widely preferred in prescriptions in accordance with legal regulations of our country. Quinolones were the second most commonly used antibiotics since they are accessible and their administration in oral form is relatively easy. Several studies have emphasized that shorter treatments ought to be applied considering the potential side effects, antibiotic resistant organisms, and increased costs.[11–13]

WBC is an indicator, which is actively used in fever identification. WBC levels elevate in IRFG, whereas they are low in NIRFG. CRP is another crucial indicator for the inflammatory response of the body. The proportion of patients with low hemoglobin and low serum albumin was higher in IRFG, while it was lower in NIRFG. In our study, we demonstrated that NIRFG patients represented significantly lower WBC, CRP, ESR, PCT, Hgb, MCV, neutrophil levels. This may be due to chronic anemia, which is a common consequence of hepcidin and cytokines such as TNF-alpha, IL1, IL6.[14,15] Additionally, lower albumin levels in IRFG may occur due to the negative phase reactant in infectious diseases.[16] Many randomized controlled trials have investigated the PCT levels to assist decisions regarding the administration of antibiotic therapy.[17] In one study, PCT and CRP levels significantly increased in cancer patients with infection compared to those who didn't have infection and significantly elevated in all gastric can-

cer groups with respect to the control group. CRP and PCT are two important markers for the diagnosis of infection in cancer patients.[18] In another study, infected inactive SLE had a significantly higher CRP level than uninfected inactive SLE.[19]

In a study by Are Naess et al., it was shown that NLR was higher in patients hospitalized due to fever due to bacterial infection compared to those due to noninfectious causes.[20] Similarly, in our study, NLR was found higher in IRFG, but lower in NIRFG. However, there was no significant difference in PLR. Pneumonia, catheter-related infection (CRI), Urinary system infections (USI), Upper respiratory tract diseases (URTD), abscess, cholangitis, cellulitis, gastroenteritis are commonly observed in IRFG since all of those diseases are infection related. It is common for diseases such as GI bleeding, anemia, diabetes, etc. to be significantly higher in the NIRFG. In community-acquired pneumonia, empirical antimicrobial therapy was applied to patients whose microbiological results have not yet been concluded. Guidelines suggest that empirical antibiotic treatment selection includes streptococci pneumonia and atypical pathogens.[21,22] In several studies, no significant difference was observed between the use of macrolides, beta lactam antibiotics and fluoroquinolones in the antibiotic regimen in CAP patients.[23] In our study, moxifloxacin antibiotics that belong to fluoroquinolone are detected to be widely used in pneumonia.

Our study has two important limiting factors, as the first being a retrospective study, and the second being a single-center study. Excluding other fever-related diseases might be another limitation of our study. However, our study makes significant contributions to the empirical antibiotic treatment of infection and non-infection related fever diseases.

Infections affect all organs and systems. People with diabetes often suffer from conditions including feet infections, malignant external otitis, rhinocerebral mucormycosis, and gangrenous cholecystitis. Infection process, in addition to increased morbidity, may be among the initial indicators of diabetes or may trigger factors for disease-specific complications such as diabetic ketoacidosis and hypoglycemia.[24] Co-occurrence of fever and GI bleeding may suggest the presence of a concomitant infection disease.

As a result of this study, empirical antibiotic treatment management should be taken into consideration in comorbid diseases such as T2DM, thyroid diseases, chronic kidney disease (CKD), non-hematological malignancies(NHM), pneumonia, urinary tract infection (UTI) accompanied by fever. In patients with diabetes mellitus, fever is a common comorbidity factor in both infectious and non-infectious conditions. The most commonly observed comorbid infections are diabetes mellitus and CKD. Thus, additional consideration is required to control infection in those patients. The anamnesis of the patients should be taken carefully and the laboratory examinations should be evaluated clearly.

CONCLUSION

Clinicians are required to avoid using wide-spectrum antibiotic selection and exposing the patients to excessive antibiotics until the culture results are revealed. Some of the hemogram parameters such as NLR and PLR are easy, fast and inexpensive to use as a marker of patient outcome, can be useful in daily clinical practice and empirical antibiotic use in developing countries.

Acknowledgments

We would like to thank Sakarya Training and Research Hospital Internal Medicine Clinic for following the patients, the laboratory staff for performing the laboratory analysis, and the hospital doctors who allowed the patients to be scanned.

Ethics approval for this study was obtained from Sakarya University Faculty of Medicine Non-Interventional Ethics Committee (Number: 71522473 / 050.01.04/47).

References

1. *Petersdorf, R. G.,Beeson, P. B. Fever of unexplainedorigin: report on 100 cases. Medicine 1961;40, 1–30.*
2. *Vanderschueren S, Knockaert D, Adriaenssens T, Demey W, Durnez A, Blockmans D, et al. From prolonged febrile illness to fever of unknown origin: The challenge continues. Archives of Internal Medicine 2003;163:1033–1041.*
3. *Unger M, Karanikas G, Kerschbaumer A, Winkler S, Aletaha D. Fever of unknownorigin (FUO) revised. Wien KlinWochenschr 2016;128(21-22):796-801.*
4. *Steele GM, Franco-Paredes C, Chastain DB. Noninfectious causes of fever in adults. Nurse Practitioner 2018;43:38–44.*
5. *Knockaert DC, Vanneste LJ, Bobbaers HJ. Fever of Unknown Origin in Elderly Patients. JAGS1993;41:1187–1192.*
6. *Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC Med 2011;9:107.*
7. *Terradas R, Grau S, Blanch J, Riu, M., Saballs, P., Castells, X. et al.Eosinophilcountand neutrophil-lymphocyte count ratio as prognostic markers in patients with bacteremia: a retrospective cohort study. PLoSOne 2012;7(8):e42860.*
8. *Ferrer R, Martin-Loeches I, Phillips G, Osborn TM, Townsend S, Dellinger RP, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: Results from a guideline-based performance improvement program. Critical Care Medicine 2014;42:1749–1755.*
9. *Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2017; 9:2(2):CD003543.*
10. *Bryan CS, Ahuja D. Fever of Unknown Origin: Is There a Role for Empiric Therapy? Infectious Disease Clinics of North America.Infect Dis Clin North Am 2007;21:1213–1220.*
11. *Katchman EA, Milo G, Paul M, Christiaens T, Baerheim A, Leibovici L, et al. Three-day vs longer duration of antibiotic treatment for cystitis in women: Systematic review and meta-analysis. American Journal of Medicine. Am J Med 2005;118:1196–1207.*
12. *Dunbar LM, Wunderink RG, Habib MP, Smith LG, Tennenberg AM, Khashab MM, et al. High-Dose, Short-Course Levofloxacin for Community-Acquired Pneumonia: A New Treatment Paradigm. Clin Infect Dis 2003;37:752–760.*
13. *Chastre J, Wolff M, Fagon JY, Chevret S, Thomas F, Wermert D, et al. Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults: A Randomized Trial. JAMA 2003;290:2588–2598.*
14. *Madu AJ, Ughasoro MD. Anaemia of Chronic Disease: An In-Depth Review. Medical Principles and Practice. S. Karger AG 2017;26:1–9.*
15. *Weiss G. Iron metabolism in the anemia of chronic disease. Biochimica et Biophysica Acta - General Subjects. Elsevier 2009;1790: 682–693.*
16. *Mackowiak PA, Bartlett JG, Borden EC, Goldblum SE, Hasday JD, Munford RS, et al. Concepts of Fever: Recent Advances and Lingering Dogma. Clin InfectDis 1997;25:119–138.*
17. *Sager R, Kutz A, Mueller B, Schuetz P. Procalcitonin-guided diagnosis and antibiotic stewardship revisited. BMC Medicine. BioMed Central Ltd 2017;15:15*
18. *Ma, Y., Zhang, L., Rong, S., Qu, H., Zhang, Y., Chang, D. W., et al.Relationbetweengastriccancer and protein oxidation, DNA damage, and lipid peroxidation. OxidMed CellLongev (2013)2013.*
19. *Zhang CF, Xu R, Li MT, Zeng XF. A clinical analysis on fever of unknown origin in in-patients with systemic lupus erythematosus. Zhonghua Nei Ke Za Zhi 2017;56(4):295-297.*
20. *Naess A, Nilssen SS, Mo R, Eide GE, Sjursen H. Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. Infection 2017;45:299–307.*
21. *Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. Clin Infect Dis 2007;44:S27–72.*
22. *Lim, W. S., Baudouin, S. V., George, R. C., Hill, A. T., Jamieson, C., Le Jeune, I.,et al.PneumoniaGuidelines Committee of the BTS Standards of Care Committee. BTS guidelines for themanagement of communityacquiredpneumonia in adults 2009;64:3, iii1–iii55.*
23. *Çilli A, Sayiner A, Çelenk B, Şakar Coşkun A, Kilinç O, Hazar A., et al. Antibiotic treatment outcomes in community-acquired pneumonia. Turk J Med Sci 2018;48:730–736.*
24. *Alves C, Casqueiro J, Casqueiro J. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian JEndocrinol Metab 2012;16:27.*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Relationship Between Self-Efficacy and Psychosocial Adjustment of Individuals with Type 2 Diabetes

Tip 2 Diyabeti Olan Bireylerin Öz Yeterlilikleri ile Psikososyal Uyumları Arasındaki İlişki

Erman Yıldız

Department of Psychiatric Nursing, Faculty of Nursing, Inonu University, Malatya, Turkey

Yazışma Adresi / *Correspondence:*
Erman Yıldız

Inonu University Faculty of Nursing, Malatya, Turkey
T: **+90 422 377 30 60 /1272** E-mail **: erman.yildiz@inonu.edu.tr**

Geliş Tarihi / Received : **04.08.2020** Kabul Tarihi / Accepted : **07.12.2020**

Orcid :
Erman Yıldız, https://orcid.org/0000-0002-6544-4847

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):32-41) DOI: 10.31832 smj.776863**

Abstract

Objective — To determine the relationship between self-efficacy and psychosocial adjustment of individuals with type 2 diabetes.

Materials and Methods — Descriptive, cross-sectional study was carried out between January 2020 and July 2020 with individuals with type 2 diabetes (N = 154). Data collection tools were identified as "Descriptive Characteristics Form", "General Self-Efficacy Scale", and "Psychosocial Adjustment to the Illness Scale – Self-Report". Data were analyzed using descriptive statistics, ANOVA, independent samples t test, Mann-Whitney U test, Kruskal-Wallis test, correlation and multiple linear regression analysis.

Results — The scores of participants on the self-efficacy and psychosocial adjustment scale are 29.42 ± 6.10 and 39.90 ± 13.94, respectively. It was determined that 33.8% of the individuals had good psychosocial adjustment, 49.4% had fair and 16.9% had poor psychosocial adjustment. There was no statistically significant relationship between self-efficacy and psychosocial adjustment scores ($p > 0.05$). It was observed that 13.1% of the change on the scores obtained with psychosocial adjustment was explained by the scores obtained in patients' age, gender, education level, marital status, economic status and working status.

Conclusion — Although the current findings do not present any relationship between psychosocial adjustment and self-efficacy in individuals with type 2 diabetes, it is emphasized in this study that it is important to support their self-efficacy and improve psychosocial adjustment so that individuals with type 2 diabetes can successfully carry out certain activities. The results may provide clues to help clinicians implement targeted strategies to support self-efficacy and psychosocial adjustment in individuals with type 2 diabetes.

Keywords — Psychosocial adjustment; Self-efficacy; Type 2 diabetes.

Öz

Amaç — *Bu araştırma tip 2 diyabeti olan bireylerin öz yeterlilikleri ile psikososyal uyumları arasındaki ilişkiyi belirlemek amacıyla yapıldı.*

Gereç ve Yöntemler — *Tanımlayıcı, kesitsel tipteki araştırma Ocak 2020- Temmuz 2020 tarihleri arasında tip 2 diyabetli bireyler (N=154) ile gerçekleştirildi. Veri toplama araçları Tanıtıcı Bilgi Formu, Genel Öz Yeterlik Ölçeği ve Hastalığa Psikosoyal Uyum-Öz Bildirim Ölçeği olarak belirlendi. Veriler tanımlayıcı istatistikler, ANOVA, Mann-Whitney U, Kruskal-Wallis ve bağımsız gruplarda t testleri ile korelasyon ve çoklu doğrusal regresyon analizleri kullanılarak değerlendirildi.*

Bulgular — *Katılımcıların öz yeterlilik ve psikososyal uyum ölçeğinden aldıkları puanlar sırasıyla 29.42±6.10 ve 39.90±13.94'dir. Bireylerin %33.8'inin iyi, %49.4'ünün orta ve %16.9'unun ise kötü psikososyal uyuma sahip olduğu belirlendi. Öz yeterlilik ve psikososyal uyum puanları arasında istatistiksel açıdan önemli düzeyde bir ilişki saptanmadı ($p>0.05$). Psikososyal uyum ile elde edilen skorlar üzerindeki değişimin %13.1'inin hastaların yaş, cinsiyet, eğitim düzeyi, medeni durum, ekonomik durum ve çalışma durumlarında elde edilen puanlar ile açıklandığı görüldü.*

Sonuç — *Her ne kadar mevcut bulgular tip 2 diyabetli bireylerde psikososyal uyum ile özyeterlilik arasında herhangi bir ilişki sunmasa da bu çalışmada tip 2 diyabetli bireylerin belirli faaliyetlerini başarıyla yürütebilmesi için öz yeterliliklerinin desteklenmesi ve psikososyal uyumlarının geliştirilmesinin önemli olduğu vurgulanmıştır. Sonuçlar, klinisyenlerin, tip 2 diyabetli bireylerde öz yeterliliği ve psikososyal uyumu desteklemek için hedeflenen stratejileri uygulamalarına yardımcı olacak ipuçları sağlayabilir.*

Anahtar Kelimeler — *psikososyal uyum; öz yeterlilik; tip 2 diyabet*

INTRODUCTION

Type 2 diabetes is a chronic condition that causes an increase in blood sugar levels. The International Diabetes Federation (IDF) estimated that 4.2 million adults will die from the disease itself and the complications it causes, which increases the risk of premature death, according to 2019 Diabetes Atlas data. This rate seems equivalent to death every eight seconds. Globally, 11.3% of deaths result from diabetes. Almost half of these deaths consist of people under the age of 60. In addition, according to the 2045 estimates, Turkey will rise to tenth place among the countries with the highest number of people with diabetes.[1] If diabetes is not properly managed, this can have serious consequences in the long run. Once diagnosed, people need to learn to manage their condition through diet and exercise, with the addition of pharmacological treatments.[2,3] People with diabetes are expected to have a sufficient level of self-efficacy to effectively deal with complex diabetes care and treatment. The concept of self-efficacy is derived from Bandura's social cognitive theory. It expresses the beliefs and judgment of the individual about his ability to perform his duties and functions. Self-efficacy means the belief that one can successfully run certain activities and expect good results to follow.[4] Previous studies has investigated effective factors and interventions in increasing the self-efficacy of diabetic patients.[3,5] Researchers have reported negative associations between poor self-efficacy and managing diabetes.[6] Similarly, negative relationships between self-efficacy and HbA1c have been reported among patients with type 2 diabetes.[7,8] For individuals with type 2 diabetes, diabetes knowledge and health literacy, along with other sociodemographic characteristics (age, gender, etc.) and health-related factors (duration of diabetes, etc.), are the main personal factors that affect diabetes management. The concepts of self-efficacy, depressive symptoms, and problem solving relate to a person's behavioral and cognitive processing and reflect behavioral factors within the scope of social cognitive theory.[4,7] The behavior of individuals with diabetes on self-care may be improved by increasing their self-efficacy levels.[2,3] From this point of view, it can be said that studies evaluating self-efficacy in individuals with type 2 diabetes are important.

It is known that individuals with diabetes are more likely to encounter psychosocial problems.[9,10] According to the findings of the recently published systematic review, anxiety, depression, stress and diabetes distress were defined as the main effective psychosocial factors in individuals with type 2 diabetes.[11] As with other chronic diseases, the ability to cope more effectively with psychosocial problems can be realized by adapting to the individual's disease. At this point, the individual's success in areas such as adjustment to health care, professional environment, home-family relations, sexual relations, extended family relationship, social environment and psychosocial oppression is also closely related to psychosocial adaptation to disease.[12,13] The literature emphasizing the importance of psychosocial adjustment in the context of chronic diseases is increasing day by day. For example, the idea that psychosocial adjustment should be determined as a treatment target in hemodialysis patients[14], liver transplant patients[15] and cancer patients[16] is emphasized. Psychosocial adjustment is recommended as an integrative model for adaptation to chronic conditions in diabetes, as in other chronic diseases.[17] In a study conducted on individuals with type 2 diabetes, a positive relationship was found between psychosocial adjustment and treatment adherence.[18] Although psychosocial adjustment is difficult to assess, every data in this area seems to be very important[13,17,19]. In addition, considering the limited number of studies evaluating psychosocial adjustment in individuals with type 2 diabetes,[13,19-21] it can be said that studies evaluating psychosocial adjustment in this population are needed. Individuals with diabetes in Turkey evaluating the structural relationship between self-efficacy with psychosocial adjustment have not been detected in any study. This research was carried out to determine the relationship between self-efficacy and psychosocial adjustment of individuals with type 2 diabetes.

MATERIALS and METHODS

Design, Sample and Participants

This study was done in descriptive, cross-sectional type. The study was carried out between January 2020 and July 2020 with individuals with type 2 diabetes who were treated at a university hospital in eastern Turkey. The population of the study consists of individuals with type 2 diabetes who were treated at the center in question between the dates of data collection. With the power analysis of the study, 0.05 error level, 0.5 effect size, ability to represent 0.95 universe were determined as 127. In the study, efforts were made to increase statistical strength and to reach the number of participants above the sample, taking into account that data forms could be completed incomplete and/or wrongly. As a result of the efforts, the study was completed with a total of 154 individuals with type 2 diabetes. The sample of the study was chosen from the universe by the simple random sampling method. The criteria to be included in the study were to be 18 or older, to take diabetes medications, and to read and write in Turkish. Those diagnosed with gestational diabetes, type 1 diabetes, cancer or psychiatric in accordance with the hospital records and the individual's own statements were excluded.

Variables and Measurement

Descriptive Characteristics Form: The form developed by the researcher contains a total of 9 questions asking the age, gender, marital status, education level, employment status, economic status, family structure, age of onset of the disease and the presence of other chronic diseases.

General Self-Efficacy Scale (GSES): Developed in 1979 by Jerusalem and Schwarzer, the scale was adapted to Turkish culture by Aypay (2010). The scale, translated into 28 languages including English, is known to be used by many researchers. The GSES is a self-report scale that tests the beliefs of different circles about their ability to cope with new and difficult situations. The scale consisting of 10 items is a 4-point Likert type. The minimum score obtained from the scale is 10, the maximum score is 40. The internal consistency of the scale was determined as α = 0.86 for all countries. High scores in the items indicate a high level of general self-efficacy.[22]

Psychosocial Adjustment of the Illness Scale – Self-Report (PAIS-SR): PAIS-SR, developed by Derogatis and Lopez, validity and reliability in Turkey were made by Adaylar. This scale measures the interaction of individuals with other individuals and institutions that make up the socio-cultural environment. PAIS-SR, which is a 4-point Likert type, consists of 7 sub-dimensions and 46 items. The subgroups are healthcare orientation, vocational environment, domestic environment, sexual relationships, extended family relationships, social environment, and psychological distress. The minimum score obtained from the scale is 0, the maximum score is 138. The cut-off scores and assessment of the PAIS-SR are as follows: Scores below 35 indicate good psychosocial adjustment; scores between 35 and 51 indicate fair psychosocial adjustment; scores between 51 and above indicate poor psychosocial adjustment.[12]

Data Collection

The data was collected by the researcher using the face-to-face interview technique with individuals with type 2 diabetes at the relevant Center following the institution's permission and ethical approval. At the beginning of the talks, participants were informed about the subject and purpose of the research and their verbal consent was obtained. It was also stated that participation in the research was voluntary and that no name information was requested in accordance with the confidentiality principle. Data collection was performed on weekdays and during working hours with each patient in approximately 15 minutes.

Data Analysis

The data of the research were evaluated and reported using SPSS 25.0. Averages, standard deviations, and percentages were used to describe the socio-demographic characteristics of the participants. In the study, Kolmogorov Smirnov test was used to examine whether the data was normally distributed. Independent samples t test and ANOVA tests were used in under normal distribution conditions, Mann-Whitney U test and Kruskal-Wallis test were used in conditions where normal distribution was not provided. Pearson correlation analysis was used to measure the relationships between self-efficacy and psychosocial adjustment. Finally, multiple linear regression analysis was performed to determine predictors of psychosocial adjustment. The results were considered statistically significant when $p < 0.05$.

Validity and Reliability

In this study, all scales had a Cronbach's Alpha above 0.70 which corresponds with an acceptable internal consistency (see Table 3).

RESULTS

Descriptive Characteristics

The distribution of the descriptive characteristics of the participants were given in Table 1. 36.4% of individuals were 56 years old or older (mean age is 59.92 ± 12.15; minimum 27, maximum 86), 62.3% were women, 90.9% were married, 83.1% lived with their spouse and children, 42.8% were determined to be primary school graduates, 89.6% of them did not work in any job, and 79.2% of them were at an intermediate level of economic level. It was determined that 35% of individuals with type-2 diabetes were diagnosed between 40 and 53 years old and 46.8% had another chronic disease (Table 1).

Table 1. Distribution of Individuals with Type 2 Diabetes by Descriptive Characteristics (N=154)

Descriptive Characteristics	n	%
Mean Age	59.92±12.15 year	(min-max=27-86)
Age		
27-55	48	31.2
56-65	50	32.5
66 and above	56	36.4
Gender		
Female	96	62.3
Male	58	37.7
Marital status		
Married	140	90.9
Single	14	9.1
People living with		
Alone	16	10.4
Parents	10	6.5
Spouse and child	128	83.1
Education level		
Illiterate	48	31.2
Literate	18	11.7
Primary education	66	42.8
High school	14	9.1
University	8	5.2
Working Status		
Working	16	10.4
Not working	138	89.6
How to perceive the economic situation		
High	20	13.0
Middle	122	79.2
Low	12	7.8
Age of Onset of Disease		
23-39	48	31.2
40-53	54	35.0
55 and above	52	33.8
Another Chronic Disease Presence		
Yes	72	46.8
No	82	53.2
Another Chronic Disease		
COPD	8	11.1
Hypertension	50	69.4
Chronic renal failure	12	61.7
Chronic liver disease	2	2.8
COPD: Chronic Obstructive Pulmonary Disease		

GSES and PAIS-SR Levels

GSES and PAIS-SR total mean scores of the participants were 29.42 ± 6.10 and 39.90 ± 13.94, respectively. It was determined that 33.8% of the individuals had good psychosocial adjustment, 49.4% had moderate and 16.9% had poor psychosocial adjustment (Table 2).

Table 2. GSES and PAIS-SR Scores (N=154)

	Mean (SD)	Min-Max
GSES	29.42 (6.10)	12-40
PAIS-SR		
Healthcare orientation	7.96 (1.99)	4-14
Vocational environment	5.44 (2.79)	0-12
Domestic environment	6.48 (4.66)	0-21
Sexual relationships	5.97 (3.23)	0-15
Extended family relationships	2.05 (2.01)	0-8
Social environment	4.19 (2.56)	0-9
Psychological distress	5.85 (3.60)	0-15
PAIS-SR total score	39.90 (13.94)	12-89
Status levels of psychosocial adjustment	n	%
Good adjustment (<35 points)	52	33.8
Fair adjustment (35–51 points)	76	49.4
Poor adjustment (>51 points)	26	16.9

GSES: General Self-Efficacy Scale; PAIS-SR: Psychosocial Adjustment of the Illness Scale – Self-Report; SD: Standard deviation; Min: Minimum; Max: Maximum

Univariate Analyses of the Factors Associated with PAIS-SR and GSES

Univariate analyzes of factors related to psychosocial adjustment and self-efficacy were presented in Table 3. It was found that the mean PAIS-SR scores of female participants were higher than that of men, and this difference was statistically significant (p = 0.001). It was found that the PAIS-SR scores of the single participants were higher than the married ones and this difference was statistically significant (p = 0.007). It was determined that the GSES mean rank of the illiterate participants was lower than those at the university education level, and this difference was statistically significant (p = 0.008). Similarly, it was determined that the PAIS-SR mean rank of the illiterate participants was higher than those at the high school level, and this difference was statistically significant (p = 0.001). It was found that the GSES mean rank of the participants with low economic status was higher than those with moderate economic status and the difference was statistically significant (p = 0.007). Finally, there was no statistically significant difference between the GSES and PAIS-SR scores of the participants according to their age, people they lived with, employment status and other chronic diseases (p> 0.05) (Table 3).

Relationship Between GSES and PAIS-SR Levels

There was no statistically significant relationship between GSES and PAIS-SR scores obtained from the participants (p> 0.05) (Table 4).

Multiple linear regression analysis was performed to explain the predictive effect of some descriptive features of individuals participating in the study on psychosocial adjustment. The model was found to be statistically significant in terms of the significance level corresponding to the F value (F = 4.842; p = 0.001). When the t coefficient and significance levels of the independent variables were examined; marital status (p = 0.007) and economic status (p = 0.031) appear to have a statistically significant effect on scores obtained by psychosocial adjustment. It was seen that 13.1% of the change on the scores obtained with psychosocial adjustment was explained by the scores obtained in patients' age, gender, education level, marital status, economic status and working status (Adjusted R^2=0.131) (p= 0.001) (Table 5).

DISCUSSION

This study has emerged as a result of current uncertainties regarding the self-efficacy and psychosocial adjustment of individuals with type 2 diabetes, who are not only a disease with organic findings, but also have psychiatric and psychosocial dimensions. Accordingly, this study was conducted to determine the relationship between the self-efficacy and psychosocial adjustment of individuals with type 2 diabetes.

Table 3. Univariate analyses of the factors associated with psychosocial adjustment and self-efficacy (N = 154).

Variables	**GSES**			**PAIS-SR**		
Age	**Mean (SD)**	**t/F**	**p**	**Mean (SD)**	**t/F**	**p**
27-55	29.83 (5.98)			42.74 (16.13)		
56-65	30.06 (6.17)	1.028	0.360	36.42 (14.06)	2.677	0.072
66 and above	28.50 (6.13)			40.56 (11.13)		
Gender						
Female	29.05 (6.01)	-0.953	0.342	42.85 (14.21)	3.500	0.001
Male	30.02 (6.25)			35.01 (12.10)		
Another Chronic Disease Presence						
Yes	28.85 (5.72)	-1.366	0.174	39.41 (14.03)	-0.513	0.609
No	30.21 (6.56)			40.58 (13.90)		
	Mean Rank	**MW/KW**	**p**	**Mean Rank**	**MW/KW**	**p**
Marital status						
Married	79.57	690.00	0.068	74.46	554.00	0.007
Single	56.79			107.93		
People living with						
Alone	78.75			94.00		
Parents	52.50	3.375	0.185	97.10	4.956	0.084
Spouse and child	79.30			73.91		
Education level						
Illiterate	55.46			90.83		
Literate	83.39			82.17		
Primary education	82.85	13.843	0.008	61.37	19.539	0.001
High school	75.90			48.90		
University	88.50			77.93		
Working status						
Working	67.63	946.00	0.349	59.75	820.00	0.093
Not working	78.64			79.56		
Economic situation						
High	92.10			68.90		
Middle	72.01	10.016	0.007	76.52	4.378	0.112
Low	109.00			101.83		

GSES: General Self-Efficacy Scale; PAIS-SR: Psychosocial Adjustment of the Illness Scale – Self-Report

Table 4. The Relationship between GSES and PAIS-SR Levels (N=154)

	α	1	2	3	4	5	6	7	8	9
GSES	0.86	-								
PAIS-SR Total Score	0.82	-0.014	-							
Healthcare orientation	0.79	0.098	0.402**	-						
Vocational environment	0.83	0.071	0.738**	0.226**	-					
Domestic environment	0.73	0.000	0.805**	0.247**	0.532**	-				
Sexual relationships	0.75	-0.116	0.695**	0.202*	0.444**	0.397**	-			
Extended family relationships	0.71	-0.146	0.547**	-0.083	0.279**	0.480**	0.284**	-		
Social environment	0.90	-0.064	0.529**	0.189*	0.392**	0.226**	0.407**	0.210**	-	
Psychological distress	0.77	0.011	0.684**	0.176*	0.429**	0.472**	0.345**	0.380**	0.113	-

* p<0.05; ** p<0.01.
GSES: General Self-Efficacy Scale; PAIS-SR: Psychosocial Adjustment of the Illness Scale – Self-Report

Table 5. Multiple Linear Regression Analysis Results for Predictors of Psychosocial Adjustment (N = 154)

Dependent Variable	Predictive Variables	ß	t	p	VIF	F	Model (p)	Adjusted R2	DW
PAIS-SR	Constant	25.156	2.206	0.029					
	Age	-0.128	-1.273	0.205	1.350				
	Gender	-4.563	-1.792	0.075	1.387				
	Education level	-1.289	-1.593	0.113	1.344	4.842	0.001	0.131	1.502
	Marital status	10.106	2.723	0.007	1.037				
	Economical situation	5.153	2.178	0.031	1.045				
	Working Status	5.580	1.433	0.154	1.427				

PAIS-SR: Psychosocial Adjustment of the Illness Scale – Self-Report.

Self-efficacy is often discussed in the chronic disease literature and is becoming increasingly important in diabetes care.[23] Since healthy behaviors have an impact on disease outcomes, approaches to supporting and maintaining diabetes self-efficacy are vital.[24] In the study, it was found that individuals at the university education level had higher self-efficacy than those at the illiterate level, while participants at the low level also had higher self-efficacy than those at the moderate economic level. Studies conducted on diabetic individuals in the literature report that the level of self-efficacy increases with the increase in education level.[10,25-27] No studies have been found in the literature comparing the economic status of individuals with type 2 diabetes and their self-efficacy. However, a study comparing their self-efficacy with their work status, which is closely related to the economic situation, was determined. In this study, it was found that individuals with type 2 diabetes who were unemployed had higher self-efficacy.[28] In light of these data, it can be argued that the findings from the existing literature support this study. The score of the participants on the self-efficacy scale was found to be 29.42±6.10, indicating a level above the intermediate level. This finding showed that individuals with diabetes maintain their belief in their ability to cope with difficult situations. It also suggests that effective strategies to increase self-efficacy in patient education in Turkey. In parallel with this finding, there were two studies in the literature that report high levels of self-efficacy in individuals with diabetes,

one at an international[29] and one at a national level. 2 In another study conducted in Turkey, it was determined that the individuals who reported adequate education about diabetes and who had regular health checks had higher self-efficacy levels.[30] However, other studies in individuals with type 2 diabetes have reported low self-efficacy.[23,31,32] Although the literature reveals contradictory data in this way, self-efficacy or belief that the person can manage his own health should continue to be an important target of healthcare providers, especially in chronic diseases such as diabetes.[33]

In the study, it was found that female individuals have a lower psychosocial adjustment than males, single individuals than married, and illiterate than high school education level. In a study conducted with individuals with type 2 diabetes in the literature, it was found that the psychosocial adjustment of single or divorced individuals was higher, while no difference was found between the variables of gender and educational status and psychosocial adjustment.[18] In another study involving the same population, it was found that psychosocial adjustment increased with the increase in educational status, but no difference was found between the gender variable and psychosocial adjustment.[13] As can be seen, the literature provides contradictory data on comparisons of demographic variables and psychosocial adjustment in individuals with type 2 diabetes. Therefore, although the data obtained from this study appeared to receive limited support from the literature, it can be said that it makes a different contribution to the limited literature on psychosocial adjustment of individuals with type 2 diabetes.

It was determined that 33.8% of individuals with diabetes had good psychosocial adjustment, 49.4% had fair adjustment and 16.9% had poor psychosocial adjustment. In a study examining psychosocial adjustment to the disease in individuals with diabetes, it was determined that 34.4% of individuals showed good adjustment, 29.5% moderate adjustment and 36.1% poor adjustment.[13] In the study conducted in individuals with type 1 diabetes in Turkey, it was reported that 99.2% of individuals' psychosocial adjustment with the disease was among the poor limits.[19] In this study, the average psychosocial adjustment score of individuals with type 2 diabetes was 29.42 ± 6.10. In the literature, in a study using the same scale in individuals with type 2 diabetes, this value was reported to be 67.78 ± 14.73. 34 In another study examining psychosocial adjustment to the disease in people with diabetes, the mean score of psychosocial adjustment of individuals was determined to be 61.01 ± 21.42. 21 In a study on the perception of disease and psychosocial adjustment of individuals with diabetes, the mean score of psychosocial adjustment obtained from individuals was 48.20 ± 23.91. 20 The value obtained from this research is lower than previous studies, but indicates a better psychosocial adjustment. This finding suggests that individuals with type 2 diabetes who participated in the study successfully overcame the psychosocial difficulties they faced. The findings of a qualitative study on the subject seem to coincide with this finding obtained from the research. In the study in question, in addition to the themes that express the obstacles faced by individuals with type 2 diabetes during the psychosocial adjustment process, they also revealed themes to deal with these obstacles.[9]

In this study, no relationship was found between self-efficacy levels and psychosocial adjustment levels obtained from individuals with type 2 diabetes. Although there are no studies examining the relationship between self-efficacy and psychosocial adjustment in individuals with diabetes in primary level, it is known that self-efficacy is a mediating variable in terms of psychosocial factors.[35] Previous cross-sectional studies reported a negative relationship between self-efficacy and diabetes distress in individuals with type 2 diabetes.[36,37] This finding from the study may seem surprising, but it has shown that self-sufficiency has no explanatory effect on psychosocial adjustment. This finding may have been influenced by the fact that the measurement tools used in the research that assess psychosocial adjustment and self-efficacy are in the form

of the self-report scale and that these instruments are not tools developed specifically for individuals with Type 2 diabetes. Although diabetes is considered among chronic diseases, it differs significantly from other chronic diseases in areas such as symptom, disease management and prognosis. For this reason, it is believed that in this population, especially in terms of effective evaluation of psychosocial adjustment, there is a need for measurement tools developed specifically for diabetes. In the study, it was determined that the marital status and economic status of the participants were the variables that predict psychosocial adjustment, together with these two variables, age, gender, educational level and working status of the individuals explained 13.1% of psychosocial adjustment. This finding appears to be consistent with the current litarature as it shows that the ability of individuals to adapt psychosocial to their disease involves more than one dynamic.

Limitations

In the scientific literature, this research is the first study to focus on the relationship between self-efficacy and psychosocial adjustment in individuals with type 2 diabetes. However, the study has its limitations that need to be addressed. Firstly, the generalizability of the findings obtained is low, as the study was conducted only in individuals with type 2 diabetes treated in one institution. If future studies aim to obtain stronger data in this population, they may plan multi-center studies. Secondly, although a valid measurement tool is used to evaluate psychosocial adjustment, a single measurement method (such as self-reporting) may not be sufficient to evaluate psychosocial adjustment. Therefore, combining at least two methods (quantitative and qualitative) may give more reliable results. Finally, these data are descriptive and the nature of the analyzes is correlative. Causality cannot be directly inferred. When the precursor property of the present data is considered, it may be appropriate for future studies to investigate this relationship with more advanced research designs.

CONCLUSIONS

The current findings suggest that individuals with type 2 diabetes have a higher-than-moderate level of self-efficacy, while their psychosocial adjustment is well within good range. Although there is no relationship between psychosocial adjustment and self-efficacy in this study, it is important to believe that individuals with type 2 diabetes can expect positive results in order to carry out certain activities successfully and that their psychosocial adjustments are important. The results may provide clues to help clinicians implement targeted strategies to support self-efficacy and psychosocial adjustment in individuals with type 2 diabetes.

Acknowledgements

The researcher would like to thank the participants for their contribution and collaboration to this study.

Funding statement

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest

No conflict of interest has been declared by the author.

Ethical Approval

Ethical approval was received from the İnönü University Health Sciences Non-Interventional Clinical Research Ethics Committee with the decision number 2019/60 on 17.12.2019 for conducting the research. In addition, written permissions were obtained from İnönü University Turgut Özal Medical Center. All participants who agreed to participate in the study were informed about the purpose, duration and scope of the study, and their verbal consent was obtained from the participants by explaining that the participation was voluntary. The study was carried out in accordance with the Helsinki Declaration Principles.

References

1. *International Diabetes Federation I. https://diabetesatlas.org/en/sections/demographic-and-geographic-outline.html. 9 ed. 2019. Access Date: 24.04.2020.*
2. *Şireci E and Karabulutlu EY. Tip 2 Diabetes Mellituslu Hastaların Hastalıklarını Kabullenme ve Kendi Bakımlarındaki Öz Yeterlilik Düzeylerinin Belirlenmesi. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi. 2017; 20: 48-55.*
3. *Bohanny W, Wu S-FV, Liu C-Y, Yeh S-H, Tsay S-L and Wang T-J. Health literacy, self-efficacy, and self-care behaviors in patients with type 2 diabetes mellitus. Journal of the American Association of Nurse Practitioners. 2013; 25: 495-502.*
4. *Bandura A. Self-efficacy mechanism in human agency. American psychologist. 1982; 37: 122.*
5. *Lee Y-J, Shin S-J, Wang R-H, Lin K-D, Lee Y-L and Wang Y-H. Pathways of empowerment perceptions, health literacy, self-efficacy, and self-care behaviors to glycemic control in patients with type 2 diabetes mellitus. Patient Education and Counseling. 2016; 99: 287-94.*
6. *Jiang X, Wang J, Lu Y, Jiang H and Li M. Self-efficacy-focused education in persons with diabetes: a systematic review and meta-analysis. Psychol Res Behav Manag. 2019; 12: 67-79.*
7. *Ji M, Ren D, Dunbar-Jacob J, Gary-Webb TL and Erlen JA. Self-Management Behaviors, Glycemic Control, and Metabolic Syndrome in Type 2 Diabetes. Nursing Research. 2020; 69: E9-E17.*
8. *Saad AMJ, Younes ZMH, Ahmed H, Brown JA, Al Owesie RM and Hassoun AAK. Self-efficacy, self-care and glycemic control in Saudi Arabian patients with type 2 diabetes mellitus: A cross-sectional survey. Diabetes Research and Clinical Practice. 2018; 137: 28-36.*
9. *Muslu L, Ardahan M and Günbayi I. Tip 2 diabetes mellituslu hastaların psikososyal uyum sürecine ilişkin görüşleri: fenomenolojik bir araştırma. Psikiyatride Güncel Yaklaşımlar. 2017; 9: 75-100.*
10. *Devarajooh C and Chinna K. Depression, distress and self-efficacy: The impact on diabetes self-care practices. PLOS ONE. 2017; 12: e0175096.*
11. *McCoy MA and Theeke LA. A systematic review of the relationships among psychosocial factors and coping in adults with type 2 diabetes mellitus. International Journal of Nursing Sciences. 2019; 6: 468-77.*
12. *Adaylar M. Kronik hastalığı olan bireylerin hastalıktaki tutum, adaptasyon, algı ve öz-bakım yönelimleri. Yayınlanmamış Doktora Tezi, İstanbul, İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü. 1995.*
13. *Türten Kaymaz T and Akdemir N. Psychosocial Adjustment to Disease in Individuals with Diabetes. J Psy Nurs. 2016; 7: 61-7.*
14. *Lee KS, Kim HY and Lee MH. Factors influencing psychosocial adjustment in hemodialysis patients. Korean Journal of Adult Nursing. 2019; 31: 38-49.*
15. *Yıldız E and Kılınç G. The relationship between anxiety-depression status and psychosocial adjustments in the patients undergoing liver transplantation. Perspectives in Psychiatric Care. 2018; 54: 221-9.*
16. *Kolokotroni P, Anagnostopoulos F and Hantzi A. The Role of Optimism, Social Constraints, Coping, and Cognitive Processing in Psychosocial Adjustment Among Breast Cancer Survivors. Journal of Clinical Psychology in Medical Settings. 2018; 25: 452-62.*
17. *Hammond LD and Hirst-Winthrop S. Proposal of an integrative model of adjustment to chronic conditions: An understanding of the process of psychosocial adjustment to living with type 2 diabetes. Journal of Health Psychology. 2018; 23: 1063-74.*
18. *Kes D and Gökdoğan F. Relationship between medication adherence and psychosocial adjustment in patients with type 2 diabetes: A cross-sectional study. Nordic Journal of Nursing Research. 2020; 40: 116-22.*
19. *Çelik S, Kelleci M, Dilek A and Temel E. Tip 1 diyabetli genç yetişkinlerin hastalığa psikososyal uyumları ve stresle başaçıkma tarzları. Florence Nightingale Hemşirelik Dergisi. 2015; 23: 105-15.*
20. *Karabulutlu EY and Gündüz F. Tip II Diyabetes Mellituslu Hastalarda Hastalık Algısı, Psikososyal Uyum ve Glisemik Kontrolün Değerlendirilmesi. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi. 2016; 19: 106-15.*
21. *Akca AT and Cinar S. Comparison of psychosocial adjustment in people with diabetes with and without diabetic foot ulceration. Australian Journal of Advanced Nursing. 2008; 25: 87-96.*
22. *Aypay A. Genel Öz Yeterlik Ölçeği'nin (GÖYÖ) Türkçe'ye Uyarlama Çalışması. İnönü Üniversitesi Eğitim Fakültesi Dergisi. 2010; 11: 113-32.*
23. *Reisi M, Mostafavi F, Javadzade H, Mahaki B, Tavassoli E and Sharifirad G. Impact of Health Literacy, Self-efficacy, and Outcome Expectations on Adherence to Self-care Behaviors in Iranians with Type 2 Diabetes. Oman Med J. 2016; 31: 52-9.*
24. *Young HM, Miyamoto S, Dharmar M and Tang-Feldman Y. Nurse Coaching and Mobile Health Compared With Usual Care to Improve Diabetes Self-Efficacy for Persons With Type 2 Diabetes: Randomized Controlled Trial. JMIR Mhealth Uhealth. 2020; 8: e16665.*
25. *Karimy M, Koohestani HR and Araban M. The association between attitude, self-efficacy, and social support and adherence to diabetes self-care behavior. Diabetology & Metabolic Syndrome. 2018; 10: 86.*
26. *Weaver R, Lemonde M and Goodman W. What shapes diabetes self-efficacy. Demographics, social relations and health perceptions J Diabetes Metab. 2014; 5: 2.*
27. *Chlebowy DO, Myers J and Mendes AN. Socio-demographic variables and self-efficacy in Caucasian and African American adults with type 2 diabetes. South Online J Nurs Res. 2010; 10: 1-13.*
28. *Kav S, Yilmaz AA, Bulut Y and Dogan N. Self-efficacy, depression and self-care activities of people with type 2 diabetes in Turkey. Collegian. 2017; 24: 27-35.*
29. *Bohanny W, Wu SF, Liu CY, Yeh SH, Tsay SL and Wang TJ. Health literacy, self-efficacy, and self-care behaviors in patients with type 2 diabetes mellitus. Journal of the American Association of Nurse Practitioners. 2013; 25: 495-502.*
30. *Özgül E and Yanık YT. Tip 2 Diyabetli Bireylerin Öz-Yeterlilik Düzeylerinin Değerlendirilmesi. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi. 2016; 19: 166-74.*
31. *Mohebi S, Azadbakht L, Feizi A, Sharifirad G and Kargar M. Review the key role of self-efficacy in diabetes care. J Educ Health Promot. 2013; 2: 36-.*
32. *Trief PM, Teresi JA, Eimicke JP, Shea S and Weinstock RS. Improvement in diabetes self-efficacy and glycaemic control using telemedicine in a sample of older, ethnically diverse individuals who have diabetes: the IDEATel project. Age and Ageing. 2009; 38: 219-25.*
33. *Messina R, Rucci P, Sturt J, Mancini T and Fantini MP. Assessing self-efficacy in type 2 diabetes management: validation of the Italian version of the Diabetes Management Self-Efficacy Scale (IT-DMSES). Health and Quality of Life Outcomes. 2018; 16: 71.*
34. *Kes D and Gökdoğan F. Relationship between medication adherence and psychosocial adjustment in patients with type 2 diabetes: A cross-sectional study. Nordic Journal of Nursing Research. 2020; 0: 2057158520937456.*
35. *Eilander MMA, de Wit M, Rotteveel J and Snoek FJ. Low Self-Confidence and Diabetes Mismanagement in Youth with Type 1 Diabetes Mediate the Relationship between Behavioral Problems and Elevated HbA1c. J Diabetes Res. 2016; 2016: 3159103-.*
36. *Kim G, Shim R, Ford KL and Baker TA. The Relation Between Diabetes Self-Efficacy and Psychological Distress Among Older Adults:Do Racial and Ethnic Differences Exist? Journal of Aging and Health. 2015; 27: 320-33.*
37. *Wardian J and Sun F. Factors Associated With Diabetes-Related Distress: Implications for Diabetes Self-Management. Social Work in Health Care. 2014; 53: 364-81.*

ARAŞTIRMA MAKALESİ / *Research Article*

Orta Büyüklükteki Rotator Manşet Kas Yırtığı Sonrası Artroskopik Omuz Cerrahisi Uygulanan Bireylerde Yenilikçi Bir Yaklaşım: Humeral Baş Depresör Kas Ko-Aktivasyon Eğitimi

An Innovative Approach in Individuals Undergoing Arthroscopic Shoulder Surgery After Medium-Sized Rotator Cuff Muscle Tear: Humeral Head Depressor Muscle Co-Activation Training

Caner Karartı[1], Anıl Özüdoğru[1], Hakkı Çağdaş Basat[2], İsmail Özsoy[3]

[1] Kırşehir Ahi Evran Üniversitesi Fizik Tedavi ve Rehabilitasyon Yüksekokulu/ KIRŞEHİR

[2] Kırşehir Ahi Evran Üniversitesi Tıp Fakültesi Ortopedi ve Travmatoloji Anabilim Dalı/ KIRŞEHİR

[3] Selçuk Üniversitesi Sağlık Bilimleri Fakültesi Fizyoterapi ve Rehabilitasyon Bölümü/KONYA

Yazışma Adresi / *Correspondence:*

Caner Karartı

Kırşehir Ahi Evran Üniversitesi Fizik Tedavi ve Rehabilitasyon Yüksekokulu/ KIRŞEHİR

T: **+90 553 223 50 30** E-mail **: fzt.caner.92@gmail.com**

Geliş Tarihi / Received : **09.09.2020** Kabul Tarihi / Accepted : **29.11.2020**

Orcid :

Caner Karartı https://orcid.org/0000-0002-4655-0986

Anıl Özüdoğru https://orcid.org/0000-0002-7507-9863

Hakkı Çağdaş Basat https://orcid.org/0000-0003-3301-2529

İsmail Özsoy https://orcid.org/0000-0001-9048-1116

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):42-52) DOI: 10.31832/ smj.792788**

Öz

Amaç Orta büyüklükte rotator manşet kas yırtığı olan hastalarda konservatif tedaviyle kombine uygulanan humeral baş depresör kas ko-aktivasyon eğitiminin etkilerini değerlendirmektir.

Gereç ve Yöntem Toplam yirmi dört katılımcı rastgele iki gruba ayrıldı. Kontrol grubundaki bireylere toplam 6 hafta olmak üzere haftada 5 gün konservatif tedavi programı uygulandı. Konservatif tedaviye ek olarak tedavi grubundaki katılımcılar için haftada 5 gün 6 haftalık humeral baş depresör kas ko-aktivasyon eğitimi uygulandı. Katılımcılar hem tedavi öncesi hem de sonrası ağrı ve eklem hareket açıklığı açısından değerlendirildiler.

Bulgular Tedavi grubunda ağrı (p=.049; p=.008; p=.009; p=.003) ve eklem hareket açıklığı skorlarındaki (p=.047; p=.007; p=.001) iyileşmenin kontrol grubuna göre daha yüksek olduğu bulundu. İç rotasyon hareket açıklığı açısından iki grup arasında anlamlı fark yoktu (p = .499).

Sonuç Bu çalışma, orta büyüklükteki rotator manşet yırtıklarının tedavisinde konservatif tedavi ile birlikte humeral baş depresör kas ko-aktivasyon eğitiminin daha iyi bir seçim olabileceğini düşündürmektedir.

Anahtar Kelimeler Omuz; Rotator Manşet; Rotator Manşet Yaralanmaları

Abstract

Objective *To evaluate the effects of humeral head depressor muscle co-activation training combined with conservative treatment in patients with medium-sized rotator cuff tears.*

Materials and methods *A total of twenty-four participants were randomly divided into two groups. A conservative treatment program was applied for the participants in the control group for 5 days per week for a total of 6 weeks. In addition to the conservative treatment, humeral head depressor muscle co-activation training was performed for 5 days per week for 6 weeks for the participants in the treatment group. Participants were assessed in terms of pain and range of motion both pre- and post-treatment.*

Results *It was found that the improvement in pain (p=.049; p=.008; p=.009; p=.003) and range of motion scores (p=.047; p=.007; p=.001) was greater in the treatment group compared to the control group. There was no significant difference between the two groups in terms of internal rotation range of motion (p=.499).*

Conclusion *The current study suggests that humeral head depressor muscle co-activation training combined with conservative treatment can be a better choice in the treatment of medium-sized rotator cuff tears.*

Keywords *: Shoulder; Rotator Cuff; Rotator Cuff Injuries*

GİRİŞ

%15-%22 arasında değişen prevalansı ile toplumda en sık görülen muskuloskeletal problemlerden ikincisi olan kronikleşmiş omuz ağrısının önemli sebeplerinden birisi, rotator manşet (RM) kas yırtıklarıdır.[1] RM yırtıklarının erken dönem tedavisi konservatif olup Level 1 ve 2 oral analjezikleri, non-steroid antiinflamatuar ilaçları, gerekli ise kortikosteroid enjeksiyonlarını ve fizyoterapi yöntemlerini içerir.[2] Bu tedavi yöntemlerinin uygulanmasına karşın RM yırtığı olan hastalarda, abdüksiyon hareketi sırasında sıklıkla ağrı şiddetinde artma gözlenir.[3] Ağrıdaki bu artış, kinetik ve kinematik faktörlerin semptomları alevlendirdiğini düşündürmektedir.[3] Çeşitli radyografi yöntemlerine dayanan çalışmalarda, bu spesifik ağrı şeklinin açığa çıkmasında, abdüksiyon hareketi sırasında yetersiz humeral baş depresyonunun etkili olduğu rapor edilmiştir.[4,5] RM yırtığı olan hastaların, humeral baş depresörleri olarak hareket eden omuz kaslarının aktif katkısıyla özellikle abdüksiyon hareketi sırasında subakromiyal dokuların mekanik boşaltılmasından fayda sağlayabilecekleri bildirilmiştir.[6]

Hem sağlıklı kişilerde hem de RM lezyonu hastalarda, deltoid aktivasyonu çoğunlukla kranial yöndeki kuvvet kolunun bir sonucu olarak subakromiyal daralmaya yol açar ve humerusu yukarı doğru çeker.[7] Sağlıklı bireylerde RM aktivitesi abdüksiyon kuvvetlerini medial yönde oryante ederek ortaya çıkan kuvveti glenoid fossa içine düşürür ve glenohumeral stabilite sağlanır. Semptomatik RM yırtığı olan hastalarda, glenohumeral eklem çevresindeki kas moment dengesi bozulur ve bu da mobilite ve stabilite arasında bir uyumsuzluğa neden olur:[8]

i) Azalan RM abdüktör kuvvetlerini telafi etmek için abdüksiyon sırasında deltoid kas aktivasyonunda artış olur.[8]
ii) RM disfonksiyonu nedeniyle glenohumeral stabilitede azalma olur.[8]

Bu mekanizma kombinasyonlarının, hastalarda humerusun aşırı kranializasyonuna (proksimal migrasyon) ve subakromiyal dokuların ağrılı sıkışmasına neden olduğu varsayılmıştır. Glenohumeral stabiliteyi eski haline getirmek için, daha kaudal olarak yönlendirilmiş moment kollarına sahip kol addüktörleri, bu subakromiyal daralmayı azaltmak için hastalarda aktif kol abdüksiyonu sırasında aktive edilmelidir.[9] Bu "out-of-phase" addüktör aktivasyonu (ko-aktivasyon) hem model simülasyon çalışmalarında hem de hasta deneylerinde, özellikle medio-kaudal olarak yönlendirilmiş kuvvet vektörlerine sahip teres majör, pektoralis major ve latissimus dorsi kasları için rapor edilmiştir.[8,9]

Subakromiyal daralma ve ağrıyı azaltmak için adduktörlerin birlikte aktivasyonunun çelişkili etkisi, net kol abdüksiyon torkunun azalması ve glenohumeral temas kuvvetinin artmasıdır.[9] Adduktor ko-aktivasyonu, hastalığın etyolojisi ve hastalıkla başa çıkma mekanizmalarına ilişkin iç görü sağlar ve aynı zamanda tanı ve klinik karar vermede uygulanabilir.[9] Semptomatik RM yırtıklarını ayırt etmede, omuz semptomları ve RM patolojileri olan hastalarda etyolojik alt grupların tanımlanması için pratik bir önlem olarak potansiyel değere sahiptir. Ayrıca tedavi etkilerinin objektif olarak değerlendirilmesinde faydalı olabilir.[7-9] Subakromiyal ağrı sendromu, RM tendinopatisi gibi çeşitli durumlarda etkisi incelenmiş olmasına karşın orta büyüklükte RM yırtığı olan kişilerde humeral baş depresör kas ko-aktivasyon eğitiminin etkisi incelenmemiştir.[8,9] Bu bağlamda literatürdeki ilk çalışma olan araştırmamızın amacı, orta büyüklükteki (1-3 cm) RM kas yırtığı sonrası artroskopik rotator manşet onarımı (ARMO) uygulanan bireylerde humeral baş depresör kas ko-aktivasyon eğitiminin etkisini incelemektir.

GEREÇ VE YÖNTEM

Çalışma Dizaynı

Bu çalışma randomize kontrollü, tek kör çalışma olarak planlandı. CONSORT 2010 Kılavuzuna dayanılarak düzenlenen çalışma protokolü, NCT04154592 (clinicaltrials.gov) ID numarası ile kayıt altına alındı. Çalışmaya katılmayı gönüllü olarak kabul eden ve orta büyüklükte RM kas yırtığı sonrası ARMO uygulanan 24 hasta Faz 1 eği-

timleri sonrası, blok randomizasyon yöntemi ile 2 gruba ayrıldı.[10,11] Bu gruplar sırasıyla tedavi grubu [Konservatif tedaviye ek olarak humeral baş depresör kas ko-aktivasyon eğitimi (KT+Ko-aktivasyon)] ve kontrol grubudur [sadece konservatif tedavi (KT)].

Her iki grubun da konservatif tedavi programı, Amerikan Omuz ve Dirsek Terapistleri Derneğinin ARMO sonrası rehabilitasyon süreçleri hakkında 2016 yılında yayınlamış oldukları rehber eğitim programına göre dizayn edildi.[12] Ev egzersizi şeklinde düzenlenen post-operatif rutin Faz 1 (0-6. haftalar arası) eğitimlerini tamamlayan ve dahil edilme kriterlerini karşılayan bireylerin Faz 2 (6-12. haftalar) eğitimleri aynı araştırmacı (CK) tarafından supervize olarak yapıldı. Çalışmaya katılmayı kabul eden hastalar, aynı araştırmacı (ÇB) tarafından Faz 1 eğitimleri sonrası (6. hafta tamamlandıktan sonra) ve Faz 2 eğitimleri sonrası (12. hafta tamamlandıktan sonra) gruplara kör olarak değerlendirildiler.

Randomizasyon Tekniği

Tanı kriterlerini karşılayan, orta büyüklükte RM kas yırtığı sonrası ARMO uygulanan ve rutin Faz 1 eğitimlerini uyum içerisinde (≥%80 uyum oranı) tamamlayan bireyler, çalışma dizaynı için uygun bulundu. Her ardışık hasta, blok randomizasyon yöntemi ile KT+Ko-aktivasyon veya sadece KT grubuna rastgele atandı. 24 hastayı KT+Ko-aktivasyon ve sadece KT olmak üzere iki farklı gruptan birine rastgele atayabilmek için çeşitli istatistik programlarından yararlanılabilir.[10,11] Çalışmamızda MedCalc 11.5.1 paket programı tercih edildi.[11] MedCalc 11.5.1 paket programında 1 ile 2 arasında rastgele 12 tane sayı üretilerek 1 geldiğinde ilk hasta KT+Ko-aktivasyon grubuna, ikinci hasta sadece KT grubuna; 2 geldiğinde ise ilk hasta sadece KT grubuna ikinci hasta KT+Ko-aktivasyon grubuna atandı. Böylece her blokta iki birey olacak şekilde atama işlemi tamamlandı.[11]

Körleme Prosedürü

Her iki grubun da Faz 2 egzersizleri ile ko-aktivasyon eğitimleri aynı araştırmacı (CK) tarafından uygulandığından çalışmamız, çift kör çalışma düzenine uygun değildi. Hastanın grup numarasının belirlendiği prosedür, çalışmaya dahil olmayan ve çalışma prosedürünü bilmeyen bir sekreter tarafından denetlendi. Daha sonra hasta, değerlendirmeleri yapan hekime (ÇB) yönlendirilerek Faz 2 eğitimleri öncesi gerekli anket ve testler tamamlandı. ÇB, bireylerin hangi grupta olduklarından habersizdi (tek kör).[10] Tüm bireyler, ilk değerlendirmelerden sonra ilgili eğitimler için fizyoterapiste (CK) yönlendirildiler. Atandıkları grubun özelliklerine göre her birey ev egzersizlerine (Faz 1) ek olarak 6 haftalık tedavi döngüsünün (Faz 2+Katılımcı tedavi grubundaysa ek olarak ko-aktivasyon eğitimi) ardından, ilk değerlendirmeyi yapan ÇB tarafından tekrar değerlendirildi.Supervize eğitimler öncesi ve sonrası değerlendirmelerde aynı prosedürler ve kayıt formları kullanıldı.[10]

Katılımcılar

Ortopedi ve Travmatoloji Polikliniğine başvuran 24 omuz hastası çalışmaya dahil edildi. Çalışmaya dahil edilme kriterleri; 18-65 yaş arasında birey olmak,Faz 1 eğitimlerini uyum içerisinde tamamlamak, radyolojik yöntemler (MRG) ve klinik testler (devamlılık testleri) sonucu hekim tarafından orta büyüklükte (1-3 cm) RM kas yırtığı tanısı almak, cerrahi yöntem olarak ARMO uygulanmak, bilgilendirilmiş gönüllü onam formu ve ilgili değerlendirme ölçekleri için Türkçe konuşma yetisine sahip olmak, Mini Mental Durum Testinden 24 üzeri skora sahip olmak ve çalışmaya katılmaya gönüllü olmak şeklinde belirlendi.[8-10] Çalışmaya dahil edilmeme kriterleri; diabetus mellitus varlığı, yağlı dejenerasyon sınıflamasına (Goutallier sınıflaması) göre evre 3 ve daha üstü seviyede olmak,mobilizasyon için kontraendikasyon oluşturabilecek herhangi bir durumun varlığı (hipermobilite, travma, inflamasyon vb.),visual, verbal, kognitif defektler (afazi, unilateral neglect vb.), nörolojik herhangi bir problemin varlığı, servikal disk hernisi varlığı, etkilenen tarafta geçirilmiş omuz fraktürleri, parsiyel RM yırtığı varlığı, etkilenen tarafta geçirilmiş cerrahi öyküsü, adeziv kapsülit varlığı, osteoartrit, romatoid artrit veya sistemik inflamatuar herhangi bir

problemin varlığı,travmatik omuz instabilitesi (subluksasyon-dislokasyon) öyküsü, tanı öncesi 6 haftalık süre içinde etkilenen taraf için kortikosteroid enjeksiyonu uygulanması şeklinde belirlendi.[8-10]

Etik Kurul İzni

Çalışmamız, Selçuk Üniversitesi Sağlık Bilimleri Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu tarafından onaylandı (2020-622). Çalışma öncesi tüm bireylerin yazılı ve sözlü onamları alındı ve ayrıca çalışma Helsinki Bildirgesi'ne uyumlu şekilde gerçekleştirildi.

Değerlendirme Yöntemleri

Tüm bireylerin sosyodemografik özellikleri kaydedildi. Supervize eğitimler öncesi ve sonrası ağrı değerleri görsel analog skala (VAS) ile; eklem hareket açıklık değerleri (ROM) ise universal gonyometre iledeğerlendirildi.[13,14]

Görsel Analog Skala (VAS)

Katılımcıların sırasıyla istirahat, aktivite, Neer Testi ve Kennedy-Hawkins testi sırasında omuz ekleminde hissettikleri ağrı şiddeti, VAS ile değerlendirildi. VAS, herhangi bir dilinin olmaması nedeniyle kullanımı kolay olan bir skaladır ve kliniklerde sıklıkla uygulanmaktadır. Bireylerden test sırasında hissettikleri ağrıyı 10 cm' lik ölçekte "0" (ağrı yok) ve "10" (dayanılmaz ağrı) olacak şekilde tariflemeleri istendi.[13]

Eklem Hareket Açıklık Değerleri (ROM)

Çalışmaya katılan tüm bireylerin fleksiyon, abduksiyon, internal rotasyon ve eksternal rotasyon olmak üzere omuz ROM'ları universal gonyometre ile değerlendirildi. Gonyometrik ölçüm, klinikte ROM değerlendirilmesinde sıklıkla kullanılan bir yöntemdir.[14] Eklem hareket sınırının değerlendirilmesine ek olarak fonksiyonel kapasiteyi saptamak, tedavi programına karar vermek ve tedavinin etkinliğini belirlemek amacıyla da kullanılmaktadır.[14]

Gonyometre ölçümleri, bireyler sırt üstü yatış pozisyonunda iken yapıldı.[14] Fleksiyon hareketinin ROM değerlendirmesinde pivot nokta humerusun büyük tüberkülü, hareketli kol ise humerusun lateral kondiline doğru, humerus orta çizgisine paralel olacak şekilde yerleştirildi. Abduksiyon hareketi için, pivot nokta akromiyona, hareketli kol ise humerusun anterior orta çizgisine paralel olacak şekilde ölçüm yapıldı. Eksternal ve internal rotasyon için ise, omuz 90º abduksiyon ve dirsek 90º fleksiyonda bireylerin üst ekstremitesi pozisyonlandı. Sabit kol yere paralel iken hareketli kol 3. metakarpofalangeal eklemin uzun eksenini takip etti.[14] Tüm ölçümlerde AROM değerlendirildi.

Tedavi Yöntemleri

Konservatif Tedavi Yöntemleri

Her iki grubun da konservatif tedavi programı, Amerikan Omuz ve Dirsek Terapistleri Derneği'nin ARMO sonrası rehabilitasyon süreçleri hakkında 2016 yılında yayınlamış oldukları rehber eğitim programına göre dizayn edildi.[12]

Faz 1 Eğitimi (0-6. haftalar)

Literatürde ARMO sonrası çoğunlukla immobilizasyon dönemi olarak düşünülen dönemdir.[12] Çalışmamızda da ev egzersizi ve immobilizasyon dönemi olarak planlanan Faz 1 dönemi, hasta eğitimini, modaliteleri, pasif ROM' u ve immobilizasyon yöntemlerini içeren dönem olarak planlandı. Bu dönem klinik çalışmaya bağlı olmaksızın ARMO sonrası benzer eğitimleri içerdiğinden bu dönemi tamamlayan 24 katılımcı çalışmaya ve randomizasyona dahil edildi.Hekim rutin olarak bu dönemde hastalardan eğitime uyum süreçlerini ve kullanmak zorunda kaldıkları medikal yöntemleri kaydetmeleri için günlük tutmalarını istedi. Günde toplam 1 saat egzersiz ve temizlik işlerine ayrıldı. Geri kalan 23 saat immobilizasyon süresi olarak düşünüldü. Bu faz sırasındaki uygulamalar sırasıyla şunlardır:

i) Hasta eğitiminde patolojinin ve tedavi prosedürünün hasta tarafından kavranılması amacıyla RM kaslarının yeri ve görevleri anatomik görseller vasıtasıyla hasta ve ailesine anlatıldı. Re-rüptür oranının sıklığı nedeniyle hekim-fizyoterapist-hasta arasında sıkı bir kooperasyon gerektiği, her bir fazda alınacak koruyucu önlemler aktarıldı. Breys

kullanım şekli, temizlik işlerinin nasıl yapılacağı konusunda bilgilendirme yapıldı.[12]

ii) Özellikle ilk 72 saatlik dönemde opioid kullanımı ve post-operatif ağrıyı azalttığı bilindiğinden hastalardan omuz bölgelerine iki saate bir 20 dakika soğuk uygulamaları istendi.[12]

iii) Kasların EMG aktivitelerini %15' in altında tutacak egzersizler seçildi. Tanımlanan her egzersiz, bir set 10 tekrar olmak üzere 3 set şeklinde yapıldı. Setler arası 1 dakika, farklı egzersizler arasında ise 3 dakika dinlenme süresi uygulandı. Faz 1 dönemi olduğu için korumanın öncelikli olduğu ve tüm egzersizlerin ağrı sınırında yapılması gerektiği belirtildi.[12] Uygulanan egzersizler sırasıyla; pendulum egzersizleri, masa kenarında pasif fleksiyon ve abduksiyon germe, ayakta maksimum 120°' ye kadar (tolere edemeyenlerde 90°) pasif öne elevasyon, maksimum 30°' ye kadar 20° abduksiyonda pasif eksternal rotasyon, self yardımlı supin pozisyonda öne elevasyon, wand ile yardımlı eksternal ve internal rotasyon ve aktif servikal hareketlerin yapılmasıdır.[12]

Çalışmamızda immobilizasyon yöntemi olarak "Velpeau bandajı" seçildi. Hastaların 23 saat boyunca bandajı kullanmaları istendi.[15]

Faz 2 Eğitimi (6-12. haftalar)

Tüm hastalar Faz 1 eğitimlerini ev ortamında tamamladıktan sonra dahil edilme kriterlerini karşılamaları durumunda supervize Faz 2 eğitimleri için Fizyoterapi ve Rehabitasyon kliniklerine başvurdular. Bu faz başlamadan önce Velpeau bandajı tekrar kullanılmamak üzere çıkarıldı. Fizyoterapist (CK) tarafından Faz 2 eğitiminin uygulanması sırasında kasların EMG aktivitelerini %29' un altında tutacak egzersizler seçildi.[12] Haftada 5 gün her seans yaklaşık 90 dakika olacak şekilde planlama yapıldı. Tanımlanan her egzersiz, bir set 10 tekrar olmak üzere 3 set şeklinde yapıldı. Setler arası 1 dakika, farklı egzersizler arasında ise 3 dakika dinlenme süresi uygulandı. Ev ortamında omuz bölgesine iki saate bir 20 dakika soğuk uygulamasına devam edildi. Belirtilen egzersizler ev ortamında da hastalara ödev şeklinde verildi ve günlük vasıtasıyla tedaviye uyum gözlemlendi.[12]

Bu faz sırasında uygulanan eğitimler sırasıyla; omuz bölgesine 20 dakika soğuk uygulama, 20 dakika Konvansiyonel TENS (60-120 Hz. arası) uygulaması, deltoid ve biseps kasları için yumuşak doku masajı (3 dakika), skapula ve glenohumeral eklem mobilizasyonları (Grade A-B), ayakta duruşta duvarda havlu kaydırma ve duvarda toz alma egzersizi, wand ile yardımlı 120°' ye kadar bilateral omuz elevasyonu, 9. haftadan sonra artan abduksiyon açılarında eksternal rotasyon, abduksiyonda internal rotasyon, horizontal adduksiyon ve fonksiyonel internal rotasyon (el dorsumu lumbalde ve daha yukarıda) egzersizleri, VAS' a göre aktivite sırasında 2 birim ve altında ağrıya ulaşıldığında sırt üstü ve yan yatış pozisyonlarında ve RM/deltoid dengesini sağlamak için dirsek fleksiyonda kısa kaldıraç kolunda kuvvetlendirme eğitimleri, parmak merdiveni egzersizleri, 0.5 kg ile başparmak yukarıda "Full Can" pozisyonunda kuvvetlendirme eğitimi, statik quadripedal pozisyonunda kapalı kinetik zincir eğitimleri, periskapular kasların, deltoidin ve trapezin izometrik egzersizleri, posterior kapsül germe, aktif elevasyon derecesi arttıkça göğüs seviyesinde deltoid, RM ve skapular kasların aktivasyon eğitimleri için dört anahtar egzersiz uygulaması:[12]

i) (Maksimum kırmızı renk elastik bant yardımı ile eksternal rotasyon (infraspinatus ve teres minör),

ii) İnternal rotasyon (subskapularis),

iii) Deltoid ve periskapular kas eğitimi,

iv) Kısa kol kaldıraçta öne elevasyon ya da öne uzanma (anterior deltoid ve supraspinatus).

Humeral Baş Depresör Kas Ko-Aktivasyon Eğitimi

Tedavi grubundaki bireylere, 6 haftalık Faz 2 (6-12. haftalar) eğitimlerine ek olarak Faz 2 eğitiminin başladığı 6. haftadan itibaren "Humeral Baş Depresör Kas Ko-aktivasyon Eğitimi" senkronize şekilde uygulandı. Ko-aktivasyon eğitimi için standart bir test ve eğitim protokolü kullanıldı.[9] Abdüksiyon hareketi sırasında skapulaya göre humerusun kraniokaudal pozisyonuna doğrudan etki eden

kasların aktivasyon modelleri temel alınarak bu modellere uygun eğitim verildi.[6] Humeral baş depresör kaslar, güçlüden zayıfa doğru sırasıyla teres majör, latissimus dorsi ve pektoralis majördür. Humeral baş depresyonuna katkıda bulunan diğer kasların (infraspinatus ve subskapularis kaslarının alt lifleri) EMG Biofeedback cihazı ile eğitilmesi invaziv iğne elektrotlar gerektirdiğinden, eğitim programı teres majör, latissimus dorsi ve pektoralis major kaslarıyla sınırlandırıldı.[2,6]

Ko-aktivasyon eğitimi için nöromusküler temelli bir eğitim aracı olan EMG Biofeedback [Chattanooga Group Inc., Chattanooga, TN] (EMG-BF) cihazından faydalanıldı. EMG-BF, yüzeyel elektrotlar vasıtasıyla kas içi myoelektriksel sinyalleri görsel ve işitsel değerlere dönüştürerek kasın re-edukasyonunu sağlayan bir cihazdır.[16] Kas kontraksiyonu sırasında sarkolemmanın depolarizasyonu ile meydana gelen Motor Ünite Aksiyon Potansiyeli (MÜAP), EMG-BF cihazının göstergesinde mikrovolt cinsinden gösterilir.[16]

Katılımcıda başarma algısının ve odaklanmanın artırılması amacıyla, ko-aktivasyon eğitimine başlanmadan önce humeral baş depresör kasların anatomisi görseller yardımı ile hastalara tariflendi. EMG-BF uygulaması için hastalar, sessiz ve sakin bir tedavi kliniğine alınarak dış ortam ile ilişkileri kesildi. Uygulama yapılmadan önce cilt alkollü pamuk ile temizlendi. Uygulamada, Stimrodes® 3.2 cm çapında elektrotlar kullanıldı.[17] Teres majör için, aktif elektrotlardan biri skapulanın inferior açısının 1 santimetre superolateraline, diğeri humerusun küçük tüberkülü üzerine yerleştirildi. Latissimus dorsi için aktif elektrotlardan biri, skapulanın alt açısının bir santimetre altındaki kas karnına, diğeri iliakkristanın 1 santimetre üzerine yerleştirildi. Pektoralis major için ise, elektrotlardan biri sternal parça venter kısmının 2/3 lateral bölümüne, diğeri ise üçüncü kostanın kostokondral eklemi üzerine yerleştirildi.[10]

Hastalar cihazı rahatlıkla görebilecek konumda ve oturur şekilde pozisyonlandılar. Çalışma hedefi "Hedefi belirle" butonu ile belirlenmeden önce katılımcılar tarafından humeral baş depresör kasların en az üç (beş adede kadar) tekrar Maksimum İzometrik Kasılması (MVIC) gerçekleştirildi. Bu alışma tekrarları arasında 1 dakika dinlenme periyodu uygulandı. En yüksek EMG-BF mikrovolt değeri, çalışma hedefini belirlemede gerekli skor olarak seçildi.

Tüm bireylerin MVIC değerlerinin hesaplanmasında, skapular düzlemde 45°'lik elevasyon hareketi esas alındı.[16,17] Teres majör ve latissimus dorsi MVIC' leri için hastalardan 45°'lik elevasyon hareketi sırasında kola iç rotasyon, adduksiyon ve ekstansiyon yaptırmaya odaklanarak omzu arkaya doğru çekmeye çalışmaları istendi. Pektoralis majör MVIC için de hastaların fleksiyon, iç rotasyon ve adduksiyon hareketine odaklanarak omuzu öne ve içeri doğru çekmeye çalışmaları istendi. Görsel geri bildirimler için cihazın ekranında yer alan kesikli çizgilerden ve işitsel geri bildirim için sinyal sesinden yararlanıldı.[16,17]

Yapılan çalışmada, humeral baş depresör kaslarda ko-aktivasyon artışı amaçlandığı için alışma tekrarları sırasında belirlenen hedef MVIC, %50 artırılarak yeni hedef belirlendi. Hastaya, ilgili hareketleri yaparken kesikli çizgilerin, hedef çizginin altında kalmaması gerektiği anlatıldı.[16,17] Her hastaya ilk gün bu 1 saatlik alışma ve odaklanma eğitimi verildikten sonra Faz 2 eğitimlerine geçildi. Faz 2 eğitimlerine geçmek için her bir hastanın ko-aktivasyonu doğru bir şekilde uygulandığından emin olundu. Faz 2 eğitimleri sırasında fizyoterapist ile her seans öncesi katılımcıların ko-aktivasyonu gerçekleştirebilme kapasiteleri değerlendirildi. Gerekirse, egzersizler doğru yapılana kadar EMG-BF cihazı kullanılarak fizyoterapist ile ek denemeler yapıldı. Haftalık telefon görüşmesi ile katılımcılara ko-aktivasyon eğitimi için odaklanmayı ev ortamında da çalışmaları gerektiği ve gereken prosedür hatırlatıldı. Ko-aktivasyon eğitiminin ev ödevi bölümüne hastaların uyumunu saptamak için günlük tutturuldu.[16,17]

KT+Ko-aktivasyon grubundaki bireylerden, Faz 2 eğitiminin glenohumeral egzersizlerinden önce EMG-BF cihazı-

nın görsel ve işitsel uyarıları ile teres majör, latissimus dorsi, pektoralis majör kaslarını yukarıda bahsedilen şekilde istemli olarak aktive etmeleri istendi. Tüm glenohumeral egzersizlerin, humeral baş depresör kasların ko-aktivasyonu bozulmadan yapılması gerektiği ifade edildi ve cihaz yardımıyla performans kontrol edildi. Öte yandan, sadece KT grubundaki bireylerin teres majör, latissimus dorsi ve pektoralis majör kaslarını hareketler sırasında aktive etmemesi gerektiğinden haftalık olarak 1 kereliğine bu hastaların sadece EMG-BF MVIC değerleri ölçülerek MVIC' in % 15' in altında olduğundan emin olundu.[16,17]

Örneklem Büyüklüğü

Orta büyüklükteki RM kas yırtığı sonrası ARMO uygulanan bireylerde humeral baş depresör kas ko-aktivasyon eğitiminin etkisinin incelendiği herhangi bir çalışma literatürde mevcut değildir. Bu nedenle çalışmamızda örneklem büyüklüğünün saptanmasında Overbeek ve ark.' nın çalışma sonuçları referans alındı.[18] Overbeek ve ark. humeral baş depresör kasların artmış ko-kontraksiyonunun, subakromiyal ağrı sendromundaki klinik seyir ile ilişkisini incelemişlerdir. Bu çalışma sonuçlarına göre geniş etki büyüklüğü hesaplandı. G*Power Software (Version 3.1.9.2, DüsseldorfUniversity, Düsseldorf, Germany) ile yapılan analizde, 0.8'lik etki büyüklüğünde, % 95 güven aralığında ve % 80 güçte 2 grupta mikst dizaynda tekrarlı ölçümler ANOVA testi yapabilmek için her gruba 12 birey olmak üzere toplam 24 bireyin dahil edilmesi gerektiği saptandı.

İstatistiksel Analiz

Verilerin istatistiksel analizinde The IBM® SPSS® Statisticsfor Windows software (ver. 22.0; IBM Corp., NY, USA) yazılımı kullanıldı. Tüm sonuçlar için tedaviye niyet prensibi ve protokol başına analizler gerçekleştirildi. Sayısal değişkenlerin normal dağılıp dağılmadıkları, görsel (histogramlar, olasılık grafikleri) ve analitik yöntemler (Kolmogorov-Simirnov/Shapiro-Wilk testi) kullanılarak belirlendi. Normal dağılım gösteren veriler için parametrik analiz yöntemleri kullanıldı. Tanımlayıcı istatistikler sürekli sayısal değişkenler için minimum-maksimum ve ortalama±standart sapma (ortalama±SS) olarak; kategorik değişkenler için oran (%) olarak ifade edildi. Gruplar açısından temel parametreler bağımsız örneklem t testi (yaş, vücut kütle indeksi) ve $\chi 2$ testi (cinsiyet dağılımı, dominant taraf, etkilenen taraf, ev egzersizleri sırasında günlük tutma vasıtasıyla tedaviye uyum) kullanılarak karşılaştırıldı. Tedavi öncesi ve sonrası grup içi farklılıkların saptanmasında eşleştirilmiş örneklem t testi kullanıldı. Mikst dizaynda iki yönlü tekrarlı ölçümler varyans analizi (ANOVA) [bağımsız faktör grup: KT+Ko-aktivasyon grubu ve sadece KT grubu; tekrarlanan faktör zaman: tedavi öncesi ve tedavi sonrası] zamana bağlı değişim ve grupxzaman etkileşimleri açısından skorları karşılaştırmak için kullanıldı. Etki büyüklükleri (f) "partial eta squared" olarak ifade edildi [f = 0.10 (küçük etki büyüklüğü), f = 0.25 (orta etki büyüklüğü) ve f = 0.40 (geniş etki büyüklüğü)]. Grup, zaman veya grupxzaman etkileşimi için saptanan önemli farklılıklarda Bonferroni post-hoc testi kullanıldı. Tüm analizler için istatistiksel anlamlılık değeri p<.05 olarak ayarlandı.

BULGULAR

Orta büyüklükte RM kas yırtığı sonrası ARMO uygulanan 24 birey çalışmaya dahil edildi. Katılımcıların tanımlayıcı istatistikleri Tablo 1' de gösterildi. İncelenen gruplar temel parametreler açısından benzerdi p>.05 ve bu durum grupların homojen dağıldığını ortaya koydu. Toplam 42 günlük ko-aktivasyon eğitiminin ev ödevi bölümüne uyum oranının ise KT+Ko-aktivasyon grubu için %90.47 olduğu bulundu.

Ağrı Değişkeni Açısından Gruplar Arası Karşılaştırma

Analizler, her iki tedavi programının da faydalı etkiler sağladığını gösterdi (p<.05). Dört farklı durum üzerinde gerçekleştirilen ANOVA, hem grup etkisi (p<.001) hem de tedavi etkisi (p<.001) ortaya çıkardı. Grup ve tedavi arasında da istatistiksel olarak anlamlı bir etkileşim saptandı (p <.05). Grup içi değerlendirmelerde tüm ölçümler için her iki tedavinin de etkili olduğu saptandı (p<.001). Tüm pozisyonlar açısından KT+Ko-aktivasyon grubundaki iyi-

Tablo 1. İlk Değerlendirmede Katılımcıların Tanımlayıcı Özellikleri (Grup Ortalamaları ve Gruplar Arası Karşılaştırmalar)			
	KT+Ko-aktivasyon	**Sadece KT**	**p**
Kadın (%)	11 (91.7)	11 (91.7)	1.0 [a]
Yaş (SS; min-max)	46.58 (7.47; 36-61)	50.25 (7.37; 36-62)	.23 [b]
VKİ (SS; min-max)	26.4 (4.48; 17.9-39.1)	25.1 (4.12; 18.4-36.5)	.21 [b]
Dominant taraf sağ (%)	12 (100.00)	12 (100.00)	1.0 [a]
Etkilenmiş taraf sağ (%)	12 (100.00)	12 (100.00)	1.0 [a]
Faz 1 egzersizlerine uyum (%)	36/42 gün (85.71)	42/42 gün (100.00)	.04 [a] *
Faz 2 egzersizlerine uyum (%)	34/42 gün (80.95)	41/42 gün (97.61)	.02 [a] *
Ko-aktivasyon eğitimine uyum (%)	-	38/42 gün (90.47)	-
VKİ: Vücut kütle indeksi; SS: Standart sapma; a $\chi 2$ testi; b Bağımsız örneklem t testi; %: Yüzde; min-max: Minimum-maksimum; KT+Ko-aktivasyon: KT+Ko-aktivasyon: Konservatif tedaviye ek olarak humeral baş depresör kas ko-aktivasyon eğitimi; KT: Sadece konservatif tedavi.			

Tablo 2. Ağrı Değişkeni Açısından Tedavi Öncesi ve Sonrası Gruplar Arası Karşılaştırma								
	Sadece KT grubu			**KT+Ko-aktivasyon Grubu**			**p^2 değeri**	
	Önce	Sonra	p^1 değeri	Önce	Sonra	p^1 değeri	Zaman	Grup×Zaman
İstirahat	5.08±1.37	3.28±1.52	<.001	5.66±1.15	2.45±0.44	<.001	<.001 (0.912)	.049 (0.311)*
Aktivite	7.16±1.33	3.96±0.82	<.001	7.50±1.00	2.48±0.58	<.001	<.001 (0.923)	.008 (0.493)*
Neer	7.33±1.43	4.49±0.99	<.001	7.16±1.19	2.88±0.86	<.001	<.001 (0.922)	.009 (0.488)*
Kennedy-Hawkins	8.33±0.88	5.78±0.87	<.001	8.16±0.57	3.87±0.48	<.001	<.001 (0.989)	.003 (0.542)*
VAS: Görsel Analog Skalası; p^1: eşleştirilmiş örneklem t testi; p^2: Mikst dizaynda iki yönlü tekrarlı ölçümler varyans analizi (ANOVA). Değerler ortalama±standart sapma şeklinde ifade edildi. Parantez içindeki veriler etki büyüklüklerini tarifler; KT+Ko-aktivasyon: KT+Ko-aktivasyon: Konservatif tedaviye ek olarak humeral baş depresör kas ko-aktivasyon eğitimi; KT: Sadece konservatif tedavi.								

leşmenin daha yüksek olduğu saptandı (p <.05, Tablo 2).

Eklem Hareket Açıklık Değerleri Açısından Gruplar Arası Karşılaştırma

Uygulanan her iki tedavinin de ROM değerleri açısından faydalı sonuçlara yol açtığı saptandı (p<.05). ANOVA, internal rotasyon hareketi dışında diğer 3 farklı ROM ölçümünde hem grup etkisi (p<.001) hem de tedavi etkisi (p<.001) ortaya çıkardı. Grup ve tedavi arasında da istatistiksel olarak anlamlı bir etkileşim bulundu (p<.05). Grup içi değerlendirmelerde tüm ölçümler için her iki tedavinin de etkili olduğu saptandı (p<.001). Fleksiyon, abduksiyon ve eksternal rotasyon hareketlerindeki iyileşme açısından KT+Ko-aktivasyon grubunun üstün olduğu görüldü (p<.05, Tablo 3).

Tablo 3. Eklem Hareket Açıklık Değerleri Açısından Tedavi Öncesi ve Sonrası Gruplar Arası Karşılaştırma								
ROM	**Sadece KT grubu**			**KT+Ko-aktivasyon Grubu**			**p^2 değeri**	
	Önce	Sonra	p^1 değeri	Önce	Sonra	p^1 değeri	Zaman	Grup×Zaman
Fleksiyon	98.66±12.40	123.23±8.75	<.001	97.25±8.51	137.42±5.12	<.001	<.001 (0.951)	.047 (0.343)*
Abduksiyon	49.66±15.82	112.21±8.9	<.001	47.91±14.20	129.84±7.58	<.001	<.001 (0.942)	.007 (0.502)*
Eksternal Rotasyon	5.66±4.84	26.13±6.44	<.001	6.16±4.62	32.48±8.78	<.001	<.001 (0.925)	<.001 (0.798)*
İnternal Rotasyon	18.83±9.00	43.25±4.88	<.001	17.75±8.13	42.65±6.14	<.001	.896 (0.004)	.499 (0.038)
ROM: Eklem Hareket Açıklığı; p^1: eşleştirilmiş örneklem t testi; p^2: Mikst dizaynda iki yönlü tekrarlı ölçümler varyans analizi (ANOVA). Değerler ortalama±standart sapma şeklinde ifade edildi. Parantez içindeki veriler etki büyüklüklerini tarifler; KT+Ko-aktivasyon: KT+Ko-aktivasyon: Konservatif tedaviye ek olarak humeral baş depresör kas ko-aktivasyon eğitimi; KT: Sadece konservatif tedavi.								

TARTIŞMA

Bu çalışma, orta büyüklükteki RM kas yırtığı sonrası ARMO uygulanan bireylerde humeral baş depresör kas ko-aktivasyon eğitiminin etkisinin incelenmesi amacıyla planlandı. Çalışma sonuçlarına göre, konservatif tedavi programına, ko-aktivasyon eğitiminin eklenmesinin ağrı ve eklem hareket açıklığı açısından olumlu etkisi vardır.

Semptomatik RM lezyonu olan hastalarda, semptomların daha da kötüleşmesine yol açan predispozan faktörlerden biri deltoid kastaki aktivasyon artışıdır.[7] Glenohumeral eklem çevresindeki kas moment dengesi anomalilerinden dolayı ortaya çıkan mobilite-stabilite uyumsuzluğu, humeral başın aşırı kranializasyonuna yol açarak akromiyohumeral mesafeyi daraltır ve fonksiyonel yetersizlikleri artırır.[8,9] Semptomların hafifletilebilmesi için çeşitli yöntemler aranmakta olup, son zamanlarda etkisinin incelenmesi konusunda çalışmalara ihtiyaç olduğu vurgulanan eğitimlerden birisi, humeral baş depresör kas ko-aktivasyon eğitimidir.[8,9] Biyomekaniksel analiz çalışmalarında teres majör, pektoralis major ve latissimus dorsi kaslarının glenohumeral egzersizler sırasında ko-aktivasyon sağlaması gerektiği ancak bu şekilde medio-kaudal moment kollarının oluşabileceği rapor edilmiştir.[8-10] Tartışmalı sonuçlar olsa da medio-kaudal moment kollarına sahip kol kol addüktörlerinin ko-aktivasyonu ile glenohumeral mobilite ve stabilitenin restorasyonunun sağlanabileceği düşüncesi önem kazanmaktadır.[9] Bu düşünce, çalışmamızın önemli çıkış noktalarından birisidir. Çalışmamız orta büyüklükteki RM kas yırtığı sonrası ARMO uygulanan bireylerde humeral baş depresör kas ko-aktivasyon eğitiminin etkisinin incelendiği ilk çalışma olma özelliği taşıdığından sonuçlarımız EMG çalışmaları ile desteklenmiştir.

Witte ve arkadaşlarının EMG' ye dayalı çalışmaları, humeral baş depresör kas ko-aktivasyon eğitiminin gerekliliği konusundaki sonuçlarımızı destekler niteliktedir.[9] Yirmi sağlıklı ve 20 tam kat RM yırtığı olan toplam 40 katılımcı ile yapmış oldukları çalışmalarında, EMG kaydı sırasında izometrik abduksiyon ve adduksiyon hareketlerini incelemişlerdir. Abduksiyon ve adduksiyon EMG sonuçları "Aktivasyon Oranı ($-1 \leq AO \leq 1$)" olarak ifade edilmiş olup daha küçük oranlar daha yüksek ko-aktivasyonu tariflemektedir. Tam kat yırtığı olan bireylerin kompansasyon mekanizması olarak abduksiyon hareketi sırasında daha yüksek adduktor kas ko-aktivasyonu gösterdiğini rapor etmişlerdir.[9] AO' lar teres majör kası için 0.3; latissimusdorsi kası için ise 0.5 olarak bulunmuştur. Eğitim olarak verilmesinin yanı sıra bu AO' ların semptomatik RM yırtığı olan kişilerin sağlıklılardan ayırt edilmesinde indikatör olarak kullanılabileceğini ifade etmişlerdir.[9]

Witte ve arkadaşları, RM disfonksiyonlu hastalarda abduksiyon hareketi sırasında akromiyohumeral mesafedeki darlığın minimize edilebilmesinde humeral baş addüktör kas ko-aktivasyonunu potansiyel bir kompansasyon mekanizması olarak görmüşlerdir.[19] Bu düşünce üzerine planladıkları bir diğer EMG çalışmasında, istirahat pozisyonunda akromiohumeral mesafeyi ve aktif abdüksiyon ve addüksiyon hareketleri sırasında humeral translasyon miktarındaki farklılıkları değerlendirmişlerdir.[19] RM yırtığı olan 20 hasta, subakromiyal sıkışması olan 30 hasta ve 10 kişilik kontrol grubu olmak üzere toplam 60 hasta ile çalışmalarını planlamışlardır. Tüm katılımcıların deltoid, pektoralis majör, latissimus dorsi ve teres majör aktivasyonları ilgili hareketler sırasında EMG ile kayıt altına alınmıştır.[19] Subakromiyal aralığın RM yırtığı olan hastalarda, diğer bireylere göre daha dar olduğunu ifade etmişlerdir.[19] Tüm deneklerde izometrik abdüksiyon sırasında ve daha az miktarda adduksiyon sırasında subakromiyal daralmada artış ve ayrıca RM yırtığı olan hastalarda daha fazla addüktör kas ko-aktivasyonu saptamışlardır.[19] Erken dönemde ko-aktivasyon artışının olması, RM kaslarındaki yetersizliğin kompanse edilmesinde önemlidir.[20] Humeral baş depresör kas ko-aktivasyon eğitiminin olumlu etkileri ile ilgili sonuçlarımız, ko-aktivasyon miktarının artırılmasıyla RM kaslarının daha hızlı iyileşmesine olanak tanınmasıyla açıklanabilir. Klinikteki eğitimler sırasında rekürrent aktivite vasıtasıyla iyileşmenin hızlanması,

ko-aktivasyon miktarını zamanla düşürecektir.[21] Yırtık olan RM kasları iyileştikçe ko-aktivasyon azalması, gereksiz kassal aktivitenin ilerleyen inhibisyonunu sağlayacak ve çalışma sonuçlarımızda olduğu gibi daha iyi fonksiyonel skorlar elde edilebilecektir.[21] Bu bağlamda Witte ve arkadaşlarının bahsedilen 2 biyomekaniksel çalışması, sonuçlarımızın geçerliliğini desteklemesi açısından önemlidir.[9,19]

Humeral baş depresör kas ko-aktivasyon artışının etkilerini inceleyen bir diğer çalışma Overbeek ve arkadaşlarına aittir.[18] Abduksiyon hareketi sırasında kol addüktör kas ko-aktivasyonunun artırılmasının subakromiyal ağrı sendromunun (SAPS) tedavisinde etkili olabileceği düşüncesiyle çalışmalarını planlamışlardır.[18] İlk değerlendirmede ve yaklaşık 4 yıllık takipten sonra, SAPS' lı 26 hastada izometrik abdüksiyon ve addüksiyon görevleri sırasında latissimus dorsi, teres major, pektoralis majör ve deltoid kasının EMG ölçümlerini kaydetmişlerdir. Klinik seyir VAS ile takip edilmiştir. Çalışma sonuçlarına göre latissimus dorsi ve teres majör kaslarının ko-aktivasyon artışı, olumlu bir SAPS seyri ile ilişkilidir. Semptomlardaki iyileşmeyi ise addüktör kas ko-aktivasyonunun artmasıyla subakromiyal mesafenin genişlemesiyle açıklamışlardır.[18]

Çalışmamızın limitasyonu yaş ile ilgilidir. Hastaların yaş dekatlarının gruplanarak skorların analiz edilmesi, sonuçların daha objektif ve genellenebilir olması açısından önemli olabilir. Sonuç olarak humeral baş depresör kas ko-aktivasyon eğitiminin konservatif tedavi programına eklenmesinin; istirahat, aktivite, Neer ve Kennedy-Hawkins olmak üzere 4 farklı pozisyonda ağrının azaltılmasına olumlu etkisi vardır. İnternal rotasyon hareketi dışında fleksiyon, abduksiyon ve eksternal rotasyon eklem hareket açıklığının artırılmasında olumlu etkisi vardır.

Çalışmamız, Selçuk Üniversitesi Sağlık Bilimleri Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu tarafından onaylandı (2020-622). Çalışma öncesi tüm bireylerin yazılı ve sözlü onamları alındı ve ayrıca çalışma Helsinki Bildirgesi'ne uyumlu şekilde gerçekleştirildi.

Kaynaklar

1. *Andersson HI, Ejlertsson G, Leden I, Rosenberg C. Chronic pain in a geographically defined general population: studies of differences in age, gender, social class, and pain localization. Clin J Pain 1993;9:174-182.*
2. *Steenbrink F, de Groot JH, Veeger HE, van der Helm FC, Rozin PM. Glenohumeral stability in simulated rotator cuff tears. J Biomech 2009;42:1740-1745.*
3. *de Witte PB, Overbeek CL, Navas A, Nagels J, Reijnierse M, Nelissen RG. Heterogeneous MR arthrography findings in patients with subacromial impingement syndrome – Diagnostic subgroups? J Electromyogr Kinesiol 2016;29:64-73.*
4. *Deutsch A, Altchek DW, Schwartz E, Otis JC, Warren RF. Radiologic measurement of superior displacement of the humeral head in the impingement syndrome. J Shoulder Elbow Surg 1996;5:186-193.*
5. *Graichen H, Bonel H, Stammberger T, Haubner M, Rohrer H, Englmeier KH, Reiser M, Eckstein F. Three-dimensional analysis of the width of the subacromial space in healthy subjects and patients with impingement syndrome. AJR Am J Roentgenol 1999;172:1081-1086.*
6. *Overbeek CL, Kolk A, de Groot JH, et al. Altered Cocontraction Patterns of Humeral Head Depressors in Patients with Subacromial Pain Syndrome: A Cross-sectional Electromyography Analysis. Clin Orthop Relat Res 2019;477(8):1862-1868.*
7. *Hinterwimmer S, Eisenhart-Rothe R, Siebert M, Putz R, Eckstein F, Vogl, T. Influence of adducting and abducting muscle forces on the subacromial space width. Med Sci Sport Exer 2003;35:2055–2059.*
8. *Steenbrink F, de Groot JH, Veeger HE, Meskers CG, van de Sande MA, Rozing PM. Pathological muscle activation patterns in patients with massive rotator cuff tears, with and without subacromial anaesthetics. Man Ther 2006;11:231–237.*
9. *de Witte PB, van der Zwaal P, Visch W, et al. Arm adductor with arm abduction in rotator cuff tear patients vs. healthy -- design of a new measuring instrument [corrected] [published correction appears in Hum Mov Sci 2013 Aug;32(4):875-6].*
10. *Boudreau N, Gaudreault N, Roy JS, Bédard S, Balg F. The Addition of Glenohumeral Adductor Coactivation to a Rotator Cuff Exercise Program for Rotator Cuff Tendinopathy: A Single-Blind Randomized Controlled Trial. J Orthop Sports Phys Ther 2019;49(3):126-135.*
11. *Kanık EA, Taşdelen B, Erdoğan S. Klinik denemelerde randomizasyon 2011.*
12. *Thigpen CA, Shaffer MA, Gaunt BW, Leggin BG, Williams GR, Wilcox RB 3rd. The American Society of Shoulder and Elbow Therapists' consensus statement on rehabilitation following arthroscopic rotator cuff repair. J Shoulder Elbow Surg 2016;25(4):521-535.*
13. *Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17(1):45-56.*
14. *Menek B, Tarakci D, Algun ZC. The effect of Mulligan mobilization on pain and life quality of patients with Rotator cuff syndrome: A randomized controlled trial. J Back Musculoskelet Rehabil 2019;32(1):171-178.*
15. *Hall MC. The Velpeau bandage. Can Med Assoc J 1963;88(2):92-93.*
16. *Juul-Kristensen B, Larsen CM, Eshoj H, et al. Positive effects of neuromuscular shoulder exercises with or without EMG-biofeedback, on pain and function in participants with subacromial pain syndrome - A randomised controlled trial. J Electromyogr Kinesiol 2019;48:161-168.*
17. *Yakut E, Dalkılınç M, Kaya D. Kanıta dayalı elektroterapi. Ankara, Pelikan Yayıncılık 2008;43-203.*
18. *Overbeek CL, Kolk A, Nagels J. Increased co-contraction of arm adductors is associated with a favorable course in subacromial pain syndrome. J Shoulder Elbow Surg 2018;27(11):1925-1931.*
19. *de Witte PB, Henseler JF, van Zwet EW, Nagels J, Nelissen RG, de Groot JH. Cranial humerus translation, deltoid activation, adductor co-activation and rotator cuff disease - different patterns in rotator cuff tears, subacromial impingement and controls. Clin Biomech (Bristol, Avon) 2014;29(1):26-32.*
20. *Busse ME, Wiles CM, Van Deursen RWM. Muscle co-activation in neurological conditions. Physical therapy reviews 2005;10(4):247-253.*
21. *Andrade R, Araújo RC, Tucci HT, Martins J, Oliveira AS. Coactivation of the shoulder and arm muscles during closed kinetic chain exercises on an unstable surface. Singapore Med J 2011;52(1):35-41.*

ARAŞTIRMA MAKALESİ / *Research Article*

Üst ve Alt Gastrointestinal Sistem Endoskopisi Yapılan Çocuklarda Gastrointestinal Kanamalarının Retrospektif Değerlendirilmesi

Retrospective Evaluation of Gastrointestinal Bleeding in Children with Upper and Lower Gastrointestinal System Endoscopy

Engin Gerçeker[1], Erhun Kasırga[2], Güzide Doğan[3], Buse Soysal[1]

[1] S.B.Ü. Dr. Behçet Uz Çocuk Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi, İzmir Türkiye
[2] Maltepe Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları AnabilimDalı, İstanbul
[3] Bezm-i Alem Vakıf Üniversitesi Tıp Fakültesi Hastanesi, İstanbul

Yazışma Adresi / *Correspondence:*
Engin Gerçeker
S.B.Ü. Dr. Behçet Uz Çocuk Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi, İzmir Türkiye
T: **+90 530 641 13 69** E-mail **: engingerceker83@gmail.com**

Geliş Tarihi / Received : **22.08.2020** Kabul Tarihi / Accepted : **04.12.2020**

Orcid :
Engin Gerçeker https://orcid.org/0000-0002-8136-2980
Erhun Kasırga https://orcid.org/0000-0002-8113-286X
Güzide Doğan https://orcid.org/0000-0003-4291-7282
Buse Soysal https://orcid.org/0000-0002-0191-5283

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):53-60) DOI: 10.31832/ smj.784167

Öz

Amaç Bu çalışma, çocuklarda gastrointestinal sistem (GİS) kanama sıklığını, kanamanın etiyolojik nedenlerini ve sosyodemografik değişkenlere göre dağılımını ortaya koymak amacıyla yürütülmüştür.

Gereç ve Yöntem Aralık 2013-Kasım 2015 tarihleri arasında Celal Bayar Üniversitesi Tıp Fakültesi Çocuk Gastroenteroloji Bölümüne GİS kanaması nedeni ile başvuran ve endoskopik inceleme (özefagogastroduodenoskopi ve kolonoskopi) yapılan 70 çocuk hastanın verileri retrospektif olarak değerlendirilmiştir.

Bulgular Hastaların (35 kız, 35 erkek) ortalama yaşları 11±4.8 yıl (2-17 yıl) idi, 43 hastada (%61.4) üst GİS kanaması, 27 hastada (%38.6) alt GİS kanaması bulundu. Üst GİS kanaması olan hastaların 16'sının (% 37.3) nonsteroidantiinflamatuar ilaç (NSAİİ) veya aspirin kullandığı ve bu hastaların 8'inin 2-5 yaş arasında olduğu saptandı. Hastaların ortalama hemoglobin değeri 11.4±2.3 (4.8-16.9) g/dL, ortalama hematokrit değeri 34.6±7.0 (15-52) idi. Üst GİS kanamalı 16 hastada (% 37.2) histopatolojik inceleme sonucunda H. pylori pozitifliği saptandı. Alt GİS kanamalı 7 hasta (% 25.9) inflamatuar bağırsak hastalığı tanısı aldı. Karaciğer sirozu olan 1 hasta özefagus varis kanaması nedeniyle kaybedildi.

Sonuç Çocukluk çağında sık kullanılan NSAİİ'ler tedavi dozlarında bile üst GİS kanamalarına neden olabilir. Gereksiz NSAİİ kullanımından kaçınılmalıdır. Adölesan dönemdeki alt GİS kanamalarının önemli nedenlerinden birisinin inflamatuar bağırsak hastalıkları olduğu unutulmamalıdır.

Anahtar Kelimeler Endoskopi; çocuk; gastrointestinal kanama

Abstract

Objective *This study was conducted to reveal the frequency of gastrointestinal system (GI) bleeding, etiological causes of bleeding, and its distribution according to sociodemographic variables in children.*

Materials and methods *Seventy pediatric patients' data who applied to Celal Bayar University Faculty of Medicine, Department of Pediatric Gastroenterology due to GIS bleeding between December 2013 and November 2015 and underwent endoscopic examination (esophagogastroduodenoscopy and colonoscopy) were evaluated retrospectively.*

Results *The patients' (35 female, 35 male) mean age was 11 ± 4.8 years (2-17 years), 43 patients (61.4%) had upper GI bleeding, and 27 patients (38.6%) had lower GI bleeding. It was found that 16 (37.3%) of the patients with upper GI bleeding were using nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin, and 8 of these patients were between 2-5 years. The mean hemoglobin level of patients was 11.4 ± 2.3 (4.8-16.9) g / dL, and the hematocrit level was 34.6 ± 7.0 (15-52). Sixteen patients (37.2%) with upper GI bleeding were positive for H. pylori at histopathological examination. Seven patients (25.9%) with lower GI bleeding were diagnosed with inflammatory bowel disease. One patient with liver cirrhosis died due to esophageal variceal bleeding.*

Conclusion *The NSAIDs are commonly used in childhood can lead to upper GI bleeding, even in therapeutic doses. Unnecessary NSAIDs use should be avoided. One of the important causes of lower GI bleeding in adolescents should be noted that inflammatory bowel disease.*

Keywords *Endoscopy; child; gastrointestinal bleeding.*

GİRİŞ

Gastrointestinal sistem (GİS) kanamaları hekimler açısından önemli pediatrik acil durumlardan biridir. Çocuklarda gastrointestinal kanama, anal fissür veya inek sütü proteini alerjisi ile ilişkili dışkıdaki az miktardaki kanamadan, portal hipertansiyon veya peptik ülser hastalığına bağlı yaşamı tehdit edici kanamalara kadar geniş bir spektrumu içermektedir. Ciddi kanama, hayatı tehdit eden acil klinik tabloya yol açabileceğinden hızlı tanı konulup uygun tedavi başlanılmalıdır.[1]

Gastrointestinal sistem kanamaları, üst ve alt olarak iki gruba ayrılmaktadır. Üst GİS kanamalar, özefagusun üst kısmı ile Treitz ligamenti arası herhangi bir yerde lümen içine kanamalardır. Treitz ligamentinin distalinden olan kanamalar ise alt GİS kanaması olarak tanımlanmaktadır.[1] GİS kanamaların çoğu üst GİS kaynaklıdır. Üst GİS kanama nedenleri yaşa, coğrafi bölgeye göre değişebilmektedir. Doğu ülkelerinde en sık neden portal hipertansiyona (PHT) bağlı iken, batı toplumlarında gastrik ve duodenal ülser gibi varis dışı nedenlere bağlı gelişebilmektedir. Çocukluk çağında sık olarak kullanılan aspirin, ibuprofen gibi non-steroid anti-inflamatuvar ilaç (NSAİİ) kullanımına bağlı kanamalar görülmektedir.[2]

Alt GİS kanamalar ise, yenidoğan döneminde anal fissür, nekrotizan enterokolit (NEK), allerjik kolit; süt çocukluğu döneminde anal fissür, invajinasyon, okul öncesi ve okul çağı döneminde juvenil polip, inflamatuar bağırsak hastalığı (İBH), Meckel divertikülü, bakteriyel enterit gibi nedenlere bağlı olabilir.[3] Pediatrik populasyonda GİS kanamalarında tanı-tedavide endoskopik ve radyolojik yöntemler gelişmişse de, GİS kanamaların etyolojisine ilişkin bilgiler yetersizdir. GİS kanaması olan çocuğunun durumu stabilleştikten sonra, kanamanın yeri, kanamaya neden olabilecek patolojilerin araştırılması oldukça önemlidir.

Bu bilgiler doğrultusunda bizim çalışmamızdaki amacımız üst ve alt GİS endoskopisi yapılan çocuklarda GİS kanama sıklığını, kanamanın etiyolojik nedenlerini ve sosyodemografik değişkenlere göre dağılımını retrospektif olarak incelemektir.

GEREÇ ve YÖNTEMLER

Bu tanımlayıcı araştırmanın örneklemini, Aralık 2013-Kasım 2015 tarihleri arasında bir üniversite hastanesinin Pediatrik Gastroenteroloji Bilim Dalında üst ve alt GİS endoskopisi yapılan 70 hasta oluşturmuştur. Yenidoğan döneminde olan, kanama diyatezi olan, sepsis öyküsü olan ve Munchausen by Proxy sendromu tanısı alan hastalar araştırmadan dışlanmıştır.

Araştırma verileri toplanmadan önce, Celal Bayar Üniversitesi Hafsa Sultan Hastanesi Yerel Etik Kurulundan onay alınmıştır (03/08/2016 20.478.486-282). Literatür doğrultusunda geliştirilen anket formu aracılığıyla, alt ve/veya üst GİS kanama teşhisiyle Pediatrik Gastroenteroloji Bilim Dalında alt veya üst GİS endoskopisi yapılan 70 hasta retrospektif olarak tanımlanmıştır. Çalışma Helsinki Deklarasyonu Prensipleri'ne uygun olarak yürütülmüştür.

Aralık 2013-Kasım 2015 tarihleri arasında endoskopi yapılan 70 hastanın dosyaları incelenerek, hastaların yaş, cinsiyet, GİS kanaması tipi, geçirilmiş GİS kanaması öyküsü, ailede GİS kanaması öyküsü, ailede ülser öyküsü, ailede geçirilmiş GİS operasyonu öyküsü, üst ve alt GİS kanama etyolojileri, üst ve alt GİS kanaması olan hastaların başvuru yakınmaları, ilaç kullanım öyküsü, fizik muayenede saptanan bulgular, hemoglobin (Hb), hematokrit (Htc), ortalama eritrosit hacmi (OEH), karaciğer ve böbrek fonksiyon testleri, koagulasyon parametreleri, histopatolojik inceleme sonuçları, *H. pylori* öyküsüne ilişkin bilgiler elde edilmiştir. Hastalara endoskopi işlemi Olympus Exera II CV180 Pediatrik Video Endoskop ve Kolonoskop ile yapılmıştır. Hastaların yaşları 2-17 arasında değişmektedir. Hastalar 2-5 yıl, 6-11 yıl ve 12-17 yıl olarak gruplandırılarak, yaş gruplarına göre alt ve üst GİS kanama etiyolojileri değerlendirilmiştir. Kanama tipine göre (alt ve üst GİS kanama) hastaların başvuru yakınmaları, ilaç kullanımı öyküsü, hastalarda görülen semptomlar, fizik muayene

bulguları değerlendirilmiştir. Hastaların Hb, Htc ve OEH değerlerine ilişkin ortalamalar hesaplanmıştır. Kanama tipi ve histopatoloji sonuçları değerlendirilmiştir. SPSS 23.0 for Windows istatistik programı kullanarak, hastaların tanıtıcı özellikleri sayı ve yüzdelik bulgular olarak değerlendirilmiştir.

BULGULAR

Hastaların yaş ortalaması 11±4.8 yıl (2-17 yıl) olup, % 55.8'i 12-17 yaş grubunda, % 50.0'si erkektir. Hastaların % 61.4'ü üst GİS kanamasıdır ve % 34.3'ünde geçirilmiş GİS kanaması öyküsü vardır. Ailelerinin % 81.1'inde GİS kanaması ya da ülser öyküsü mevcuttur (Tablo 1).

Tablo 1. Gastrointestinal kanaması olan çocukların tanıtıcı özellikleri

Değişkenler	**Sayı**	**%**
Yaş Grubu		
2-5 yaş	14	20.0
6-11 yaş	17	24.2
12-17 yaş	39	55.8
Yaş ortalaması	**M ± SS**	**Min.-Max.**
	11 ± 4.8 yıl	2-17
Cinsiyet	**Sayı**	**%**
Kız	35	50.0
Erkek	35	50.0
Kanamanın tipi		
Alt GİS	27	38.6
Üst GİS	43	61.4
Geçirilmiş GİS kanaması		
Evet	24	34.3
Hayır	46	65.7
Ailede GİS kanaması öyküsü		
Evet	9	12.9
Hayır	61	81.1
Ailede ülser öyküsü		
Evet	9	12.9
Hayır	61	81.1
Ailede geçirilmiş GİS operasyonu öyküsü		
Evet	5	7.1
Hayır	65	92.9
Toplam	**70**	**100.0**
M: Ortalama, SS:Standart sapma, GİS:Gastrointestinal		

Üst GİS kanamalı hastaların etyolojisi incelendiğinde; % 69.8'inde eroziv gastrit/bulbit, % 16.2'sinde gastrik-duodenal ülser, % 7'sinde özefageal varis, % 4.7'sinde özefajit ve % 2.3'ünde vasküler malformasyon saptanmıştır. Yaş gruplarına göre etyoloji incelendiğinde ise, 2-5 yaş grubunda (% 55.6), 6-11 yaş grubunda (% 81.9), 12-17 yaş grubunda (% 69.6) en sık eroziv gastrit, bulbit saptanmıştır.

Alt GİS kanamalı hastaların etyolojisi incelendiğinde; % 29.6'sında İBH, % 14.8'sinde hemoroid, % 14.8'sinde anal fissür, % 14.8'sinde rektal polip, % 11.1'inde soliter rektal ülser, % 7.4'ünde normal kolonoskopik inceleme (Meckel divertikülü), % 3.7'sinde familyal polipozis koli ve % 3.7'sinde arteriovenöz malformasyon saptanmıştır. Yaş gruplarına göre etyoloji incelendiğinde ise, 2-5 yaş grubunda en sık anal fissür (% 40.0) ve rektal polip (% 40.0), 6-11 yaş grubunda en sık İBH (% 33.3) ve anal fissür (% 33.3), 12-17 yaş grubunda en sık İBH (% 31.3) ve hemoroid (% 25.0) saptanmıştır.

Alt GİS kanamalı hastaların % 92.6'sında rektal kanama, % 70.4'ünde kabızlık, üst GİS kanamalı hastaların ise % 83.7'sinde ağızdan kan gelmesi, % 51.2'sinde bulantı, % 48.8'inde karın ağrısı, %39.5'inde siyah dışkıen sık başvuru yakınmaları idi (Tablo 2).

Tablo 2: Gastrointestinal kanaması olan çocuklarda kanamanın tipine göre görülen semptomlar

	Kanama Tipi			
	Alt GİS kanaması		Üst GİS kanaması	
Semptomlar	**Sayı**	**%**	**Sayı**	**%**
Ağızdan kan gelmesi				
Evet	3	11.1	36	83.7
Hayır	24	88.9	7	16.3
Siyah Dışkı				
Evet	2	7.4	17	39.5
Hayır	25	92.6	26	60.5
Karın ağrısı				
Evet	7	25.9	21	48.8
Hayır	20	74.1	22	51.2
Bulantı				
Evet	2	7.4	22	51.2
Hayır	25	92.6	21	48.8
Halsizlik				
Evet	6	22.2	10	23.3
Hayır	21	77.8	33	76.7
Baş Dönmesi				
Evet	1	3.7	8	19.0
Hayır	26	96.3	34	81.0
Dispepsi				
Evet	-	0.0	6	14.0
Hayır	27	100.0	37	86.0
Rektal kanama				
Evet	25	92.6	1	2.3
Hayır	2	7.4	42	97.7
Kabızlık				
Evet	19	70.4	-	0.0
Hayır	8	29.6	43	100.0
Toplam	**27**	**100.0**	**43**	**100.0**

Üst GİS kanama nedeni ile endoskopi yapılan hastalardan 16'sının (% 37.3) NSAİİ veya aspirin kullandığı ve bu hastaların 8'inin 2-5 yaş arasında olduğu saptanmıştır (2-5 yaşta 8 hasta, 6-11 yaşta 3 hasta, 12-17 yaşta 5 hasta). Alt GİS kanamalı hastaların % 48.2'inde rektal tuşede kitle, % 33.3'ünde solukluk, üst GİS kanamalı hastaların ise % 58.1'inde solukluk, % 41.9'unda taşikardi, % 39.5'inde rektal tuşede melena en sık fizik muayene bulguları idi (Tablo 3).

Tablo 3: Gastrointestinal kanaması olan çocuklarda kanama tipine göre görülen fizik muayene bulguları

	Kanama Tipi			
	Alt GİS kanaması		Üst GİS kanaması	
Semptomlar	**Sayı**	**%**	**Sayı**	**%**
Fizik muayene bulguları				
Hepatomegali				
Evet	2	7.4	4	9.3
Hayır	25	92.6	39	90.7
Splenomegali				
Evet	-	0.0	3	7.0
Hayır	27	100.0	40	93.0
Rektal tuşede melena				
Evet	1	3.7	17	39.5
Hayır	26	96.3	26	60.5
Taşikardi				
Evet	2	7.7	18	41.9
Hayır	24	92.3	25	58.1
Solukluk				
Evet	9	33.3	25	58.1
Hayır	18	66.7	18	41.9
Siroz				
Evet	-	0.0	2	4.7
Hayır	27	100.0	41	97.1
Batında Kitle				
Evet	-	0.0	1	2.3
Hayır	27	100.0	42	97.7
Rektal tuşede kitle				
Evet	13	48.1	-	0.0
Hayır	14	51.9	43	100.0
Toplam	**27**	**100.0**	**43**	**100.0**

GİS: Gastrointestinal

Hastaların ortalama hemoglobin değeri 11.4±2.3 (4.8-16.9) g/dL, ortalama hematokrit değeri % 34.6±7.0 (15-52) ve ortalama OEH değeri 80.8±7.6 fl (62.5-97.3) idi. Karaciğer, böbrek fonksiyon testleri ve koagülasyon parametreleri normaldi. Üst GİS kanamalı 16 hastada (% 37.2) histopatolojik inceleme sonucunda *H. pylori* pozitifliği saptandı ve hastalara eradikasyon tedavisi verildi. Hastaların % 60.5'inde normal patoloji saptanmıştır. Tirozinemiye bağlı hepatoselüler karsinom ve karaciğer sirozu olan 1 hasta bant ligasyonu yapılmasına rağmen özefagus varis kanaması nedeniyle kaybedildi.

Alt GİS kanamalı 7 hasta (% 25.9) histopatolojik inceleme sonucunda İBH (2 hasta crohn hastalığı, 5 hasta ülseratif kolit) tanısı almıştır. Hastaların % 14.8'inde polip, % 7.4'ünde Meckel divertikülü saptanmıştır (Tablo 4). Üst GİS kanamalı hastalarda histopatolojik inceleme sonucunda *H. pylori* saptananların % 68.8'inde karın ağrısı saptanmıştır.

Tablo 4: Gastrointestinal kanaması olan çocuklarda kanama tipine göre histopatoloji sonuçları

	Kanama Tipi			
	Alt GİS kanaması		**Üst GİS kanaması**	
Histopatoloji Sonuçları	**Sayı**	**%**	**Sayı**	**%**
Helikobakter pylori	-	0.0	16	37.2
İBH	7	25.9	-	0.0
Meckel divertikülü	2	7.4	-	0.0
Polip	4	14.8	1	2.3
Granülomatoz kolit	1	3.7	-	0.0
Normal patoloji	13	48.1	26	60.5
Toplam	**27**	**100.0**	**43**	**100.0**

GİS:Gastrointestinal, İBH: inflamatuar bağırsak hastalığı

TARTIŞMA

Üst ve alt GİS endoskopisi yapılan çocuklarda GİS kanamalarının etiyolojik nedenlerini ve sosyodemografik değişkenlerle ilişkisini retrospektif olarak incelediğimiz çalışmamızda, üst GİS kanamaları alt GİS kanamadan daha sık görülmüştür. Çocuklarda GİS kanamalarının sıklığı konusunda yeterli veri bulunmamaktadır. Yapılan çalışmalar genellikle pediatrik yoğun bakım ünitelerinde gerçekleştirilmiştir. Chaibou ve ark.'nın çalışmasında çocuk yoğun bakım ünitesine yatırılan 1006 çocuğun % 10.2'sinin üst GİS kanama tanısı aldığı bildirilmiştir.[4] Lacroix ve ark.'nın çalışmasında çocuk yoğun bakım ünitesinde yatırılan 984 çocuğun % 6.4'ünde üst GİS kanama gözlenmiştir.[5] Pant ve ark.'nın Amerika'da hastanelerde yatırılarak tedavi edilen çocuklarda GİS kanama epidemiyolojisini araştırdığı çalışmasında, 23383 çocuk hastanın GİS kanama tanısıyla taburcu edildiği ve bu sayının tüm taburcuların % 0.5'ini oluşturduğu saptanmıştır.[6]

Yaklaşık iki yıllık süreçte, araştırma kriterlerine uyan tüm hastaları incelediğimiz çalışmamızda, GİS kanamalar 12-17 yaş grubunda daha sık görülmüş olup, hastaların yaş ortalaması 11 yıl idi. Pant ve ark.'nın çalışmasında da, GİS kanama insidansı en sık 11-15 yaş grubunda görülmüş olup, en az 1 yaşından küçüklerde görülmüştür.[6] Çocukluk döneminde, yaş gruplarına göre GİS kanama nedenleri değişebilmekte ve her yaşta çocukta kanama görülebilmektedir. Çalışmamızda GİS kanamaları her iki cinsiyette de eşit olarak saptanmıştır. Literatürde ise, erkek cinsiyette daha sık görüldüğü belirtilmekte olup, nedenine ilişkin bir veri mevcut değildir.[6,7] Akçam ve ark.'nın çalışmasında, bizim çalışmamıza benzer olarak, üst GİS kanama nedeniyle endoskopi yapılan 54 çocukta da, cinsiyet açısından fark saptanmamıştır.[8]

Üst GİS kanamalı hastaların etyolojisi incelendiğinde en sık eroziv gastrit/bulbit saptanmıştır. Yu ve ark.'nın 1218 Çinli çocuğu üst GİS kanama açısından inceledikleri retrospektif çalışmalarında, çocukların % 76.4'ünde kanama kaynağı saptanmış olup, en sık rastlanan endoskopik bulgu eroziv gastrit (% 33.5) ve duodenal ülser (% 23.2) idi. Eroziv gastritin yaşla birlikte azaldığı, duodenal ülserin ise yaşla birlikte arttığını bildirmişlerdir.[9] Bizim çalışmamızda ise, yaş gruplarına göre etyolojilerin benzer olduğu görülmüştür. Ünal ve ark.'nın çocuklarda üst GİS kanamalarının etyolojisini inceledikleri çalışmalarında, üst GİS kanamalarının %15.1'inin varis ve %70.5'inin varis dışı kaynaklı olduğunu saptamışlardır.[2] Rafeey ve ark.'nın çalışmasında üst GİS kanamalı 447 çocuk hastada, en sık rastlanan endoskopik tanının özefajit ve eroziv özefajit olduğu belirtilmiştir.[10] Mrad ve ark.'ı üst GİS kanamasıyla başvuran çocuklarda, süt çocuklarının % 27.8'inde peptik özefajit, çocukların ise %10'unda peptik özefajit, %1.6'sında peptik ülser, % 1.8'inde Mallory-Weiss yırtığı ve %1.6'sında varis tipi lezyonlar olduğunu bildirilmişlerdir.[11] Literatüre benzer olarak, bizim çalışmamızda üst GİS kanamalı hastaların % 69.8'i eroziv gastrit/bulbit, % 16.2'si gastrik-duodenal ülser, % 7'si özefageal varis, % 4.7'si özefajit ve % 2.3'ü vasküler malformasyon tanısı almıştır.

Alt GİS kanamalı hastaların etyolojisi incelendiğinde en sık İBH saptanmıştır. Alt GİS kanamalı 7 hasta (% 25.9) histopatolojik inceleme sonucunda İBH (2 hasta crohn hastalığı, 5 hasta ülseratif kolit) tanısı almıştır. İBH, çocuklarda alt GİS kanamalarının en sık karşılaşılan sebeplerinden biridir. Çin'de her yaş grubunu içeren 53.951 hastayla yapılan bir çalışmada, kolerektal kanser-polip, kolit, anorektal hastalık ve İBH'nin yetişkin ve yaşlı populasyonunda; kolerektal polip, kronik kolit, invajinasyon ve İBH'nin de Çinli çocuklarda alt GİS kanamaların ana nedenleri olduğu belirtilmiştir.[12]

Khushdil ve ark.'nın 80 çocuk hastada alt GİS kanamaların etyolojisini inceledikleri çalışmalarında, en sık saptanan kolonoskopik tanı polipti (% 58.7) ve kolon yerleşimliydi. Hastaların % 21.2'sinde de kolit saptanmış olup çoğu 2-6 yaş arasındaydı.[13] Polipler çocuklardaki GİS tümörlerinin en sık nedenidir ve alt GİS kanamanın önemli bir sebebidir.[14] Çinli çocuklarla yapılan bir çalışmada, kolonoskopi yapılan 82 çocuğun %50.6'sı (n=40) tanı almış olup, 23 çocukta polip, 12 çocukta ise Crohn hastalığı saptanmıştır. Poliplerin % 80'inin rektosigmoid kolonda olduğu belirtilmiştir. Aynı çalışmada, İBH'li çocukların yaş ortalaması 11.3 yıl, polipli çocukların yaş ortalaması ise 4.3 yıl olarak saptanmıştır.[15] Bizim çalışmamızda da, yaş gruplarına göre alt GİS kanamalarının etyolojileri incelendiğinde ise, 2-5 yaş grubunda en sık anal fissür ve rektal polip , 6-11 yaş grubunda en sık İBH ve anal fissür, 12-17 yaş grubunda en sık İBH ve hemoroid saptanmıştır. İran'da 363 çocukla yapılan bir çalışmada da, alt GİS kanamalarının 2-10 yaş aralığında yaygın olduğunu, en sık kolonoskopik bulgunun sigmoid kolon polipi (% 25.1) ve en sık patolojik bulgunun da juvenil polip (% 23.1) olduğu belirtilmiştir.[16] Aktif rektal kanaması olan 2-12 yaş arası 174 Mısırlı çocukla yapılan bir çalışmada da, hastaların % 57.4'ünde rektal polip saptanmıştır.[17] Rektal kanamalı 194 Mısırlı çocukta yapılan bir diğer çalışmada da, rektal kanamanın en sık sebebi enfeksiyöz enterokolit (% 37.1) olup diğer sebepler sırasıyla kolerektal polip (% 21.1), kronik kolit (% 16), alerjik kolit (% 2.6), soliter rektal ülser sendromu (% 1.5) ve nonspesifik kolit (% 6.7) idi.[18] Thakkar ve ark.'nın çalışmasında alt GİS yakınması ile başvuran hastaların % 12'sinde kolorektal polip saptadıkları, polipi olan hastaların yaşlarının, olmayanlardan daha küçük ve erkek cinsiyetin hakim olduğu (% 58.3) bildirilmiştir.[19] Bizim çalışmamızda da benzer olarak, rektal polip 2-5 yaş grubunda daha sıktır. Ek olarak hastaların %14.8'inde polip, %7.4'ünde Meckel divertikülü, % 3.7'sinde granülomatoz kolit saptanırken, % 48.1'inde patoloji sonucu normal bulunmuştur.

Üst GİS kanamalı hastaların başvuru yakınmaları incelendiğinde; % 83.7'sinin hematemez, % 51.2'sinin bulantı-kusma, % 48.8'inin karın ağrısı, % 39.5'inin melena, % 23.3'ünün halsizlik ve % 19'unun baş dönmesi nedeniyle başvurdukları saptanmıştır. Rafeey ve ark.'nın çalışmasında üst GİS kanamalarında klinik bulgular sırasıyla, hematemez (% 26.8), melena (% 13.4) ve hematokezya (% 2.4) olarak saptanmıştır.[10] Diğer bir çalışmada da, klinik bulgular sırasıyla, hematemez (% 59.3), melena (% 22.6) ve her iki bulgu birden hastaların % 18.12'sinde saptanmıştır. Diğer önemli semptomlar ise abdominal ağrı (% 46.2) ve halsizlik (% 6.3) olup, hastaların % 2.2'sinde hipovolemik şok saptanmış, % 11'ine transfüzyon uygulanmıştır.[9] Çalışmamızda, hematemez en sık rastlanan semptomdu. Bu durum diğer araştırmalarda da gözlenmektedir. [9,10]

Hematemez ve melena her ikisi de ciddi kanamalardır, çalışmamızda tüm hastaların ortalama hemoglobin değeri 11.4±2.3 (4.8-16.9) g/dl, ortalama hematokrit değeri % 34.6±7.0 (15-52) ve ortalama OEH değeri 80.8±7.6 (62.5-97.3) fl idi. Yu ve ark.'nın çalışmasında hematemez ve melenanın her ikisinin birden görüldüğü grupta, Hb, OEH değerlerinin sadece hematemez ya da melena görülen gruptan daha düşük olduğu saptanmıştır.[9]

Alt GİS kanamalı hastaların başvuru yakınmaları incelendiğinde; %92.6'sının hematokezya, % 70.4'ünün kabızlık, % 25.9'unun karın ağrısı, % 22.2'sinin halsizlik, %7.4'ünün melena ve bulantı-kusma ve % 3.7'sinin baş dönmesi nedeniyle başvurdukları saptanmıştır. İran'da yapılan bir ça-

lışmada da, alt GİS kanamalı hastaların %80.2'sinde hematokezya, %18.1'inde kanlı diyare ve %1.7'sinde pozitif gizli kan bulgusu saptanmıştır.[16] Aktif rektal kanaması olan 174 Mısırlı çocukla yapılan bir çalışmada da, aktif rektal kanamanın yanısıra 74 çocukta farklı nedenler saptanmıştır. Bu nedenler intestinal amebiazis (42), diyare (18), ciddi konstipasyon (2) ve intestinal şistosomiazis (2) idi.[17] Okul öncesi ve okul çağı çocuklarında rektal kanamanın en sık sebebi fissür formasyonu ile birlikte konstipasyon olabilir. Alt GİS kanamaları yaşa göre farklı bulgular sergileyebilir. Eğer çocukta hipovolemi bulgusu varsa, hemodinamik stabilizasyon sağlanmalı, aktif kanama durdurulmalı ve tekrarlayan kanama önlenmelidir.[20]

Üst GİS kanama nedeni ile endoskopi yapılan hastalardan 16'sının (% 37.3) NSAİİ veya aspirin kullandığı ve bu hastaların 8'inin 2-5 yaş arasında olduğu saptanmıştır. Kalyoncu ve ark.'nın 2 yaşından küçük 34 çocukta GİS kanama etyolojisini incelediği çalışmasında da, hastaların %56'sının NSAİİ aldığı belirtilmiştir.[7] Ünal ve ark.'ı da çalışmalarında, hastaların %26.6'sında ilaç kullanım öyküsünün mevcut olduğu, en sık 3-9 yaş grubu hastaların ilaç kullanmakta olduğunu saptamışlardır (% 25.9).[2] Küçük yaş gruplarında antipiretik kullanımına bağlı olarak üst GİS kanama insidansının çalışmamızdakine benzer olarak artmış olabileceği düşünülmektedir.

Bu çalışmada, üst GİS kanamalı 16 hastada (% 37.2) histopatolojik inceleme sonucunda *H. pylori* pozitifliği saptandı ve hastalara eradikasyon tedavisi verildi. Hastaların % 2.3'ünde vasküler malformasyon saptanırken, % 60.5'inde normal patoloji saptanmıştır. Mrad ve ark.'ı üst GİS kanamasıyla başvuran çocuklarda, 614 endoskopik değerlendirmenin % 20.6'sında endoskopik olarak etyoloji saptamamışlardır.[11] Üst GİS endoskopisi, üst GİS kanamalarının altında yatan nedeni saptamada tanısal bir prosedürdür, bu sayede çeşitli endoskopik lezyonlar görülerek uygun tedavi sağlanabilir.[10] Akçam ve ark.'nın çalışmasında da, hastaların % 40'ında *H. pylori* pozitifliği saptanmıştır.[8] Ülkemizde yapılan bir çalışmada da, GİS yakınması olan endoskopi yapılan 357 çocuğun % 13.2'sinde peptik ülser hastalığı saptandığı, 47 peptik ülser hastasının 38'inde H.pylori pozitif olduğu bildirilmiştir.[21] Çalışmamızda, üst GİS kanamalı hastalarda patoloji sonucunda *H. pylori* saptananların % 68.8'inde karın ağrısı saptanmıştır. Ecevit ve ark.'nın çalışmasında endoskopi yapılan 902 çocuk hastanın % 3.4'ünde peptik ülser hastalığı saptanmış olup, ülseri olan hastaların % 61'inde *H.pylori* pozitifliği bildirilmiştir.[22] Bu çalışmada *H.pylori* pozitif grupta üst GİS kanaması ve ağrı major semptomlar olarak belirtilmiştir. Ağrı semptomu ve *H. pylori* ilişkisini açıklayabilecek çalışmalara ihtiyaç duyulmaktadır.

Sonuç olarak NSAİİ kullanımına bağlı üst GİS kanaması olgularının yarısının 2-5 yaş döneminde ortaya çıktığı ve ergenlik dönemdeki alt GİS kanamalarının önemli nedenlerinden birisinin İBH olduğu saptanmıştır. Buna göre NSAİİ kullanımında dikkatli olunması ve ergenlik dönemindeki alt GİS kanamalarında İBH açısından değerlendirme yapılmasının önemli olduğu düşünülmüştür.

Çalışmanın Kısıtlılığı

Çalışmanın tek bir hastanede yürütülmesi ve katılımcı sayısının az olması araştırmanın sınırlılıklarını oluşturmaktadır.

Çıkar Çatışması

Yazarlar çıkar çatışması bildirmemiştir.

Etik onay

Çalışma protokolü Celal Bayar Üniversitesi Hafsa Sultan Hastanesi Yerel Etik Kurulu tarafından onaylanmıştır (03/08/2016 20.478.486-282).

Kaynaklar

1. *Wyllie R, Hyams JS, Kay M. Pediatric gastrointestinal and liver disease. 5th ed., Elsevier Health Sciences; 2015.*
2. *Ünal F, Şahin G, Ecevit Ç, Semizel E, Cebe A, Erdoğan H, et al. Çocuklarda Üst Gastrointestinal Sistem Kanamalarına Tanısal ve Tedavi Edici Endoskopik Yaklaşımlar. Güncel Pediatr 2012;10:1–7.*
3. *Kasırga E. Çocukluk Çağında Gastrointestinal Sistem Kanamaları. Türkiye Klin J Pediatr Sci 2005;1(8):21–31.*
4. *Chaïbou M, Tucci M, Dugas MA, Farrell CA, Proulx F, Lacroix J. Clinically significant upper gastrointestinal bleeding acquired in a pediatric intensive care unit: a prospective study. Pediatrics 1998;102:933–8.*
5. *Lacroix J, Nadeau D, Laberge S, Gauthier M, Lapierre G, Farrell CA. Frequency of upper gastrointestinal bleeding in a pediatric intensive care unit. Crit Care Med 1992;20(1):35–42.*
6. *Pant C, Sankararaman S, Deshpande A, Olyaee M, Anderson MP, Sferra TJ. Gastrointestinal bleeding in hospitalized children in the United States. Curr Med Res Opin 2014;30(6):1065–9.*
7. *Kalyoncu D, Urganci N, Cetinkaya F. Etiology of upper gastrointestinal bleeding in young children. Indian J Pediatr 2009;76(9):899–901.*
8. *Akçam M, Yılmaz A, Artan R. Üst gastrointestinal kanama nedeniyle endoskopi yapılan çocuklar: 54 hastanın retrospektif değerlendirilmesi. SDÜ Tıp Fak Derg 2006;13(1):22–6.*
9. *Yu Y, Wang B, Yuan L, Yang H, Wang X, Xiao Y, et al. Upper Gastrointestinal Bleeding in Chinese Children: A Multicenter 10-Year Retrospective Study. Clin Pediatr 2015;(197):1–6.*
10. *Rafeey M, Shoaran M, Majidy H. Diagnostic endoscopy and clinical characteristics of gastrointestinal bleeding in children: a 10-year retrospective study. Iran Red Crescent Med J 2013;15(9):794–7.*
11. *Mrad SM, Boukthir S, Brini I, Hachicha S, Samoud A. Endoscopic diagnosis in a Tunisian pediatric population with upper gastrointestinal bleeding. Tunis med 2013;91(11):655–60.*
12. *Bai Y, Peng J, Gao J, Zou D-W, Li Z-S. Epidemiology of lower gastrointestinal bleeding in China: single-center series and systematic analysis of Chinese literature with 53,951 patients. J Gastroenterol Hepatol 2011;26(4):678–82.*
13. *Khushdil A, Ali S, Malik R, Farrukh H. Etiology Of Lower Gastrointestinal Bleeding In Paediatric Patients, A Colonoscopic Surgery. Armed Forces Med J 2014;64(3):484–7.*
14. *Nikpour S, Ali Asgari A. Colonoscopic evaluation of minimal rectal bleeding in average-risk patients for colorectal cancer. World J Gastroenterol 2008;14(42):6536–40.*
15. *Tam YH, Lee KH, Chan KW, Sihoe JDY, Cheung ST, Mou JWC. Colonoscopy in Hong Kong Chinese children. World J Gastroenterol 2010;16(9):1119–22.*
16. *Zahmatkeshan M, Fallahzadeh E, Najib K, Geramizadeh B, Haghighat M, Imanieh MH. Etiology of lower gastrointestinal bleeding in children:a single center experience from southern iran. Middle East J Dig Dis 2012;4(4):216–23.*
17. *El-Shabrawi MHF, El Din ZE, Isa M, Kamal N, Hassanin F, El-Koofy N, et al. Colorectal polyps: a frequently-missed cause of rectal bleeding in Egyptian children. Ann Trop Paediatr 2011;31(3):213–8.*
18. *El-Khayat HA, El-Hodhod MA, Abd El-Basset FZ, Tomoum HY, El-Safory HA, Hamdy AM. Rectal bleeding in Egyptian children. Ann Trop Paediatr 2006;26(4):337–44.*
19. *Thakkar K, Alsarraj A, Fong E, Holub JL, Gilger MA, El Serag HB. Prevalence of colorectal polyps in pediatric colonoscopy. Dig Dis Sci 2012;57(4):1050–5.*
20. *Leung AKC, Wong AL. Lower gastrointestinal bleeding in children. Pediatr Emerg Care 2002;18(4):319–23.*
21. *Uğraş M, Pehlivanoğlu E. Helicobacter pylori infection and peptic ulcer in eastern Turkish children: is it more common than known? Turk J Pediatr 2011;53(6):632–7.*
22. *Ecevit ÇÖ, Özgenç F, Yüksekkaya HA, Ünal F, Arikan Ç, Yağci RV. Peptic ulcer disease in children: an uncommon disorder with subtle symptomatology. Turkish J Gastroenterol 2012;23(6):666–9.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Relationship Between the Coronary Artery Bypass Graft Operation and the Levels of Ceruloplasmin Enzymatic Activity as an Antioxidant

Koroner Arter Baypas Greft Operasyonu ile Antioksidan Olarak Seruloplazminin Enzimatik Aktivitesi Arasındaki İlişki

Özgür Altınbaş[1], Abdullah Tuncay Demiryurek[2], Mehmet Salih Aydın[3], Aydemir Koçarslan[4], Ata Niyazi Ecevit[5], İlker Mercan[6], Abdussamet Hazar[7], Erdal Ege[8]

[1] Gaziantep University, Vocational School of Health Services, Department of Operating Room Services, Gaziantep, Turkey
[2] Gaziantep University, Medical Faculty, Department of Medical Pharmacology, Gaziantep, Turkey
[3] Sanliurfa Harran University, Medical Faculty, Department of Cardiovascular Surgery, Sanliurfa, Turkey
[4] Kahramanmaras Sutcu Imam University, Medical Faculty, Department of Cardiovascular Surgery, Kahramanmaras, Turkey
[5] Ankara City Hospital, Department of Cardiovascular Surgery, Ankara, Turkey
[6] Tepecik Training and Research Hospital, Department of Congenital Heart Surgery, İzmir, Turkey
[7] Konya City Hospital, Department of Cardiovascular Surgery, Konya, Turkey
[8] Necmettin Erbakan University, Meram Medical Faculty, Department of Cardiovascular Surgery, Konya, Turkey

Yazışma Adresi / *Correspondence:*
Özgür Altınbaş

Gaziantep University, Vocational School of Health Services, Department of Operating Room Services, Gaziantep, Turkey
T: **+90 505 657 05 77** E-mail **: ozgur_altinbas@yahoo.com**

Geliş Tarihi / Received : **08.10.2020** Kabul Tarihi / Accepted : **17.12.2020**

Orcid :

Özgür Altınbaş https://orcid.org/0000-0002-6819-2454
Abdullah Tuncay Demiryurek https://orcid.org/0000-0002-9994-8541
Mehmet Salih Aydın https://orcid.org/0000-0002-6652-6035
Aydemir Koçarslan https://orcid.org/0000-0003-3874-8762
Ata Niyazi Ecevit https://orcid.org/0000-0002-8820-9305
İlker Mercan https://orcid.org/0000-0002-0295-2641
Abdussamet Hazar https://orcid.org/0000-0001-6245-8664
Erdal Ege https://orcid.org/0000-0002-2763-6223

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):61-66) DOI: 10.31832/smj.807518

Abstract

Objective	Ceruloplasmin is the major copper-carrying protein in the blood, and in addition plays a role in iron metabolism. Moreover, its antioxidant activity was showed in several studies. In this study, we investigated the relationship between coronary artery bypass graft operation and the levels of ceruloplasmin enzymatic activity.
Materials and Methods	The study included 120 patients who underwent coronary artery bypass graft operation. Peripheral blood samples were taken preoperatively, peroperatively –before and after cardiopulmonary bypass-, at postoperative 4th hour, 3rd day and 5th day. Blood samples before and after cardiopulmonary bypass were also taken from the coronary sinus. The enzymatic activity of ceruloplasmin levels were measured by Erel method.
Results	There was a gradual decrease in the enzymatic activity of ceruloplasmin levels after cardiopulmonary bypass. In the postoperative 4th hour and the 1st day, reduction was statistically significant in the blood samples taken peripherally (p=0.025). Activities increased in the postoperative 3rd and 5th days, respectively. According to the coronary sinus blood samples, there was also a significant decrease in the enzymatic activity of ceruloplasmin after cardiopulmonary bypass (p=0,035).
Conclusion	Our study showed significant differences in preoperative, peroperative and postoperative levels of the enzymatic activity of ceruloplasmin. The reduction in postoperative period during the 3rd day which was probably due to consumption as a respond to oxidant activity, demonstrated that cardiovascular bypass significantly increased oxidative stress. Enzymatic activity of the ceruloplasmin may be one of the parameters that reflect the response of inflammatory and oxidative stress associated with cardiopulmonary bypass.
Keywords	ceruloplasmin; cardiopulmonary bypass; coronary artery bypass graft operation; enzymatic activity; oxidative stress

Öz

Amaç	*Seruloplazmin, kanda bakır taşıyan başlıca proteindir ve demir metabolizmasında da rol oynar. Ayrıca antioksidan aktivitesi birçok çalışmada gösterilmiştir. Bu çalışmada koroner arter baypas greft operasyonu ile seruloplazminin enzimatik aktivite düzeyleri arasındaki ilişkiyi araştırdık.*
Gereç ve Yöntemler	*Çalışmaya koroner arter baypas greft operasyonu geçiren 120 hasta dahil edildi. Periferik kan örnekleri ameliyat öncesi, ameliyat sonrası - kardiyopulmoner baypas öncesi ve sonrası-, ameliyat sonrası 4. saat, 3. gün ve 5. gün alındı. Koroner sinüsten de kardiyopulmoner baypas öncesi ve sonrası kan örnekleri alındı. Seruloplazmin düzeylerinin enzimatik aktivitesi Erel yöntemi ile ölçüldü.*
Bulgular	*Kardiyopulmoner baypas sonrası seruloplazmin düzeylerinin enzimatik aktivitesinde kademeli bir azalma oldu. Postoperatif 4. saat ve 1. gün periferden alınan kan örneklerinde azalma istatistiksel olarak anlamlıydı (p = 0,025). Aktiviteler sırasıyla postoperatif 3. ve 5. günlerde arttı. Koroner sinüs kan örneklerine göre de, kardiyopulmoner baypas sonrası seruloplazmin enzimatik aktivitesinde önemli bir azalma vardı (p = 0.035).*
Sonuç	*Çalışmamız, seruloplazmin enzimatik aktivitesinin preoperatif, peroperatif ve postoperatif düzeylerinde önemli farklılıklar gösterdi. Muhtemelen oksidan aktiviteye yanıt olarak tüketime bağlı olan postoperatif 3. gündeki azalma, kardiyovasküler baypasın oksidatif stresi önemli ölçüde artırdığını göstermiştir. Seruloplazmin enzimatik aktivitesi, kardiyopulmoner baypas ile ilişkili enflamatuar ve oksidatif stresin tepkisini yansıtan parametrelerden biri olabilir.*
Anahtar Kelimeler	*seruloplazmin; kardiyopulmoner baypas; koroner arter baypas greft operasyonu; enzimatik aktivite; oksidatif stres*

INTRODUCTION

Morbidity and mortality are highly related with ischemia/reperfusion injury, surgical trauma and patient characteristics in cardiac surgery.[1] Oxidative stress is caused by an imbalance between antioxidants and free radicals and commonly seen in major surgical operations and especially in coronary artery bypass graft operation (CABG) and alters normal endothelial functions. It induces proinflammatory, proliferative, prothrombotic, and vasoconstrictor mechanisms that form atherogenic processes. Beside these, oxidative stress and inflammatory response caused by cardiopulmonary bypass may result in myocardial damage and variable grade myocardial dysfunction.[2,3] In the literature, insufficient antioxidant defense and oxidative stress are reported in the pathogenesis of cardiovascular diseases.[4] Advanced age, significant co-morbidities and the cardiopulmonary bypass procedures are also associated with postoperative complications, increased length of hospital stay and enhanced degree of oxidative stress.[5]

The formation of Reactive Oxygen Species (ROS) after ischemic reperfusion triggers a chain of complex events. These oxidative events lead to increased lipid peroxidation, decrease of plasma antioxidants and the formation of other harmful metabolites.[1]

Ceruloplasmin (Cp) is an acute phase reactant with alpha-2-glycoprotein structure with a molecular weight of about 132 kDa.[6] It has ferro-O^2-oxidoreductase activity directed towards ferrous ion stimulated lipid peroxidation and formation of hydroxyl radical in Fenton reaction.[7] Cp has diverse functions. The known functions of Cp include copper transportation, iron metabolism, anti-oxidation, angiogenesis and coagulation. Cp is also effective in regulating vascular tone.[6] Since Cp inhibits nitric oxide (NO) synthesis, it can modify the vascular responses through NO.[8] Cp can also act as a pro-oxidant or an antioxidant. It catalyzes the oxidation of Fe^{+2} to Fe^{+3}.[9] It has also an antioxidant effect on LDL by blocking Cu^{+2}-induced lipid oxidation.[2]

The current study was designed to establish the relationship between cardiopulmonary bypass operation and the enzymatic activity of Cp levels in preoperative, preoperative and postoperative period in patients underwent CABG.

MATERIALS and METHODS

Patient Selection

The study was conducted prospectively between January 2016 to June 2018. The study was approved by the ethics committee of clinical research of Harran University with the decision no: 02-12-2010-06. The study population consisted of 120 consecutive patients undergoing coronary artery bypass graft surgery. Written informed consent was obtained from all participants. Patients' demographics were recorded. Patients with low ejection fraction (<25%), neoplastic disease, systemic inflammatory disease, infection, chronic obstructive pulmonary disease, major depression, liver and kidney disease, cardiac valve procedure, congenitally cardiac procedure, emergency cardiac procedure, off-pump CABG and recurrent cardiac surgery were excluded from the study.

Anesthetic and Surgical Techniques

Midazolam (10 mg/kg) 3 hours before the operation was administered intravenously to the patients for premedication. No other premedication was applied. Anesthesia consisted of a balanced opiate based general anesthesia technique. Propofol (1.5-2.2 mg/kg), rocuronium (0.6 mg/kg), and fentanyl (3 mg/kg) infusions were administered in induction. During the operation, anesthesia was maintained with continuous propofol infusion (10-20 ml/h), remifentanil (0.25-1 mg/kg) and rocuronium. Hemodynamic parameters were kept constant. Median sternotomy was performed under general anesthesia. The cannulation was done with aortic cannula and two stage venous cannula. Standard cardiopulmonary bypass was applied with mild hypothermia (26-32°C) and isothermic blood cardioplegia. Cardioplegia was performed by antegrade way from the aorta and retrograde way from the coronary si-

nus. Cardioplegia application was repeated in every 15-20 minutes. All the cases were applied with perfusion pressure was kept control of at 60-70 mm Hg. Full cardiac flow was maintained with 2,4 L/m^2. Routine heparinization was performed in operation (300 IU/kg). Throughout the operation, activated clotting time (ACT) was kept over 480 seconds. Standard protamine sulfate was applied at the exit from the cardiopulmonary bypass (120-150 IU). Intensive care follow-up of all patients were performed as standard. Cross clamp time, total operation time, cardiopulmonary bypass time, intensive care and hospitalization duration were recorded.

Blood Sample Collection and Enzymatic Activity of Ceruloplasmin Measurements

Blood samples were taken peripherally from all patients 24 hours before the operation, intraoperative-before cardiopulmonary bypass, after cardiopulmonary bypass-, postoperative 4th hour, postoperative 24th hour, postoperative 3rd day and postoperative 5th day for biochemical analysis. Blood samples before and after cardiopulmonary bypass was also taken from coronary sinus. Samples were kept at room temperature for 30 minutes and then separated from the cells by centrifugation at 3000 rpm for 5 minutes. Serum samples were stored at -80°C until the day of biochemical analysis. The enzymatic activity of Cp was measured by Erel method.[10,11] In this method, the iron ion is oxidized to ferric ion by Cp ferroxidase activity. Results were recorded as U/ml.

Statistical Analysis

SPSS 11.5 software was used for statistical analysis (SPSS Inc., Chicago, IL, USA). Student's t test was used in the statistical analysis of coronary sinus blood samples. Repeated measurement of variance was performed of Cp level of venous blood samples. Arithmetic averages of all parameters were given with standard deviation values. P values less than 0.05 were considered significant.

RESULTS

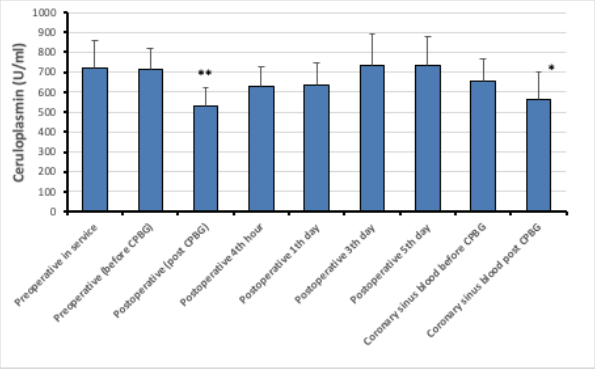
Mean cross clamp time was 88.13 ± 31.70 (min-max 46-175) minutes, mean cardiopulmonary bypass time was 133.83 ± 45.67 (min-max; 70-210) minutes, mean hospital stay was 10.53 ± 5.28 (min-max; 1-27) days, mean duration in intensive care unit was 2.33 ± 1.56 (min-max 0-9) days. The mean ejection fraction was 47.63 ± 11.35% (min-max 25-73). The mean number of anastomosis was 2.73 ± 0.69 (min-max; 2-4). Demographic data, duration of operation, postoperative intensive care and hospital stays are summarized in Table 1.

Table 1: Demographic data, duration of operation, postoperative intensive care and hospital stays of the patients

Variables	Patients (n=120)	S.D. or %
Age(years)	61.80 (41-77)	±9.88
Gender (M/F)	67/53	%56.25
Diabetes (yes/no)	37/83	%31.2
Hypertension (yes/no)	63/57	%53.2
Smoking status (yes/no)	60/60	%50
Dyslipidemia (yes/no)	57/63	%46.8
Mean X-clemp time (min)	88.13(46-175)	±31.70
Mean CPBP time(min)	133.83(70-210)	±45.67
Hospital stay (length)(day)	10.53(1-27)	±5.28
ICU stay (length)(day)	2.33(0.00-9.00)	±1.56
Ejection fraction (%)	47.63(25-73)	±11.35
Previous MI (yes/no)	60/60	%50
Number of anastomosis	2.73(2-4)	± 0.69

CPBP: Cardiopulmonary bypass pump
ICU: Intensive care unit
CABG: Coronary artery bypass graft
MI: myocardial infarction

In our study, there was a decrease in enzymatic activity of ceruloplasmin levels immediately after cardiopulmonary bypass both in the samples taken peripherally and from coronary sinus. This decrease continued until 24 hours after the operation ($p < 0.05$). Postoperative 3rd day, the enzymatic activity of the ceruloplasmin becomes the normal values. Reduction in blood samples from the coronary sinus was observed to be more apparent ($p < 0.05$). Enzymatic activity of Cp levels are presented in Figure 1.



**p=0,035

* p=0,025

Figure 1:Enzymatic activity of ceruloplasmin levels

DISCUSSION

Ceruloplasmin (Cp) is an acute phase reactant and it acts as a pro-oxidant or an antioxidant. Many investigators have reported that coronary artery bypass graft operation leads to increase in oxidative stress.[1] Normotensive-normotermic condition followed by hypotensive-hypothermic period leads to ischemia-reperfusion injury and this mechanism causes oxidative stress especially in on-pump CABG.[12] Mumby and colleagues studied the enzymatic activity of Cp levels in 65 patients with congenital heart disease. They investigated the enzymatic activity of Cp before, during and after cardiopulmonary bypass. It was showed that the enzymatic activity of Cp levels decreased during cardiopulmonary bypass and increased postoperatively.[13] Jeremy et al.[14] studied the enzymatic activity of Cp levels in 55 adult patients with coronary artery disease. They evaluated the enzymatic activity of Cp levels at preoperative, postoperative 1st day, postoperative 6th day and postoperative 6th week. They detected a decrease in levels on the postoperative 1st day. On postoperative 6th day and at postoperative 6th week, they found that the enzymatic activity Cp values are higher than preoperative Cp values.[14] Lull et al. studied on the enzymatic activity of Cp values in 10 pediatric patients with congenital heart disease. They reported that levels were reduced by 40% during cardiopulmonary bypass but after 24 hours, it reached normal levels.[15] According to the study conducted by Melnikov et al. in patients with congenital heart disease, the levels of Cp enzymatic activity decreased during cardiopulmonary bypass and returned to normal after 24 hours after cardiopulmonary bypass.[16] Hepponstall et al. reported that in children with tetralogy of Fallot, levels of the enzymatic activity of Cp decreased at the 6th and 12th hours after cardiopulmonary bypass.[17]

Our study demonstrates preoperative and postoperative marked changes in the enzymatic activity of Cp levels. Reduction continued until 24 hours and returned to preoperative levels on postoperative 3rd day. Significant reduction was also observed in coronary sinus blood sample after cardiopulmonary bypass. Decreased Cp levels in blood samples taken before and after cardiopulmonary bypass, except coronary sinus, indicate that cardiopulmonary bypass increases oxidative stress in all organ systems. Significant decrease in the level of Cp enzymatic activity in the coronary sinus blood before and after cardiopulmonary bypass showed reduction in the local myocardial antioxidant levels due to consumption as a respond to oxidant stress. This decline is indicative of an increase in oxidative stress on the heart due to cardiopulmonary bypass. These results suggest that Cp may play an important role in the evaluation of the oxidative stress of the heart. In addition, normalization of Cp levels on postoperative 3rd day revealed that the destructive effect of cardiopulmonary bypass disappeared and the antioxidant level returned to normal. This indicates that the patients undergoing cardiopulmonary bypass should be monitored carefully until the third day of operation.

In conclusion, enzymatic activity of the Cp is a parameter that can be important in determination of antioxidant capacity in cardiovascular procedures especially in coronary artery bypass graft operations. Further studies with large number of patient population are required to improve our knowledge on this subject.

The study was approved by the Clinical Studies Ethical Committee of Harran University by the decision no 02-12-2010-06.

Written informed consent was obtained from patients who participated in this study.

There are no conflicts of interest.
This study has received no financial support.

References

1. *Kurban S, Mehmetoglu I, Ege E. Effect of preoperative atorvastatin therapy on paraoxonase activity and oxidative stress after coronary artery bypass grafting. Perfusion 2009;24(4):271-76.*
2. *Jean-Jacques G, Gaelle C, Olivier G, et al. In High-Risk Patients, Combination of Antiinflammatory Procedures During Cardiopulmonary Bypass can Reduce Incidences of Inflammation and Oxidative Stress. J Cardiovasc Pharm 2007;49(1):39-45.*
3. *Gurol G, Aslan A. Lipid peroxidation and antioxidant enzymes. Sakaryamj 2013; 3(1):5-7*
4. *Hammadh M, Fan Y, Wu Y, Hazen SL, Tang WW. Prognostic Value of Elevated Serum Ceruloplasmin Levels in Patients with Heart Failure. J Card Fail 2014;20(12): 946-52.*
5. *Leong JY, van der Merwe J, Pepe S, et al. Perioperative Metabolic Therapy Improves Redox Status and Outcomes in Cardiac Surgery Patients: a randomized trial. Heart Lung Circ 2010;19(10):584-91.*
6. *Buyukhatıpoglu H, Sezen Y, Yildiz A, et al. Effects of Statin Use on Total Oxidant and Anti-oxidant Capacity and Ceruloplasmin Activity. Clin Invest Med 2010;33(5): 313-20.*
7. *Sarkar A, Dash S, Barik BK, et al. Copper and Ceruloplasmin Levels In Relation to Total Thiols And Gst in Type 2 Diabetes Mellitus Patients. Ind J Clin Biochem 2010;25(1):74-76.*
8. *Patti MC, Cutone A, Polticelli F, et al. The Ferro-portin-ceruloplasmin System and the Mammalian Iron Homeostasis Machine: regulatory pathways and the role of lactoferrin. BioMetals 2018;31(5):399-414.*
9. *Gocmen AY, Sahin E, Semiz E, Gumuslu S. Is Elevated Serum Ceruloplasmin Level Associated with Increased Risk of Coronary Artery Disease? Can J Cardiol 2008;24(3):209-12.*
10. *Erel O. Automated Measurement of Serum Ferroxidase Activity. Clin Chem 1998;44(2):2313–19.*
11. *Neselioglu S, Ergin M, Erel O. A New Kinetic, Automated Assay to Determine the Ferroxidase Activity of Ceruloplasmin. Anal Sci 2017;33(12):1339-44.*
12. *Ata EC, Dereli Y, Durgut K, Ozpinar C. The Effect of Lidocaine Enriched Cardioplegia on Myocardial Ischemia Reperfusion Injury. JCAM 2016;7(3):191-96*
13. *Mumby S, Chaturvedi R, Brierley J, Lincoln C, Petros A, Redington A, Gutteridge JM. Antioxidant Protection against Iron Toxicity: plasma changes during cardiopulmonary bypass in neonates, infants, and children. Free Radic Res 1999;31(2):141-48.*
14. *Jeremy JY, Shukla N, Angelini GD, et al. Sustained Increases of Plasma Homocysteine, Copper, and Serum Ceruloplasmin after Coronary Artery Bypass Grafting. Ann Thorac Surg 2002;74(5):1553-37.*
15. *Lull ME, Carkaci-Salli N, Freeman WM, et al. Plasma Biomarkers in Pediatric Patients Undergoing Cardiopulmonary Bypass. Pediatr Res 2008;63(6):638-44.*
16. *Melnikov P, Zanoni LZ, Poppi NR. Copper and Ceruloplasmin in Children Undergoing Heart Surgery with Cardiopulmonary Bypass. Biol Trace Elem Res 2009;129(1-3):99-106.*
17. *Hepponstall M, Ignjatovic V, Binos S, et al. Cardiopulmonary Bypass Changes the Plasma Proteome in Children Undergoing Tetralogy of Fallot Repair. Perfusion 2015;30(7):556-64.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Congenital Thoracic Abnormalities: Contribution of Prenatal Magnetic Resonance Imaging to Ultrasound Diagnosis

Konjenital Toraks Anomalileri: Prenatal Manyetik Rezonans Görüntülemenin Ultrasonografik Tanıya Katkısı

Gülseren Dinç[1], Deniz Öztürk Koçakgöl[2]

[1] Department of Obstetrics and Gynecology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey,
[2] Department of Radiology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

Yazışma Adresi / *Correspondence:*
Gülseren Dinç

Department of Obstetrics and Gynecology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey
Tel **:**+90 462 377 54 94 E-mail **: gulserendinc1@gmail.com**

Geliş Tarihi / Received : **23.09.2020** Kabul Tarihi / Accepted : **01.01.2021**

Orcid :

Gülseren Dinç https://orcid.org/0000-0001-6513-0656
Deniz Öztürk Koçakgöl https://orcid.org/ 0000-0003-3780-2173

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):67-76) DOI: 10.31832/smj.798874**

Abstract

Objective We aimed to evaluate the contribution of prenatal magnetic resonance (MR) imaging to ultrasound (US) in the diagnosis of congenital thoracic abnormalities.

Materials and Methods Thirty-three out of 984 pregnant women, with fetal thoracic anomalies detected at US and subsequently underwent fetal MR imaging were analyzed retrospectively. In the present methodological study, prenatal MR imaging and US findings are compared with postnatal imaging, autopsy, surgical pathologic examination, physical examination or clinical follow-up. Diagnostic sensitivities were calculated for US, MR imaging and combinations of both methods by comparing US and MR results with postnatal definite diagnoses.

Results The sensitivities of US and MR imaging in detecting thoracic anomalies were 53.3% and 66.7%, respectively. Both US and MRI findings were consistent in prenatal imaging in a total 27 (82%) of cases. Both US and MR imaging made correct diagnosis in 48% of cases. MR imaging confirmed the suspected US diagnosis in 3%. Prenatal MR imaging positively contributed to US with revealing additional findings such as pulmonary hypoplasia and mediastinal shift in 30% cases. Main contribution (90%) of MR imaging to US was in congenital diaphragmatic hernia (CDH) cases. In all cases with CDH, MRI showed reduction in T2 signal consistent with pulmonary hypoplasia. MR imaging completely altered the diagnosis in 9% of cases. Total contribution rate of prenatal MR imaging to US was 42%. Sixty-seven percent of prenatally detected congenital cystic adenomatoid malformation (CCAM) and congenital lobar fluid overload (CLFO) cases exhibited spontaneous resolution before birth.

Conclusion MR imaging as a complementary to US can be used successfully in the prenatal diagnosis of congenital thoracic pathologies. It can provide additional findings, confirm the suspected diagnosis or completely alter the prenatal US diagnosis. The most additional contribution of MRI to US was provided in cases of CDH.

Keywords prenatal diagnosis; magnetic resonance imaging; ultrasound; thorax abnormalities

Öz

Amaç *Çalışmada konjenital torasik anomalikleri olan fetüslerde prenatal manyetik rezonans görüntüleme (MRG)'nin prenatal ultrason (US)'na olan katkısını ortaya koymayı amaçladık.*

Gereç ve Yöntemler *Prenatal dönemde ultrason (US) de fetal torasik anomaliler tespit edilen ve ardından fetal MRG yapılan 984 gebenin 33'ü retrospektif olarak analiz edildi. Metadolojik çalışmada, prenatal MR görüntüleme ve US bulguları doğum sonrası görüntüleme, otopsi, cerrahi patolojik inceleme, fizik muayene veya klinik takip ile karşılaştırıldı. US, MRG ve her iki yöntemin kombinasyonları için tanısal duyarlılıklar, US ve MR sonuçları, doğum sonrası kesin tanılarla karşılaştırılarak hesaplandı.*

Bulgular *US ve MRG'nin torasik anomalileri saptamadaki duyarlılıkları sırasıyla % 53.3 ve % 66.7 bulundu. Prenatal görüntülemede olguların %82'sinde hem MR hem de US bulguları birbiriyle uyumluydu. Olguların %48'inde hem MR hem de US doğru tanıyı koydu. MRG, %3 olguda şüpheli US tanısını doğruladı. Prenatal MRG, %30 vakada primer tanıya ek olarak pulmoner hipoplazi ve mediastinal şift gibi ek bulguları ortaya çıkararak US'ye ilave katkıda bulunmuştur. MRG'nin US'ye en fazla katkısı (% 90) konjenital diyafram hernilerinde (KDH) oldu. KDH'li olguların tümünde pulmoner hipoplazi ile uyumlu olarak T2 ağırlıklı MRG'de sinyal azalması saptandı. MRG, %9 olguda US tanısını tamamen değiştirdi. Prenatal MRG'nin US'ye toplam katkı oranı %42 idi. Doğum öncesi kistik adenomatoid malformasyon (CCAM) veya doğumsal lober sıvı yüklenmesi (CLFO) tanısı konan fetüslerin %67'sinde doğum sonrasında spontan rezolüsyon saptandı.*

Sonuç *US'ye tamamlayıcı yöntem olarak MRG görüntüleme doğumsal toraks patolojilerinin prenatal tanısında başarıyla kullanılabilir. MRG prenatal dönemde US'ye ek bulgular sağlayabilir, şüpheli tanıyı doğrulayabilir veya tanıyı tamamen değiştirebilir. Çalışmada MRG'nin US'ye en fazla (%90) katkı sağladığı patoloji konjenital diyafram hernileri bulundu.*

Anahtar Kelimeler *prenatal tanı; manyetik rezonans görüntüleme, ultrason; toraks anomalileri*

INTRODUCTION

Algorithmically, prenatal ultrasonography (US) remains the primary imaging modality in detection, diagnosis and characterization of fetal anomalies.[1,2] In the last 15 years, prenatal magnetic resonance (MR) imaging has frequently been used as an adjunct to US for the evaluation of challenging fetal pathologies. It has the capability to improve diagnostic accuracy of prenatal US in most of the body systems. New MR imaging techniques with high temporal, spatial and contrast resolution and sequences used for metabolic imaging increased the contributive role at MR imaging to US.[3-5]

Although there have been numerous studies concerning fetal MR imaging, fewer have investigated the contribution of MR imaging to US with postnatal correlation in fetal thoracic pathologies.[1,6,7] Most of these publications are case reports or small case series mainly focusing on a specific pathology.[8-10] The purpose of this study was to evaluate the contribution of MR imaging to US in fetuses with various congenital thoracic abnormalities with postnatal correlation.

MATERIALS and METHODS

The study protocol was approved by the Karadeniz Technical University Faculty of Medicine Ethical Committee and the institutional review board which is responsible for all patient data and images available in hospital information system (approved date 20.09.2019 and number 24237859/657). Informed consent had been obtained from all pregnant women before MR imaging. Nine hundred eighty-four pregnant women over 12 week-gestational age with fetal anomaly that is detected or suspected at obstetric US and then underwent fetal MR imaging between April 2007 and December 2019 were analyzed retrospectively. Thirty-three of those cases had fetal thoracic anomalies that were imaged both with US and MR imaging in our center were included in the study. Cases with lung hypoplasia due to renal agenesis and oligohydramnios without thoracic anomaly were excluded from the study. In the present methodological study, prenatal US and MR images and patient data were retrieved from our hospital database. Prenatal findings were correlated by postnatal findings obtained from physical examination, postnatal imaging, autopsy, surgical pathologic examination and/or clinical follow-up.

Three high resolution US scanners, GE Voluson Expert (General Electric, Waukesha, Wisconsin), or Siemens Sonoline Antarest (Siemens Medical Systems, Erlangen, Germany), or Toshiba Aplio 500 (Toshiba Medical Systems Corporation, Tochigi, Japan), were used for prenatal US examinations. All US examinations were performed according to the international society of ultrasound in obstetrics and gynecology (ISUOG) practical guidelines.[2]

Our standard for anatomic examination of the fetus in the second or third trimesters at US includes the fetal head, face and neck (cerebellum, choroid plexus, cistern magna, lateral ventricles, falx cerebri, cavum septum pellucidum, and upper lip), heart axis, four-chamber view of the heart, outflows of the main vessels from the heart, bilateral lung parenchyma, stomach, kidneys, bladder, umbilical cord localization, umbilical cord number, as well as evaluation of the entire spine, and upper and lower extremities. Additionally, fetal US and MR imaging protocols and parameters were adopted as a reference in a previous study conducted in our hospital.[6]

Between 2007 and 2015, MR images were obtained with a 1.5 Tesla MR unit (Magnetom, Symphony; Siemens, Erlangen, Germany), while after 2015, it was performed with a 3 T MR unit (Magnetom Skyra Siemens Healthcare, Erlangen, Germany). All cases were examined using body phase array coils. Patients were placed in the supine or lateral decubitus position. No sedation or contrast agent was used. Our conventional MR imaging protocol included steady-state free precession (SSFP), true fast imaging with steady-state free precession (TRUFI) and half Fourier acquisition single shot turbo spin-echo (HASTE). Images were

acquired in the axial, coronal and sagittal planes relative to the fetal head and trunk. Additionally, a single plane T1-weighted spoiled gradient-echo (fast low angle shot: FLASH) image was obtained in sagittal fetal plane.

Statistical analysis

MR imaging and US findings were evaluated based on postnatal definite diagnoses. In comparison of fetal MR imaging and US findings the following evaluations were made; 1) Both methods make the correct diagnosis, 2) MR correct and US failure, 3) US correct and MR failure, 4) MR imaging made accurate diagnosis in cases where US findings are suspicious, 5) both MR imaging and US were inconsistent with postnatal findings. Diagnostic sensitivities were calculated for US, MR and combinations of both methods by comparing US and MR results with postnatal definite diagnoses.

RESULTS

Over the 12-year period, fetal MR imaging was performed on 984 pregnant women in whom congenital anomaly was observed or suspected at prenatal US. Of them 33 fetuses with congenital thoracic pathology were included to the present study. Gestational ages ranged from 20 to 36 weeks (mean 25.6 ± 5.1 weeks). Prenatal US, MR imaging findings and postnatal diagnosis and findings are summarized in Table 1.

Postnatal diagnoses were provided with postoperative pathologic examination in 11 cases those underwent surgery, with autopsy in two cases and with combination of findings from physical examination, chest radiography

Table 1. Patients' prenatal MRI, US findings and postnatal diagnoses

		Prenatal MR findings	Prenatal US findings	Postnatal diagnosis
1	27	R-CDH, med. shift, BL hypoplasia, polyhyd	R-CDH, med. shift, polyhyd.	Operation (CDH), res. distress, O2 support
2	24	L-CDH, excessive med. shift, LL hypoplasia	L-CDH	Operation (CDH), res. distress, O2 support
3	23	L-CDH, LL pleural effusion, LL hypoplasia	L-CDH, L-sided pleural effusion	Operation (CDH)
4	21	R-CDH, RL hypoplasia, pleural effusion, liv. her.	R-CDH	CXR (CDH), PP exitus
5	22	L-CDH, LL hypoplasia, liv. her.	L-CDH	CXR (CDH), PP exitus
6	23	L-CDH, trisomy 18, LL hypoplasia, polyhyd.	L-CDH, trisomy 18, LL hypoplasia, polyhyd.	Autopsy (trisomy 18, CDH)
7	33	L-CDH, LL hypoplasia	L-CDH	CXR (CDH), PP exitus
8	24	L-CDH, LL hypoplasia	L-CDH	Operation (CDH), res. distress, O2 support
9	35	L-CDH, LL hypoplasia	L-CDH	Operation (CDH)
10	35	L-CDH, LL hypoplasia	L-CDH	Operation (CDH), res. distress, O2 support
11	20	LL BPS, excessive med. Shift	LL BPS	Operation (BPS)
12	36	LL BPS	LL BPS or CCAM	Operation (BPS)
13	21	RL BPS, excessive med. Shift	RL CCAM	Operation (BPS)
14	33	RL agenesis, med. Shift	RL agenesis, med. Shift	CXR (RL agenesis)
15	29	Bronchogenic cyst	Bronchogenic cyst	Operation (Bronchogenic cyst)
16	28	Neurenteric cyst	Neurenteric cyst	Medical abortus
17	28	RL upper lob atelectasis	RL CLFO	CXR/MRI/atelectasis
18	34	LL upper lob atelectasis	Normal	CXR/MRI/atelectasis
19	25	LL CCAM (macrocystic)	LL CCAM (macrocystic)	Operation, CCAM

Table 1. Patients' prenatal MRI, US findings and postnatal diagnoses

		Prenatal MR findings	Prenatal US findings	Postnatal diagnosis
20	29	RL CCAM (microcystic), hydrops fetalis	RL CCAM (microcystic), hydrops fetalis	Autopsy (CCAM)
21	22	RL CCAM (microcystic), excessive med. Shift	RL CCAM (microcystic), med. Shift	Intrauterine exitus (no pathology)
22	24	LL CCAM (microcystic)	LL CCAM (microcystic)	PE and CXR normal
23	27	LL CCAM (microcystic)	LL CCAM (microcystic)	PE and CXR normal
24	22	RL CCAM (macrocystic)	RL CCAM (macrocystic)	PE and CXR normal
25	23	RL CLFO, BL hypoplasia, renal agenesis	Renal agenesis	Medical abortus (no pathology)
26	25	RL CLFO	RL CLFO	PE, CXR and CT normal
27	24	RL CLFO	RL CLFO	PE and CXR normal
28	23	RL CLFO	RL CLFO	PE and CXR normal
29	24	LL CLFO	LL BPS, CLFO	PE and CXR normal
30	20	RL CLFO, CCAM	RL CLFO, CCAM	Intrauterine exitus (no pathology)
31	22	RL CLFO, CCAM	RL CLFO, CCAM	PE, CXR and CT normal
32	20	LL CLFO, CCAM	LL CLFO, CCAM	PE, CXR and CT normal
33	22	LL CLFO, CCAM	LL CLFO, CCAM	PE and CXR normal

R= right, L= left, LL= left lung, RL = right lung, BL = bilateral lung, R-CDH = right-sided congenital diaphragmatic hernia, med. shift = mediastinal shift. L-CDH = left sided congenital diaphragmatic hernias, BPS = bronchopulmonary sequestration, CCAM = congenital cystic adenomatoid malformation of the lung. CLFO = congenital lobar fluid overload, PE = physical examination, CXR = chest x-ray, MRI= magnetic resonance imaging, CT = computed tomography, PP = postpartum. polyhyd. = polyhydramnios. liv. her. =liver herniation, US = ultrasonographic

(CXR), computed tomography (CT) and/or MR imaging in 16 cases. Unfortunately, no postnatal correlation could be obtained in four fetuses those were medically aborted or died intrauterine.

Congenital diaphragmatic hernia (CDH) was present in 10 (33%) of the 33 fetuses (Figure 1). Herniation was left sided in eight and right sided in two cases. Both prenatal US and MR imaging successfully detected CDH in all cases. In nine (90%) of the 10 cases with CDH, prenatal MR imaging contributed to US with the detection of accompanying pulmonary hypoplasia, liver herniation and/or mediastinal shift. While pulmonary hypoplasia was documented in all CDH cases (one bilateral, nine unilateral) at MR imaging, US detected it in only one case. Decreased volume and T2 signal according to gestational age or compared to normal side were the criteria used in the diagnosis of pulmonary hypoplasia on MR imaging. Three of those CDH cases died postnatally. Four of the cases, although developed respiratory problems postnatally, successfully operated.

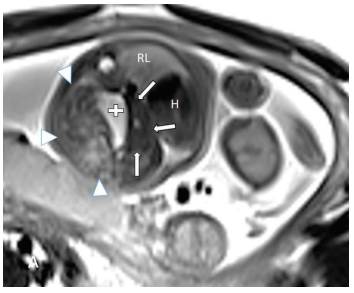


Figure 1 a

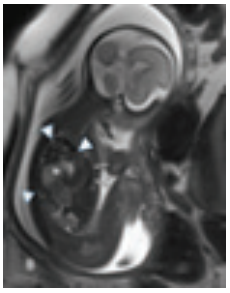


Figure 1 b

Figure 1. Congenital diaphragmatic hernia. Axial (a) and sagittal (b) T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) images show that the stomach (+), bowels (white arrowheads) and portions of the liver (white arrows) are herniated into the left thorax whereas heart (H) is displaced into the right thorax. There is very little lung tissue at the apices (b). The right lung (RL) also shows hypoplasia due to compression of the herniated structures.

Bronchopulmonary sequestration (BPS) was present in three cases. They were correctly diagnosed with MR imaging (100%) by the demonstration of systemic feeding vessel (Figure 2). On the other hand, US successfully showed the abnormal vascular supply and yielded the correct diagnosis just in one case. Two cases of upper lobe atelectasis were misdiagnosed by US. However, MR imaging achieved accurate diagnosis in these cases. Both US and MR imaging correctly diagnosed one case of unilateral lung agenesis, one bronchogenic cyst and one neuroenteric cyst.

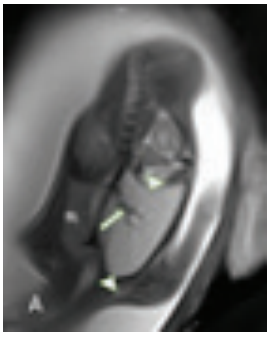


Figure 2 a

Figure 2 b

Figure 2. Bronchopulmonary sequestration (BPS). Coronal (a) and axial (b) MR images revealed homogenous T2- hyperintense lesion (white arrowheads) that fill the whole left thorax and herniation in to the right thorax with normal right lung. The feeding artery (white arrow) from aorta supports the diagnosis of BPS. Postpartum operation was consistent with BPS.

There were 15 cases of congenital cystic adenomatoid malformation (CCAM)/congenital lobar fluid overload (CLFO) cases diagnosed prenatally. Just in one of these cases US could not provide the diagnosis. In other 14 cases US and MR imaging were correlated. However, just in two of these cases the diagnosis could be confirmed postnatally by autopsy and operation. Three cases died intrauterine or medically aborted. The postnatal imaging findings of remaining 10 cases were normal probably due to the intrauterine resolution of prenatally diagnosed pathologies. Both US and MRI findings were consistent in prenatal imaging in a total 27 (82%) of cases. Both US and MR imaging established the correct diagnosis in 16 (48%) cases compared with postnatal findings (Table 2).

Table 2. Comparision of US and MRI with postnatal findings

	Number of cases (%)
Both US and MRI correct	16 (48%)
MR correct, US failed	3 (9%)
MRI confirmed the suspicious US diagnosis	1 (3%)
*Both US and MRI were not consistent with postnatal findings	10 (30%)
Patients without radiologic and pathologic confirmation	3 (9%)

US= ultrasound, MRI= magnetic resonance imaging.
*= Both methods in prenatal imaging were compatible with each other in 10 cases and made the same diagnosis. However, due to the resolution of the lesions, incompatibility was observed in the postnatal period.

Prenatal diagnoses in 10 of these cases were CCAM and/or CLFO. The physical and radiological examinations of these cases were all normal postnatally probably related to total resolution of the pathology (Figure 3).

Figure 3 a

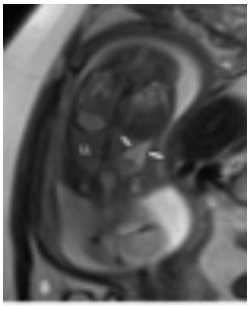


Figure 3 b

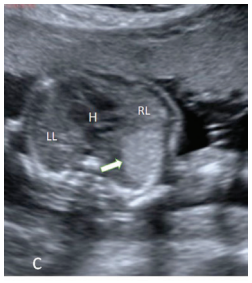


Figure 3 c

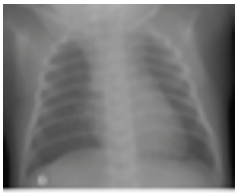


Figure 3 d

Figure 3. CCAM and/or CLFO. Sagittal (a) and coronal (b) T2-weighted HASTE images revealed hyperintense lesion and axial US image (c) revealed hyperechoic lesion in the right lung consistent with CCAM and/or CLFO. The fetus was followed up with the diagnoses of CCAM and/or CLFO in the prenatal period. Both physical examination and chest x-ray/CT (d) were normal in the postnatal period.

Unfortunately, due to the absence of serial radiological follow-ups the resolution of the lesions could not be documented prenatally. In these 10 cases, prenatal MR imaging and US diagnoses were correlated but prenatal and postnatal findings were not. Therefore, we had to record these 10 cases (30%) as prenatal imaging failed cases. There were 15 cases prenatally diagnosed with CCAM and CLFO in the present study and 67% of them seem underwent spontaneous resolution before birth. In three cases (9%) with prenatally diagnosed thoracic anomalies postnatal diagnosis could not be obtained. Prenatal US and MR imaging were totally correlated with postnatal diagnosis just in 16 (48%) cases.

In one (3%) fetus (case 12), MR imaging confirmed the suspected US diagnosis. Prenatal MR imaging contributed to US with revealing additional findings of pulmonary hypoplasia, liver herniation and/or mediastinal shift in addition to primary diagnosis in 10 (30%) cases (Figure 4). However, since additional findings did not change the diagnosis, these cases were evaluated in the correct diagnostic group for both methods (Table 2). MR imaging completely altered the US diagnosis in 9% of cases. As a result, total contribution rate of MR imaging to prenatal US in the diagnosis of congenital thoracic abnormalities was 42%.

Of the 30 anomalies that have definitive diagnosis postnatally, 16 were accurately diagnosed by US and 20 by MR imaging during prenatal period. Sensitivities of US and MR imaging in detecting thoracic anomalies were 53.3% and 66.7%, respectively. We did not have a case where MR imaging was wrong and US diagnosed correctly. Therefore, the sensitivity obtained with the combination of both methods was the same as the sensitivity of MR imaging (66.7%).

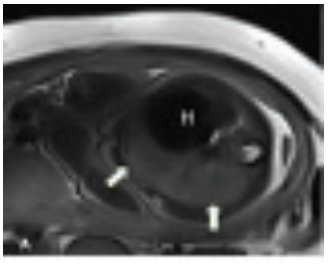


Figure 4 a

Figure 4 b

Figure 4. Right lung agenesis. Axial (a) and coronal (b) T2-weighted HASTE MR images revealed absence of right lung. The left lung (white arrows) has been herniated into the left thorax due to the right lung agenesis.

DISCUSSION

In the present study of congenital thoracic pathologies, the sensitivities of US and MR imaging in detecting thoracic

anomalies were 53.3% and 66.7%, respectively. Both MR imaging and US provided the same diagnosis in 48% of cases, prenatally. MR imaging contributed to US diagnosis in 42% of the cases either by confirmation of suspicious US diagnosis or by completely altering the US diagnosis or by detecting some accompanying abnormalities. The most prominent contribution of MRI to US was provided in cases of CDH by documenting the accompanying pulmonary hypoplasia, liver herniation or mediastinal shift.

Although US is the initial method of choice for fetal imaging, due to its multiplanar capabilities and excellent soft tissue contrast resolution, MR imaging allow more accurate analysis of the fetal anatomy and pathological processes. As a result, in recent years MR imaging has frequently been used as a complementary imaging method in the evaluation of the fetal pathologies. Following neurological abnormalities, thorax pathologies is one of the most common indications for fetal MR imaging.[4,11] Compared with US, fetal MR imaging can change the diagnosis or add additional information that cannot be obtained with US in the evaluation of thoracic abnormalities. Although there are many publications concerning MR imaging of fetal thorax in the literature, little of them correlate prenatal findings with postnatal ones and document contribution of MR imaging to US clearly in this context.[7,12,13]

Congenital diaphragmatic hernia (CDH) is the most common thoracic anomaly reported prenatally and the main indication for thoracic fetal MR imaging. It occupied 30% of our cases. It is commonly (70-90%) located posterolaterally on the left side and less frequently on the right side (13%) or bilaterally (2%).[14-16] Algorithmically, US is the primary screening modality in the diagnosis of CDH. The sensitivity of US in the diagnosis of CDH varies, depending on the examiner's experience, gestational age, fetal position, presence or absence of abdominal organs in the thorax, and the presence of additional anomalies.[14] Both US and MR imaging correctly diagnosed 100% of CDH cases in our series but MRI made an additional contribution to US in 90% of these cases. With its large field of view, MR imaging provided detailed and complete documentation of the fetal anatomy, diaphragmatic contours and herniated organs even in the late weeks of gestation, independent of fetal position. The majority of patients with CDH present with pulmonary hypoplasia and persistent pulmonary hypertension. Pulmonary hypoplasia usually occurs ipsilateral or less commonly bilateral secondary to physical compression of the lung by the herniated abdominal organs.[15] In our study, pulmonary hypoplasia was documented in all CDH cases (one bilateral, nine unilateral) at MR imaging, while US diagnosed it in only one patient. Consistent with the literature, MR imaging was superior to US in the demonstration of pulmonary hypoplasia in the present study.[15,17] Decrease in T2 MR signal with decreased lung volume was used as the MR imaging criterion for the diagnosis of pulmonary hypoplasia. Normal lungs exhibit homogeneous and moderately high signal intensity on T2-weighted images. Signal intensity must be higher than that of the chest wall muscles but lower than that of amniotic fluid.[13] If the lung is compressed, the T2 signal decreases compared to the normal lung, since fluid production in the alveoli will decrease.[4,17,18] Postpartum lung hypoplasia is difficult to diagnose and is usually established by lung volume measurements and imaging findings.[18,19] In recent years, lung volume measurement in CDH cases has been shown to be useful in determining the degree of pulmonary hypoplasia. It is reported that the most validated method for the prediction of pulmonary hypoplasia is prenatal measurement of the lung-to-head ratio (LHR) by using US and MR imaging.[19] In addition, there are studies using prenatal lung volume measurements for postnatal outcome prediction.[4] Unfortunately, we used quantitative lung volume measurements method in neither of our prenatal imaging methods.

Congenital fetal cystic lung lesions are rare, and the most common lesions include CCAM, BPS and CLFO.[4,17,20] CCAM is the most common of them and considered a hamartomatous malformation or a localized developmen-

tal arrest in fetal terminal bronchioles.[21,22] There is both pathologic and radiologic classification for CCAM. On ultrasonographic classification it is divided into two subgroups, depending on cyst size; microcystic (<5 mm cysts) and macrocystic (≥5 mm cysts).[21,23] At US, CCAM generally appears as a cystic (macrocystic form) or solid echogenic mass (microcystic form).[21,24] In our series, two of the six CCAM cases were macrocystic and four were microcystic. At MRI, macrocytic CCAM appeared as a lobulated, non-homogenous hyperintense mass and microcystic form as a lobulated, homogeneous hyperintense mass both without a feeding artery.[20] From six cases of our CCAM cases two died before birth. There were accompanying hydrops and excessive mediastinal shift in these two fetuses diagnosed both with MRI and US prenatally.

CLFO is also known as congenital lobar emphysema and is a rare cystic lung lesion characterized by overinflation of lung tissue.[25,26] The proposed etiological causes are bronchial cartilage hypoplasia or absence, and intrinsic or extrinsic bronchial obstruction producing a one-way valve effect resulting in air-trapping and progressive lobar and segmental alveolar hyperinflation.[10,20,25,26] The most common US finding is a solid-appearing uniformly hyperechoic lesion with absence of identifiable cyst and a systemic blood supply.[26] Prenatal MR imaging findings were a homogeneous hyperintense lesion with or without mass effect on mediastinum and intact lung architecture with stretching or elongation of non-displaced hilar vessels.[20,25,26]

Prenatal differential diagnosis of cystic lung lesions may not be possible based on imaging findings alone. Some CCAM cases may give similar MR imaging findings to CDH and CLFO, and sometimes to BPS.[21,25] Differential diagnosis of CLFO and CCAM was not possible with prenatal US and MR imaging findings in four of our cases. In 10 (30%) of our cases diagnosed as CCAM and/or CLFO on prenatal imaging, postnatal examination and images were normal. This condition might be explained with resolution of these pathologies during intrauterine period which is a very common occurrence reported in these pathologies. Partial or complete regression can be observed in CCAM and CLFO lesions prenatally. In their studies of Laberge JM et al. and Ierullo AM et al. reported spontaneous regression of CCAM in 56% of the 48 and 76% of 34 cases, respectively.[21,27] In the study of Liu YP et al. spontaneous regression was detected in five out of six CCAM cases.[20] Due to the absence of serial prenatal radiological follow-up during the intrauterine period, we couldn't be sure, however we thought 10 (67%) out of 15 CCAM and/or CLFO cases in our series went to spontaneous resolution prenatally.

BPS is a nonfunctional pulmonary tissue that does not communicate with the normal tracheobronchial tree.[1,4,17] It can be either extralobar or intralobar.[17] Although the intralobar type is more common, most prenatal diagnoses are extralobar. The intralobar type do not have its own pleura whereas extralobar type surrounded by a separate pleura. Both types receive their vascular supply from the systemic circulation. Venous drainage occurs via pulmonary veins for intralobar and systemic veins for extralobar type.[1] Fetal MR imaging contributes to the detection, characterization of BPS and identification of additional anomalies.[17] But most of the time it is unable to differentiate between two types. MR imaging shows a well-defined homogeneous, triangular, hyperintense mass compared to a normal lung. The diagnosis is certain if abnormal vascular supply arising from the large systemic arteries is recognized.[15,20] These MRI findings were present in all our three cases with BPS and were correctly diagnosed. On the other hand, US misdiagnosed one of them as CCAM and could not differentiate between CCAM and BPS in another case. BPS can also be in the form of hybrid lesions combined with CCAM and CLFO and may sometimes regress, partially or completely, during pregnancy.[16,20] Partial and near-complete regression rates in Liu YP et al. series were 82% and 61%, respectively.[20] Decreased signal intensity, signal inhomogeneity and marginal lobulation can be ob-

served during regression. Our BPS cases were isolated lesions, and two had mass effect. Our three cases diagnosed as BPS were operated postnatally since no regression was observed.

Limitations of the Study

There are some limitations to the present study. The main limitation is its retrospective nature. Second, the small numbers of patients in anomaly groups restricted statistical comparison of these groups. Our study results were therefore expressed as numbers. Third, since serial US and MR imaging examinations were not performed in the prenatal period, spontaneous resolution of CCAM and CLFO lesions could not be documented prenatally. The fourth limitation was that failure to establish the diagnosis of pulmonary hypoplasia with imaging findings in the postnatal period. Prenatally, lack of pulmonary volume measurements in the evaluation of pulmonary hypoplasia in CDH cases was another limitation. Lastly, fetuses undergoing fetal MR imaging had definite US diagnoses. This selection bias might cause an advantage in favor of MR imaging.

CONCLUSION

Our results show that MR imaging might be a helpful complementary tool to prenatal US in fetuses with congenital thoracic lesions. Fetal MRI can either alter or clarify the suspected US diagnoses or can yield accompanying abnormalities that might affect the prognosis or care of the fetuses.

Disclosure statement

The author reports no conflicts of interest in this work.

Author contributions

All authors contributed to the manuscript. GD-project development, manuscript writing/editing, literature search, data analysis and DÖK- project development, manuscript writing/editing, literature search, data analysis

Funding

No financial support was received for this study.

Ethical approval

This retrospective study was approved by the institutional review board responsible for all patient data and images available in the hospital information system.

Informed consent

informed consent was obtained from all patents included in the study.

Acknowledgement

The authors would like to thank to Dr. S.K. for her kind support in the organization of the manuscript.

Conflicts of interest

The author has no conflict of interest of this article.

The study protocol was approved by the Karadeniz Technical University Faculty of Medicine Ethical Committee and the institutional review board which is responsible for all patient data and images available in hospital information system (approved date 20.09.2019 and number 24237859/657).

References

1. *Pacharn P, Kline-Fath B, Calvo-Garcia M, Linam LE, Rubio EI, Salisbury S, Brody AS. Congenital lung lesions: prenatal MRI and postnatal findings. Pediatr Radiol. 2013 Sep;43(9):1136-43.*
2. *The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG). Practice Guidelines: ultrasound assessment of fetal biometry and growth Ultrasound Obstet Gynecol 2019;53: 715–723.*
3. *Daltro P, Werner H, Gasparetto TD, Domingues RC, Rodrigues L, Marchiori E, Gasparetto EL. Congenital chest malformations: a multimodality approach with emphasis on fetal MR imaging. Radiographics 2010; 30:385-95*
4. *Hibbeln JF, Shors SM, Byrd SE. MR imaging: is there a role in obstetrics? Clin Obstet Gynecol 2012; 55:352-66.*
5. *Torrents-Barrena J, Piella G, Masoller N, Gratacós E, Eixarch E, Ceresa M, Gonzalez Ballester MA. Segmentation and classification in MRI and US fetal imaging: Recent trends and future prospects. Med Image Anal 2019; 51:61-88.*
6. *Kul S, Korkmaz HA, Cansu A, Dinc H, Ahmetoglu A, Guven S, Imamoglu M. Contribution of MR imaging to ultrasound in the diagnosis of fetal anomalies. J Magn Reson Imaging 2012; 35:882-90*
7. *Breysem L, Bosmans H, Dymarkowski S, Schoubroeck DV, Witters I, Deprest J, Demaerel P, Vanbeckevoort D, Vanhole C, Casaer P, Smet M. The value of fast MR imaging as an adjunct to ultrasound in prenatal diagnosis. Eur Radiol 2003; 13(7):1538-48.*
8. *Matsuoka S, Takeuchi K, Yamanaka Y, Kaji Y, Sugimura K, Maruo T. Comparison of magnetic resonance imaging and ultrasonography in the prenatal diagnosis of congenital thoracic abnormalities. Fetal Diagn Ther 2003; 18(6):447-53.*
9. *Johnston JH, Kline-Fath BM, Bitters C, Calvo-Garcia MA, Lim FY. Congenital overinflation: prenatal MR imaging and US findings and outcomes. Prenat Diagn 2016; 36(6):568-75.*
10. *Khatib N, Beloosesky R, Ginsberg Y, Lea B, Michal G, Weiner Z, Bronshtein M. Early sonographic manifestation of fetal congenital lobar emphysema. J Clin Ultrasound 2019; 47:225-227*
11. *Martin C, Darnell A, Escofet C, Duran C, Pérez V. Fetal MR in the evaluation of pulmonary and digestive system pathology. Insights Imaging 2012; 3(3):277-93.*
12. *Alamo L, Gudinchet F, Reinberg O, Vial Y, Francini K, Osterheld MC, Meuli R. Prenatal diagnosis of congenital lung malformations. Pediatr Radiol 2012; 42(3):273-83*
13. *Hubbard AM, Adzick NS, Crombleholme TM, Coleman BG, Howell LJ, Haselgrove JC, Mahboubi S. Congenital chest lesions: diagnosis and characterization with prenatal MR imaging. Radiology 1999; 212:43-8*
14. *Alamo L, Gudinchet F, Meuli R. Imaging findings in fetal diaphragmatic abnormalities. Pediatr Radiol 2015; 45 (13) :1887-900.*
15. *Mehollin-Ray AR, Cassady CI, Cass DL, Olutoye OO. Fetal MR imaging of congenital diaphragmatic hernia. Radiographics 2012; 32 (4):1067-84.*
16. *Aksoy Ozcan U, Altun E, Abbasoglu L. Space occupying lesions in the fetal chest evaluated by MRI. Iran J Radiol 2012;9(3):122-9.*
17. *Levine D, Barnewolt CE, Mehta TS, Trop I, Estroff J, Wong G. Fetal thoracic abnormalities: MR imaging. Radiology 2003 Aug;228(2):379-88.*
18. *Kuwashima S, Nishimura G, Iimura F, Kohno T, Watanabe H, Kohno A, Fujioka M. Low-intensity fetal lungs on MRI may suggest the diagnosis of pulmonary hypoplasia. Pediatr Radiol 2001;31(9):669-72.*
19. *Deprest J, Brady P, Nicolaides K, Benachi A, Berg C, Vermeesch J, Gardener G, Gratacos E. Prenatal management of the fetus with isolated congenital diaphragmatic hernia in the era of the TOTAL trial. Semin Fetal Neonatal Med 2014;19(6):338-48.*
20. *Liu YP, Chen CP, Shih SL, Chen YF, Yang FS, Chen SC. Fetal cystic lung lesions: evaluation with magnetic resonance imaging. Pediatr Pulmonol 2010;45(6):592-600.*
21. *Labege JM, Flageole H, Pugash D, Khalife S, Blair G, Filiatrault D, Russo P, Lees G, Wilson RD. Outcome of the prenatally diagnosed congenital cystic adenomatoid lung malformation: A Canadian experience. Fetal Diagn Ther 2001;16 (3):178-86.*
22. *Ankers D, Sajjad N, Green P, McPartland JL. Antenatal management of pulmonary hyperplasia (congenital cystic adenomatoid malformation). BMJ Case Rep 2010;21; 1-5.*
23. *Mashiach R, Hod M, Friedman S, Schoenfeld A, Ovadia J, Merlob P. Antenatal ultrasound diagnosis of congenital cystic adenomatoid malformation of the lung: spontaneous resolution in utero. J Clin Ultrasound 1993; 21:453-7.*
24. *Daventport M, Warne SA, Cacciaguerra S, Patel S, Greenough A, Nicoliaides K. Current outcome of antenatally diagnostic cystic lung disease. J Pediatr Surg 2004; 39 (4):549-556.*
25. *Tsai PS, Chen CP, Lin DC, Liu YP. Prenatal diagnosis of congenital lobar fluid overload. Taiwan J Obstet Gynecol 2017;56 (4): 425-431.*
26. *Oliver ER, DeBari SE, Horii SC, Pogoriler JE, Victoria T, Khalek N,Howell LJ, Adzick NS, Coleman BG. Congenital Lobar Overinflation: A Rare Enigmatic Lung Lesion on Prenatal Ultrasound and Magnetic Resonance Imaging. J Ultrasound Med 2019; 38 (5):1229-1239.*
27. *Ierullo AM, Ganapathy R, Crowley S, Craxford L, Bhide A, Thilaganathan B. Neonatal outcome of antenatally diagnosed congenital cystic adenomatoid malformations. Ultrasound Obstet Gynecol 2005;26(2):150-3.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Comparison of Different Topographic Reference Surfaces in Keratoconus Cases

Keratokonus Olgularında Farklı Topografik Referans Yüzeylerin Karşılaştırılması

Ahmet Elbeyli[1], Sucattin Ilker Kocamis[2], Hasan Basri Cakmak[3], Emine Dogan[4]

[1] 1 Department of Ophthalmology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey
[2] Sakarya Yenikent State Hospital, Sakarya, Turkey
[3] Ophthalmology Department, Hitit University, Faculty of Medicine, Corum, Turkey
[4] Ophthalmology Department, Sakarya Training and Research Hospital, Sakarya, Turkey

Yazışma Adresi / *Correspondence:*
Ahmet Elbeyli
Department of Ophthalmology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey
T: **+90 326 291 10 00** E-mail **: ahmetelbeyli@yahoo.com**

Geliş Tarihi / Received : **03.06.2020** Kabul Tarihi / Accepted : **26.12.2020**

Orcid :

Ahmet Elbeyli https://orcid.org/0000-0002-5520-4591
Sucattin Ilker Kocamis https://orcid.org/ 0000-0001-8731-0471
Hasan Basri Cakmak https://orcid.org/ 0000-0001-6877-8773
Emine Dogan https://orcid.org/ 0000-0002-6505-3328

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):77-84) DOI: 10.31832 smj.747560**

Abstract

Objective To compare the sensitivity and specificity of corneal elevation maps obtained from different topographical reference surfaces used in the diagnosis of keratoconus.

Materials and Methods In this prospective study, 40 eyes of 23 patients with keratoconus (keratoconus group) and 40 eyes of 25 refractive surgery candidates without keratoconus (control group) were included. Flat keratometry (K1), steep keratometry (K2) and apex curvature keratometry (Kmax) values were obtained for both groups using the Scheimpflug camera system. Both anterior and posterior elevation maps were obtained from the spherical, aspherical and aspherotoric reference surfaces by assessing an 8 mm central corneal area. Topographic data were used to determine a more sensitive and specific corneal elevation mapping method to use in the differentiation of normal and keratoconic corneas.

Results The ROC curve analysis showed that posterior elevation measured from the aspherical and aspherotoric surfaces had a higher area under the ROC curves (0.987, 0.973 respectively) than the value obtained from the spherical reference surfaces. According to the data obtained from the ROC curve analysis, the posterior elevation maps obtained from the aspherical and aspherotoric reference surfaces had the highest sensitivity (97.5% for both) and the posterior elevation map obtained from the aspherical reference surface had the highest specificity (90%).

Conclusion The highest sensitivity and specificity values were obtained from the aspherical and aspherotoric reference surfaces compared to the spherical reference surface. When compared to the anterior elevation values, the posterior elevation values were found to be more sensitive and specific. Therefore, aspherical and aspherotoric reference surfaces and a posterior elevation map are seen more accurately in the differentiation of keratoconus and normal cornea.

Keywords Cornea; Keratoconus; Scheimpflug camera; Reference surface selection; Corneal topography.

Öz

Amaç *Keratokonus tanısında kullanılan topografik referans haritalama yöntemlerinin duyarlılık ve özgüllüğünün karşılaştırılması amaçlanmıştır.*

Gereç ve Yöntemler *Keratokonuslu 23 hastanın 40 gözü (keratokonus grubu) ile keratokonus olmayan ve rastgele seçilen refraktif cerrahi adayı 25 hastanın 40 gözü (kontrol grubu) Scheimpflug (Sirius CSO-Italy) topografi cihazı ile analiz edildi. Her iki grup için düz keratometri (K1), dik keratometri (K2) ve apeks eğrilik keratometri (Kmax) değerleri elde edildi. Sferik, asferik ve asferotorik referans yüzeyler kullanılarak ön ve arka korneal elevasyon haritaları (8 mm'lik santral korneal alanda) elde edildi. Normal ve keratokonuslu korneaların ayrımında daha duyarlı ve daha özgül olan korneal elevasyon haritalama yöntemini belirlemek için topografik veriler kullanıldı.*

Bulgular *ROC eğri analizlerine göre; asferik ve asferotorik yüzeylerden elde edilen posterior elevasyon verilerinin her ikisinin de keratokonusu saptamadaki duyarlılığı (97,5%), sferik referans yüzeyden elde edilen verilere göre anlamlı olarak daha yüksekti. Asferik referans yüzeyin keratokonus tanısında en yüksek özgüllüğe (90%) sahip olduğu sonucuna ulaşıldı.*

Sonuç *Çalışmaya göre yüksek duyarlılık ve özgüllük değerleri asferik ve asferotorik referans yüzeylerden elde edildi. Posterior elevasyon değerleri ile anterior elevasyon değerleri kıyaslandığında posterior yüzeyin daha değerli olduğu görüldü. Bu yüzden asferik ve asferotorik referans yüzeyin keratokonusu saptamada posterior elevasyon ile birlikte daha doğru sonuçlar vereceği sonucuna ulaşıldı.*

Anahtar Kelimeler *keratokonus; kornea; korneal topografi; referans yüzey seçimi; scheimpflug kamera*

INTRODUCTION

Keratoconus is the progressive ectasia of the cornea and causes a decrease in visual acuity by leading to high myopia and astigmatism. An accurate and more sensitive and specific method is crucial for diagnosis, follow-up the prognosis of the disease and planning the treatment options. The efficiency of diagnosis is more important in refractive surgery cases that may develop postoperative ectasia.[1-2]

Corneal topography is currently the gold standard diagnostic method in keratoconus cases. Although some limitations; placido disc-based corneal topographies have been widely used for a long time. Placido-disc based topographies only evaluate the anterior corneal surface and measurements are greatly affected by the angle and position of the surface.[2] Many studies on keratoconus have revealed that the morphological changes also occur on the posterior corneal surface.[3-5] It is now known that the morphological changes begin to occur primarily on the posterior corneal surface.[5] Corneal elevation change is one of the most important parameters and there have been some previous studies related to this issue.[6-9]

Scheimpflug-based corneal tomography comprises a rotating camera and slit scanning system and provides both the anterior and the posterior corneal surface elevation data.[5] Early and accurate diagnosis of keratoconus is provided by using Scheimpflug-based topographies and elevation maps. The evaluation of the cases is done according to reference mapping methods offered by topography devices. One of the reference surfaces (spherical, aspherical, aspherotorical) is chosen by the clinician for keratoconus diagnosis and classification. Of them, aspherical reference surface is usually preferred by most of the clinicians for keratoconus diagnosis.

There have been few studies about the comparison of the accuracy of the elevation data obtained from the spherical, aspherical and aspherotorical reference surfaces of the anterior and the posterior elevation maps in the diagnosis and classification of keratoconus. This study aimed to compare the sensitivity and specificity of various reference surfaces used in corneal elevation maps to provide a more accurate diagnosis of keratoconus.

MATERIALS and METHODS

This study was conducted at the Ankara Atatürk Training and Research Hospital between June 2011 and August 2011. The study was carried out in accordance with the principles of the Declaration of Helsinki, and approval of the ethics committee was obtained (Ankara Atatürk Education and Research Hospital, 16.06.2011, no:68)

Patients diagnosed with keratoconus and patients candidates for refractive surgery without keratoconus were enrolled in this prospective, methodological study. Control group was consisted of randomly selected age and gender-matched patients who admitted to the eye clinic for refractive surgery and had no ocular surface pathology, and a history of surgery/trauma.

40 eyes of 23 patients with keratoconus and 40 eyes of 25 refractive surgery candidates without keratoconus were included in the study. Subjects over 40 years of age (for both groups) and with history of previous eye surgery or a history of systemic disease were excluded from the study. Patients with any additional eye disease (glaucoma, corneal scar, dry eye, etc) and those with advanced keratoconus were also excluded. Patients who used contact lenses were examined 15 days after removing the lenses.

Comprehensive ocular examination, including best-corrected visual acuity measurement with a Snellen chart, slit lamp examination, topographic measurements using a Scheimpflug camera system were performed in all subjects. Keratoconus was diagnosed with clinical and topographic signs. In addition the topographic data, patients had at least one clinical sign, including Munson sign, scissor reflex during retinoscopy, Fleischer ring, Vogt striae,

increased visibility of the corneal nerves, and Rizzuti sign. For topographic measurements, Sirius Scheimpflug analyzer (Phoenix software, CSO-Italy) was used and measurements were obtained by a single experienced examiner. Images were confirmed under a quality-specification window and good-quality scans were included. Flat keratometry (K1), steep keratometry (K2) values (in a central corneal ring, 3 mm in diameter), and apex curvature keratometry (Kmax) values (in 8mm central corneal area) were obtained for both groups using the Scheimpflug camera system. Both anterior and posterior elevation maps were obtained from the spherical, aspherical and aspherotoric reference surfaces by assessing an 8 mm central corneal area.

Topographic data were used to determine a more sensitive and specific corneal elevation mapping method to use in the differentiation of normal and keratoconic corneas.

Statistical Analyses: Statistical analyses were performed using SPSS v. 17.0 software. The corneal elevation values, age, gender, and K values were used as variables. Numerical values were stated as mean ± standard deviation (SD). The parametric distribution of the continuous variables in the keratoconus and control groups was confirmed by the Kolmogorov- Smirnov test. The comparison of the two groups in terms of continuous variables was analyzed using the t-test in the independent groups. The Chi-square test was used for the gender comparison of the two groups. The specificity, sensitivity, cut-off point and area under the curve of height data obtained from all the reference surface maps were calculated using receiver operator characteristics (ROC) curves. A value of $p< 0.05$ was accepted as statistically significant.

RESULTS

There was no statistically significant difference between the keratoconus group and the control group in respect of demographics (age, gender) ($p>0.05$). The Control group included 18 males (78%) and 5 females (22%) with a mean age of 26.9±6.31 years. Keratoconus group was consisted of 16 males (64%) and 9 females (36%) with a mean age of 23.7±8.16 years (Table 1).

Table 1. The main clinical and demographic findings of the keratoconus and control

	Keratoconus		**Control**	
	Male	**Female**	**Male**	**Female**
Gender, n (%)	16(64)	9(36)	18(78)	5(22)
Age, years (mean±sd)	23.7±8.16		26.9±6.31	
Miyopi, (mean±sd), (D)	5.05±1.85		4.43±1.54	
Astigmatism, (mean±sd), (D)	4.67±2.05		1.68±1.38	
Munson sign (n)	2	1	0	0
Vogt stria (n)	3	1	0	0
Scissors reflex (n)	3	1	0	0
Fleischer ring (n)	2	0	0	0
Rizutti sign (n)	3	1	0	0
Corneal thickness <500 µm, (n)	2	1	1	0
D=Diopter				

In the keratoconus group the mean K1, K2 and Kmax values were 50.35±7.6, 54.35±9.3, 58.64±9.32 D respectively. In the control group, the K1, K2, and Kmax values were 41.94±1, 42.61±1.04 and 43.28±1 D respectively. There was a statistically significant difference between the groups in terms of K1, K2 and Kmax values ($p<0.05$, Table 2).

Table 2. The mean and standard deviation keratometry values of the keratoconus and control group

	Keratoconus (n=40)	Control group (n=40)	p values
K1 (D)	50.35±7.60	41.94±1.00	0.001
K2 (D)	54.35±9.30	42.61±1.04	0.001
Kmax (D)	58.64±9.32	43.28±1.00	0.001
K1= flat keratometry, K2= steep keratometry, Kmax= apex keratometry value			

The anterior and posterior corneal elevation values of the keratoconus and the control group were assessed according to the spherical, aspherical and aspherotorical refer-

ence surface. The differences between the keratoconus group and the control group were found to be statistically significant in terms of the mean anterior and posterior elevation values obtained with all of the three reference surfaces ($p<0.05$) (Table 3).

Table 3. The mean anterior and posterior elevation values obtained from different reference surfaces in the keratoconus and control groups.

	Keratoconus (n=40)	Control (n=40)	p values
PE Spherical (µm)	16.65±30.49	5.15±2.97	0.020
PE Aspherical (µm)	53.07±24.14	6.97±2.30	0.001
PE Aspherotoric (µm)	53.10±24.70	5.80±2.45	0.001
AE Spherical (µm)	11.72±10.56	1.50±1.01	0.001
AE Aspherical (µm)	26.45±14.85	3.05±1.39	0.001
AE Aspherotoric (µm)	25.30±14.17	2.32±1.27	0.001
AE; Anterior elevation, PE; Posterior elevation			

The cut-off point, sensitivity and specificity values of each reference surface were analyzed and compared between the groups (Table 4). As shown in Table 4, the highest sensitivity and specificity values were obtained from the aspherical and aspherotorical reference surfaces rather than the spherical reference surface. It was also observed that posterior elevation values were found to be more sensitive and specific than the anterior elevation values.

Table 4. The cut-off point, sensitivity and specificity values of the anterior and posterior elevation maps obtained from different reference surfaces.

	Cut off point (µm)	Sensitivity (%)	Specificity (%)
PE Spherical	7.5	75	80
PE Aspherical	9.5	97.5	90
PE Aspherotoric	7.5	97.5	80
AE Spherical	2.5	85	85
AE Aspherical	4.5	95	82.5
AE Aspherotoric	3.5	95	85
AE; Anterior elevation, PE; Posterior elevation			

The predictive accuracy of the anterior and posterior corneal elevation maps was defined as the area under the ROC curves and it was high for the aspherical and aspherotorical reference surfaces in the keratoconus group ($p>0.90$) (Table 5).

Table 5. The estimated accuracy of the anterior and posterior corneal elevation maps was defined as the area under the ROC curves

	Area Under the Curve	Standard Error
PE Spherical	0.819	0.057
PE Aspherical	0.987	0.012
PE Aspherotoric	0.973	0.023
AE Spherical	0.858	0.053
AE Aspherical	0.969	0.022
AE Aspherotoric	0.971	0.021
AE: Anterior elevation, PE: Posterior elevation		

Statistical analysis results of both the posterior and anterior elevation map values obtained with three reference surfaces in the keratoconus and control groups were plotted as ROC curves in figures 1 and 2. Also, posterior elevation maps for different reference surfaces of a patient are shown in Figures 3,4 and 5.

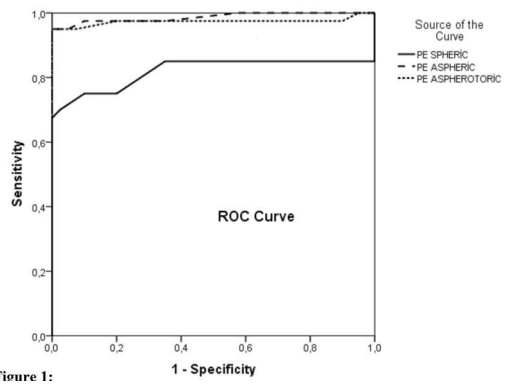


Figure 1:

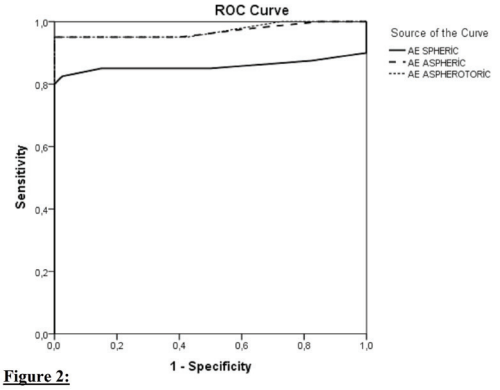


Figure 2:

Figure 1 and 2. The statistical analysis results of both the posterior and anterior elevation map values produced from the three reference surfaces in the keratoconus and control groups

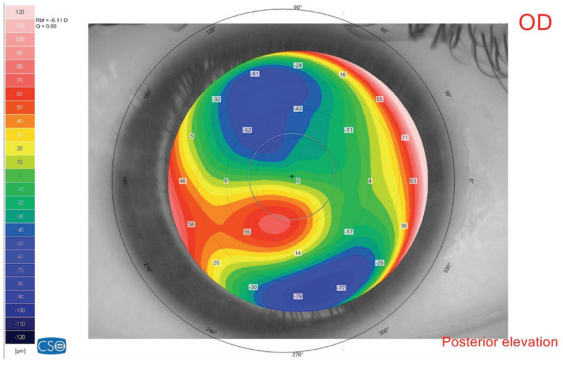


Figure 3

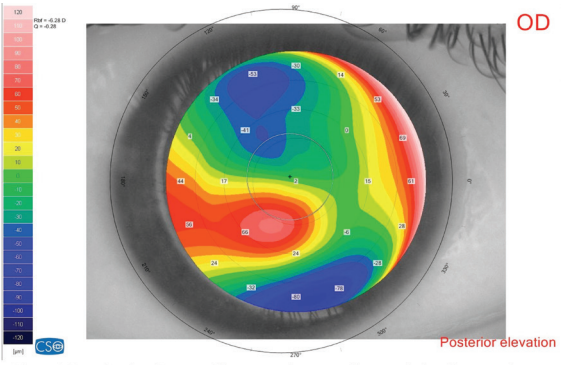


Figure 4

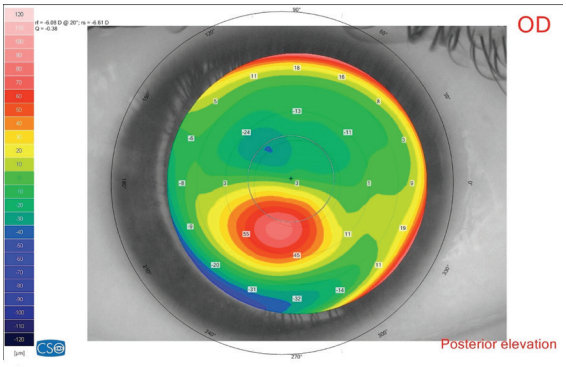


Figure 5

Figure 3, 4, 5. Posterior elevation maps for different reference surfaces of a patient

DISCUSSION

The results of this study demonstrated that the highest sensitivity and specificity values were obtained from the aspherical and aspherotoric reference surfaces rather than the spherical reference surface. Also, our study results showed that posterior elevation values were found to be more sensitive and specific than the anterior elevation values.

Evaluation of the elevation values of the anterior and posterior cornea obtained with Scheimpflug imaging systems in keratoconus diagnosis has gained favor recently. Corneal elevation analyses provide a better assessment of the corneal surface due to the fact that these analyses are inde-

pendent of the axis, orientation and position.[10-13]

In our study, the difference between the keratoconus and control group was found to be statistically significant in terms of both anterior and posterior elevation values according to all three reference surfaces. In a study, anterior and posterior corneal power, elevation and thickness values were analyzed with the Scheimpflug imaging system and a significant difference was found between ectatic and normal corneas in these parameters.[14] Jafarinasab et al. demonstrated that anterior and posterior elevation maps measured with Galilei analyzer in the 3-mm zone can effectively discriminate keratoconus from normal corneas.[15] Ishii et al. stated that anterior and posterior corneal surface elevation data obtained with elevation-based tomography provide useful information to improve keratoconus diagnostic accuracy and to grade the severity of keratoconus.[16] The results of the current study are consistent with these studies showing that the elevation data of the anterior and posterior corneal surface are an important criterion in the detection of keratoconus. However, there is no consensus yet on which of the different reference surfaces is better at the determination of keratoconus in elevation mapping. The sensitivity and specificity of the elevation values in the posterior elevation map to spherical, aspherical and aspherotorical reference surfaces were 75%-80%, 97.5%-90%, and 97.5%- 80% respectively. The areas under curve (AUC) values of the spherical, aspherical and aspherotoric maps of the posterior cornea were 0.819, 0.987 and 0.973, respectively. Of the reference surfaces used in the posterior elevation map, the aspherical and aspherotoric reference surface measurements appeared to be more sensitive than those of the spherical reference surface and the most accurate reference surface was the aspherical reference surface. According to the results of this study, posterior elevation values were found to be more sensitive and specific than anterior elevation values on aspherical and aspherotoric reference surfaces. The advantage of the posterior surface measurement is that it is not affected by tear film irregularities. The assessment of the posterior cornea is important in the diagnosis of keratoconus because epithelial compensation may hide the cone formation on the anterior surface.[17] Various studies had shown that posterior corneal elevation data were more accurate than anterior elevation data and also that the aspherical and aspherotoric reference surfaces were superior to the spherical reference surface in keratoconus detection. In a study performed with Galilei dual Scheimpflug analyzer; different reference surfaces were compared. It was reported that the best-fit torical and aspherical reference surface were more effective than the best fit spherical surface in forme fruste and keratoconus diagnosis. They also reported that posterior surface elevation maps relative to best-fit toric and aspherical were more sensitive than the anterior surface maps.[18] In a study by Kovacs et al., posterior corneal elevation was assessed using a Scheimpflug camera, and it was reported that posterior corneal elevation maps could be effectively used in discriminating keratoconic and normal corneas. Furthermore, the toric ellipsoid reference surface was found to be the most sensitive method in identifying keratoconus.19Sideroudi et al. suggested that the toric ellipsoid reference surface, with a diameter of 8 mm and an eccentricity of 0.4, should be used in the diagnosis and follow-up of keratoconus cases.[20]

Assessing an aspherotoric normal cornea in relation to an aspherotoric reference surface is expected to reveal less topographic differences compared to spherical reference surfaces. In other words, the best-fit contact lenses for a normal cornea would be contact lenses with an aspherotoric surface. Asphericity and toricity induce a rigid pattern seen in elevation maps compared to the spherical reference surface, therefore affect the precise assessment of the elevation data.[17] This aspherotoricity becomes more prominent in keratoconic cornea. Therefore, evaluation of the aspherotoric reference surface minimizes the influence of the corneal aspherotoricity which could result in miscalculation of the elevation data, and it also helps to detect subtle differences on a normal aspherotoric corneal surface.

This study contained some limitations. Firstly there was a limited number of patients and the patients were at different stages of keratoconus which could affect the analysis results. It is possible to obtain clearer results by carrying out further studies involving a greater number of patients of a similar stage and a larger control group.

In conclusion, the selection of an appropriate reference surface is very important in the diagnosis and classification of keratoconus in Scheimpflug systems. According to the current study results, a topographic assessment of the posterior cornea based on the aspherical and aspherotoric reference surfaces appears to be more effective in determining keratoconus.

References

1. *Swartz T, Marten L, Wang M. Measuring the cornea: the latest developments in corneal topography. CurrOpinOphthalmol. 2007;18:325–33.*
2. *Konstantopoulos A, Hossain P, Anderson DF. Recent advances in ophthalmic anterior segment imaging: a new era for ophthalmic diagnosis? Br J.Ophthalmol. 2007;9:1551–7*
3. *Tomidokoro A, Oshika T, Amano S, Higaki S, Maeda N, Miyata K. Changes in anterior and posterior corneal curvatures in keratoconus. Ophthalmology. 2000;107:1328–32.*
4. *Rao SN, Raviv T, Majmudar PA, Epstein RJ. Role of Orbscan II in screening keratoconus suspects before refractive corneal surgery. Ophthalmology.2002;109:1642-6.*
5. *Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr, Guell JLet al. Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases. Global consensus on keratoconus and ectatic diseases. Cornea. 2015;34:359-69.*
6. *am HB, Lim KL. Corneal elevation indices in normal and keratoconic eyes. J Cataract Refract Surg. 2006;32:1281–7.*
7. *de Sanctis U, Loiacono C, Richiardi L, Turco D, Mutani B, Grignolo FM. Sensitivity and specificity of posterior elevation measured by Pentacam in discriminating keratoconus/subclinical keratoconus. Ophthalmology 2008;115:1534–9.*
8. *Mihaltz K, Kovacs I, Takacs A, Nagy ZZ. Evaluation of keratometric, pachymetric, and elevation parameters from keratoconic corneas with Pentacam. Cornea. 2009;28:976–80.*
9. *Tanabe T, Oshika T, Tomidokoro A, Amano S, Tanaka S, Kuroda T et al. Standardized color-coded scales for anterior and posterior elevation maps of scanning slit corneal topography. Ophthalmology 2002; 109:1298–302.*
10. *Wang JC, Hufnagel TJ, Buxton DF. Bilateral keratectasia after unilateral laser in situ keratomileusis: a retrospective diagnosis of ectatic corneal disorder. J Cataract Refract Surg. 2003;29:2015-8.*
11. *Nilforoushan MR, Speaker M, Marmor M, Abramson J, Tullo W, Morschauser Det al. Comparative evaluation of refractive surgery candidates with Placido topography, Orbscan II, Pentacam, and wavefront analysis. J Cataract Refract Surg. 2008;34:623–31.*
12. *Rufer F, Schröder A, Arvani MK, Erb C. Central and peripheral corneal pachymetry standard evaluation with the Pentacam system. KlinMonatsblAugenheilkd. 2005;222:117–22.*
13. *Ho JD, Tsai CY, Tsai RJ, Kuo LL, Tsai IL, Liou SW. The validity of the keratometric index: evaluation by the Pentacam rotating Scheimpflug camera. J Cataract Refract Sur. 2008;34:137–45.*
14. *Ucakhan O, Cetinkor V, Ozkan M, Kanpolat A. Evaluation of Scheimpflug imaging parameters in subclinical keratoconus, keratoconus, and normal eyes. J Cataract Refract Surg. 2011;37:1116–24.*
15. *Jafarinasab MR, Feizi S, Karimian F, Hasanpour H. Evaluation of corneal elevation in eyes with subclinical keratoconus and keratoconus using Galilei double Scheimpflug analyzer. Eur J Ophthalmol. 2013;23:377-84.*
16. *Ishii R, Kamiya K, Igarashi A, Shimizu K, Utsumi Y, Kumanomido T. Correlation of corneal elevation with the severity of keratoconus by means of anterior and posterior topographic analysis. Cornea. 2012;31:253-8.*
17. *Reinstein DZ, Archer TJ, Gobbe M. Corneal epithelial thickness profile in the diagnosis of keratoconus. J Refract Surg 2009;25:604–10.*
18. *Smadja D, Santhiago MR, Mello GR, Krueger RR, Colin J, Touboul D. Influence of the reference surface shape for discriminating between normal corneas, subclinical keratoconus, and keratoconus. J Refract Surg. 2013;29:274-81.*
19. *Kovács I, Miháltz K, Ecsedy M, Nemeth J, Nagy ZZ. The role of reference body selection in calculating posterior corneal elevation and prediction of keratoconus using rotating Scheimpflug camera. Acta Ophthalmol.2011; 89:251–6.*
20. *Sideroudi H, Labiris G, Giarmoukakis A, Bougatsou N, Kozobolis V. Contribution of reference bodies in the diagnosis of keratoconus. Optom Vis Sci. 2014;91: 676-81.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Assesment of Optic Nerve Sheath Diameter in Healthy Adults in Turkey

Türkiye'de Sağlıklı Erişkinlerde Optik Sinir Kılıfı Çapının Değerlendirilmesi

Emre Gökçen[1], İbrahim Çaltekin[1], Levent Albayrak[1], Atakan Savrun[2], Dilek Atik[1], Sevilay Vural[1], Nuray Kılıç[1], Mikail Kuşdoğan[1], Hasan Burak Kaya[1]

[1] Acil Tıp Anabilim Dalı, Bozok Üniversitesi Tıp Fakültesi
[2] Acil Tıp Anabilim Dalı, Ordu Üniversitesi Tıp Fakültesi

Yazışma Adresi / *Correspondence:*
Emre Gökçen

Yozgat Bozok Üniversitesi, Erdoğan Akdağ Yerleşkesi, Atatürk yolu 7. Km, Merkez-Yozgat /Türkiye
T: **+90 505 571 86 88** E-mail **: emregokcenacl@gmail.com**

Geliş Tarihi / Received : **29.08.2020** Kabul Tarihi / Accepted : **05.01.2021**

Orcid :

Emre Gökçen https://orcid.org/0000-0002-6018-6105
Hasan Burak Kaya https://orcid.org/0000-0001-8851-2614
İbrahim Çaltekin https://orcid.org/0000-0002-3973-0655
Levent Albayrak https://orcid.org/0000-0002-4288-8170
Atakan Savrun https://orcid.org/0000-0001-7468-4159
Mikail Kuşdoğan https://orcid.org/0000-0003-4075-8601
Nuray Kılıç https://orcid.org/0000-0003-1371-3600
Sevilay Vural https://orcid.org/0000-0002-1722-7987
Dilek Atik https://orcid.org/0000-0002-3270-8711

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):85-90) DOI: 10.31832 smj.787427**

Abstract

Objective	The ultrasonographically detected optic nerve sheath diameter (ONSD) measurement is a practical and non-invasive method for the detection of increased intracranial pressure. However, it is important to know the normal ONSD values of a healthy population in the interpretation of pathological ONSD values. In this study, we aimed to investigate how the normal values of ONSD are distributed in normal healthy volunteers in Turkish population.
Materials and Methods	This descriptive cross sectional type design study was planned between November 15, 2019 and April 15, 2020. The study included 160 healthy volunteers who were over 18 years of age and didn't have acute and chronic systemic disorders. ONSD of the subjects were measured from both eyes ultrasonographically.
Results	ONSD means (median, IQR) of right and left eyes of the subjects were measured as 4.87 (0.41) mm and 4.86 (0.32) mm, respectively. Right and left eye ONSD measurements were detected lower in female gender than men, and this difference was statistically significant. (p = 0.017 and p = 0.031, respectively).
Conclusion	It was found ONSD value as 4.87 (0.41) for the right eye and 4.86 (0.32) mm for the left eye in healthy individuals in Turkish population in our study. Determination of ONSD optimal reference values in healthy individuals would benefit in predicting increase in intracranial pressure in clinical practice.
Keywords	optic nerve sheath diameter; ultrasonography; healthy volunteer

Öz

Amaç	*Artmış intrakranial basınç artışının tespitinde ultrasonografik olarak tespit edilen optik sinir kılıf çapı (OSKÇ) ölçümü pratik ve non invaziv bir yöntemdir. Bununla birlikte patolojik OSKÇ değerlerinin yorumlanmasında sağlıklı bir popülasyonun normal OSKÇ değerlerinin bilinmesi önem arz eder. Biz bu çalışmada Türk popülasyonundaki normal sağlıklı gönüllülerde OSKÇ normal değerlerinin nasıl dağıldığını araştırmak istedik.*
Gereç ve Yöntemler	*Bu kesitsel tipte tanımlayıcı araştırma, 15 Kasım 2019 ile 15 Nisan 2020 tarihleri arasında planlandı. Çalışmaya 18 yaş üstü, akut ve kronik sistemik rahatsızlığı bulunmayan 160 sağlıklı gönüllü dahil edildi. Deneklerin her iki gözden ultrasonografik olarak OSKÇ'ları ölçüldü.*
Bulgular	*Deneklerin sağ ve sol göz OSKÇ ortalamaları (median, IQR) sırasıyla 4,87 (0,41) mm ve 4,86 (0,32) mm olarak ölçüldü. Sağ göz ve sol göz OSKÇ ölçümleri bayan cinsiyette erkeklere göre daha düşük saptandı ve bu fark istatiksel olarak anlamlıydı. (p=0,017 ve p=0,031, sırasıyla).*
Sonuç	*Çalışmamızda Türk popülasyonunda sağlıklı erişkinlerde OSKÇ ölçümleri sağ göz için 4.87 (0.41) mm sol göz için 4.86 (0.32) mm olarak tespit edildi. Sağlıklı bireylerde OSKÇ optimal referans değerlerinin belirlenebilmesi klinik pratikte kafa içi basınç artışını öngörmede fayda sağlayacaktır.*
Anahtar Kelimeler	*optik sinir kılıf çapı; ultrasonografi; sağlıklı gönüllü*

INTRODUCTION

Increased intracranial pressure (ICP) is one of the common conditions in patients admitted to the emergency service, and close clinical follow-up is often required for these patients.[1-3] In addition, early and accurate diagnosis is of great importance in preventing possible complications and determining treatment strategies in these patients.[4-6] ICP can be measured with tools that can be placed intraparenchymal and intraventricular. Although ICP can be measured directly with these tools, there are dangerous complications of it such as bleeding and infection. Moreover, they are not cost-effective, require intensive care conditions and are therefore preferred in selected patients.[4,5,7,8]

The optic nerve sheath can be described as a continuation of the intracranial dura surrounding the subarachnoid space.[9] Changes occurred in ICP are also reflected in the optic nerve sheath via subarachnoid fluid.[9,10] The optic nerve sheath diameter (ONSD), which can also be measured ultrasonographically, has taken its place as a non-invasive method used to predict ICP. Being easily applicable, inexpensive, repeatable and non-interventional procedure is one of the reasons why ultrasonography is preferred in the emergency service.[11,12] Although the expansion in the optic nerve sheath can be visualized with increased intracranial pressure, an optimal ONSD value has not yet been reached in the representation of increase in ICP. Moreover, potential factors such as genetic structure and racial differences that may affect the optic nerve sheath have not been fully investigated due to the lack of studies performed on this subject. In the light of current information, there is no study conducted on ONSD on normal healthy volunteers in Turkish population in the literature. In this study, it was aimed to investigate how the normal values of ONSD are distributed in normal healthy volunteers in Turkish population.

MATERIALS and METHODS

This descriptive cross sectional type design study was conducted in emergency service of a tertiary hospital between November 15, 2019 and April 15, 2020. During the study, the principles of Helsinki Declaration were adhered to, and written informed consents of all participants were obtained. Approval was obtained by Bozok University Faculty of Medicine Ethics Committee before the study started (Ethics Committee date / number: 30.10.2019 / 2019-10-244).

Healthy volunteers who were over 18 years of age and didn't have acute and chronic systemic disorders were enrolled in the study. Study individuals were composed of the relatives of the patients admitted to emergency service and university hospital staff volunteering to participate in the study. The individuals who were under the age of 18, had a history of cardiovascular disease, had neurological problems, had endocrinological diseases such as hypertroidism, hypotroidism and diabetes mellitus, had immunological and rheumatological diseases, had ocular disorder (vasculitis, tumor, glaucoma etc.) affecting the optic nerve and intraocular pressure, and used drugs affecting ICP and intraocular pressure were excluded from the study.

Heights, weights, ages and genders of the subjects accepted to the study were recorded. Then, ONSD measurements of the patients were performed ultrasonographically. HM70A with Plus ultrasound system (Samsung Medison Co., Ltd., Seoul, Korea) and 7-16 Mhz linear probe were used for the ultrasonographic examination. The subjects were placed on a stretcher in a supine position with a comfortable head. The eye socket was filled with a water-soluble and conductive gel when eyes were closed. The linear probe was placed on the eyeball filled with gel. The optic nerve was detected 3 mm behind the optical disc displayed behind the eyeball. Measurements were performed using an electronic caliper from this line. Optical nerve arachnoid differentiation was determined on ultrasonographic imaging (Figure 1). Measurements were realized by 4 emergency medicine specialists. Three measurements were taken for each eye and the mean of these measurements was recorded.

Statistical analysis: Statistical analyzes were performed using IBM SPSS statistics version 22 software. The suitability of variables to normal distribution was examined with Kolmogorov-Smirnov test. Descriptive analyzes were given using the median and interquartile ranges for non-normally distributed variables. Comparison of independent variables that did not show normal distribution was made using Man-Whitney U test. Correlation coefficients and statistical significance were calculated for the associations between non-normally distributed variables using Spearman test. P-values below 0.05 were considered statistically significant.

Table 1. Demographic characteristics and ONSD measurements of healthy subjects.

Study Group		n=160
Gender, n (%) :		
	Male	74 (46.2)
	Female	86 (53.8)
Age		35 (11)
Height , (m)		1.68 (0.1)
Weight , (kg)		75 (15)
BMI, (kg/m2)		25.8 (3.97)
R-ONSD, mm		4.87 (0.41)
L-ONSD, mm		4.86 (0.32)

BMI: Body mass index, R-ONSD: Right eye optic nerve sheath diameter, L-ONSD: Left eye optic nerve sheath diameter, Data were expressed as n (%) and median (interquartile range).

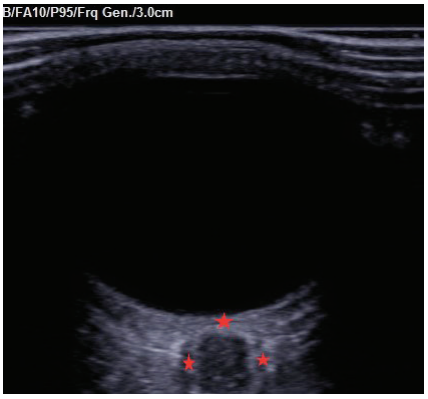


Figure 1: Ultrasonographic view of the optic nerve sheath diameter of a 25-year-old young individual

RESULTS

The average age of the subjects participating in the study was 35 (11), and 74 were male (46.2%) and 86 (53.8%) were female of them. Mean ONSD values of the subjects were measured as 4.87 (0.41) mm (median, IQR) for the right eye and 4.86 (0.32) mm for the left eye. The demographic data of the patients were shown in . Right eye and left eye ONSD measurements were lower in female gender than men, and this difference was statistically significant (p = 0.017 and p = 0.031, respectively) (Table 2) (Figure 2).

Table 2. Comparison of ONSD measurements between gender and right eye/left eye

ONSD, mm	Between gender		p-value
	Male	Female	
Right eye	4.92 (0.3)	4.81 (0.54)	0.017
Left eye	4.89 (0.2)	4.81 (0.49)	0.031
	Between right/left eye		
	Right eye	Left eye	
ONSD,mm	4.87 (0.41)	4.86 (0.32)	0.636

ONSD: Optic nerve sheath diameter, Data were expressed as median (interquartile range)

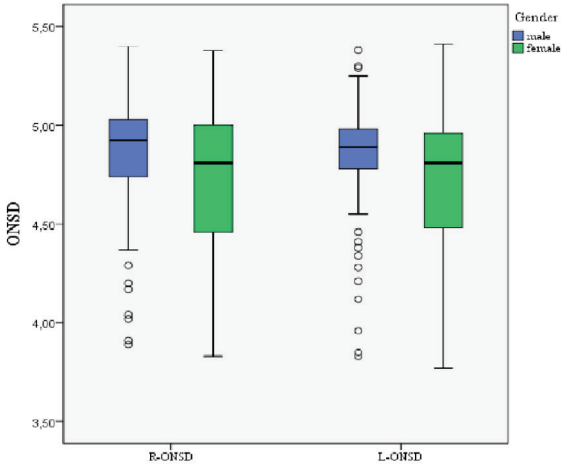


Figure 2: Box plot of the ONSD of different genders according to right and left eye.

The association between the patients' mean ONSD values and age, height, weight and BMI values were examined. No association was found between ONSD values of both

right and left eyes, and age, height, weight and BMI values (Table 3).

Table 3. Correlation analysis of optic nerve sheath diameter between weight, height and body mass index

	p-value	r-value
Right eye		
Weight, (kg)	0.301	0.082
Height, (m)	0.238	0.094
BMI, (kg/m2)	0.592	0.043
Age	0.490	0.055
Left eye		
Weight, (kg)	0.299	0.083
Height, (m)	0.339	0.076
BMI, (kg/m2)	0.514	0.052
Age	0.506	0.053

BMI: Body mass index, r-value: Correlation coefficient

DISCUSSION

In this study, the normal ranges of ONSD values in healthy individuals in Turkish population were investigated. The main findings of this study can be summarized as follows. 1) ONSD value in healthy volunteers was found to be 4.87 (0.41) for the right eye and 4.86 (0.32) mm for the left eye. 2) No statistically significant association was detected between ONSD values and height, weight, BMI and age. 3) ONSD values were observed lower in female gender.

In the studies performed so far, ONSD reference range has differed in healthy volunteers. In the study performed on Chinese healthy volunteers by Chen et al., they reported mean ONSD value as 5.1 ± 0.5 mm.[13] Goeres et al. found the mean of ONSD to be 3.68 ± 0.36 mm in their study conducted on 120 healthy volunteers.[14] In the study realized on 101 healthy volunteers of Bangladesh origin by Maude et al., the mean ONSD value was 4.41 (4.24–4.83) mm.[15] Bauerle et al. observed the mean ONSD value as 5.4 ± 0.6 mm in their study performed on 40 healthy volunteers in Germany.[16] In our study, although the mean ONSD values were close to the values in these two studies[13,15] performed, they were less than the average value found by Chen et al.[13], but more than the mean value reported by Maude et al.[15] These differences in ONSD values may be due to the differences in ethnic origin or ultrasonographic measurement techniques. Sargsyan et al. argued that it is not correct to measure only the 'black stripe' behind the globe without visualizing the differentiation of the optic nerve and arachnoid in ONSD measurement in their study.[17] Goeres et al. reported that they took the 'black stripe' as a basis in their measurements. Although there is no definitive judgment, measurement methods may also have an impact on the lower ONSD values observed by Goeres et al.[14] Optic nerve and arachnoid differentiation were taken into consideration in ONSD measurement in our study.

Chen et al. presented that there was no significant linear association between ONSD-age and ONSD-weight.[13] They also found a statistically significant correlation between ONSD and height but detected that the correlation coefficient was too low. They therefore argued that this association should be considered independent of clinical interpretation. Goeres et al. revealed that there was an association between ONSD and gender, but reported that there was no association between age, weight or height and ONSD.[14] ONSD values were lower in female patients than in men in their study. Bauerle et al. stated that there was no correlation between ONSD and age, BMI and gender.[16] Any correlation between ONSD and age, height, weight and BMI was not found in our study. However, in accordance with the results of Goeres et al.[14], ONSD values were observed lower in female individuals than in men in our study. The difference in ONSD values between women and men may indicate that different threshold values are needed to predict ICP increase. Also, there was no difference between the right and left eyes in terms of ONSD measurement in our study. This may mean that a single eye measurement is sufficient to predict ICP increase.

Limitation: There were some limitations in this study. Firstly, direct measurement methods were not used for ICP estimation of the subjects. According to medical his-

tories and physical examination findings of the subjects, it was concluded that their ICPs were normal. The study was conducted only on adult subjects with BMIs below 30kg / m2. Therefore, our study cannot predict the mean ONSD values of the obese and pediatric age groups. New studies are needed to clarify this issue.

Conclusion: Predicting ICP is critical in many patients admitted to the emergency service. It was found ONSD value as 4.87 (0.41) for the right eye and 4.86 (0.32) mm for the left eye in healthy individuals in Turkish population in our study. Secondly, there was no association between ONSD and age, height, weight and BMI, but ONSD values were lower in female subjects than in men. Determination of ONSD optimal reference values in healthy individuals will benefit in predicting ICP increase in clinical practice. However, larger studies on healthy volunteers to define ONSD normal values are needed.

This study was approved by Bozok University Faculty of Medicine Ethics Committee (Ethics Committee date / number: 30.10.2019 / 2019-10-244).

References

1. *Çökük A, Kozacı N, Ay MO, Açıkalın A, Seviner M, Satar S. Acil Servise Başvuran Kafa Travması Olgularının Değerlendirilmesi. Cukurova Medical Journal. 2013;38(1):63-71.*
2. *Dölen D, Sabanci PA. Kafa Travmasında Beyin Ödemi ve İntrakranyal Basınç Değişimleri. Türk Nöroşir Derg. 2020;30(2):187-193.*
3. *Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med. 2008;15(2):201-204.*
4. *Emmez ÖH, Egemen E. Kafa içi basınç artışı tedavisinde pratik yaklaşımlar. Yoğun Bakım Derg. 2010; 9(2):77-84.*
5. *Harary M, Dolmans RG, Gormley WB. Intracranial pressure monitoring—review and avenues for development. Sensors. 2018;18(2):465.*
6. *Changa AR, Czeisler BM, Lord AS. Management of Elevated Intracranial Pressure: a Review. Curr Neurol Neurosci Rep 2019;19(12):99.*
7. *Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. 2012;367(26):2471-2481.*
8. *Aiolfi A, Benjamin E, Khor D, Inaba K, Lam L, Demetriades D. Brain trauma foundation guidelines for intracranial pressure monitoring: Compliance and effect on outcome. World J Surg. 2017;41(6):1543-1549.*
9. *Hansen H, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surg Radiol Anat. 1996;18(4):323-338.*
10. *Komut E, Kozacı N, Sönmez BM, Yılmaz F, Komut S, Yıldırım ZN, et al. Bedside sonographic measurement of optic nerve sheath diameter as a predictor of intracranial pressure in ED. Am J Emerg Med. 2016;34(6):963-967.*
11. *Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL. Optic nerve ultrasound for the detection of raised intracranial pressure. Neurocrit Care. 2011;15(3):506-515.*
12. *Robba C, Santori G, Czosnyka M, Corradi F, Bragazzi N, Padayachy L, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 2018;44(8):1284-1294.*
13. *Chen H, Ding G-S, Zhao Y-C, Yu R-G, Zhou J-X. Ultrasound measurement of optic nerve diameter and optic nerve sheath diameter in healthy Chinese adults. BMC Neurol. 2015;15(1):106.*
14. *Goeres P, Zeiler FA, Unger B, Karakitsos D, Gillman LM. Ultrasound assessment of optic nerve sheath diameter in healthy volunteers. J Crit Care. 2016;31(1):168-171.*
15. *Maude RR, Hossain MA, Hassan MU, Osbourne S, Sayeed KLA, Karim MR, et al. Transorbital sonographic evaluation of normal optic nerve sheath diameter in healthy volunteers in Bangladesh. PloS one. 2013;8(12):e81013.*
16. *Bäuerle J, Lochner P, Kaps M, Nedelmann M. Intra-and interobsever reliability of sonographic assessment of the optic nerve sheath diameter in healthy adults. J Neuroimaging. 2012;22(1):42-45.*
17. *Sargsyan A, Blaivas M, Geeraerts T, Karakitsos D. Ocular ultrasound in the intensive care unit. Lumb P,Karakitsos D. Critical Care Ultrasound. Vol.1. Philadelphia, Elsevier Saunders. 2014. p. 45-50.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Can Mortality Be Predicted With Semi-Quantitative Visual Scoring In Coronavirus Disease?

Koronavirus Hastalığında Yarı Kantitatif Görsel Skorlama ile Mortalite Öngörülebilir Mi?

Keziban Karacan[1], Alper Karacan[2]

[1] Departmant of Anatomy, Faculty of Medicine, University of Sakarya, TURKEY
[2] Department of Radiology, Faculty of Medicine, University of Sakarya, TURKEY

Yazışma Adresi / *Correspondence:*
Keziban Karacan

Department of Anatomy, Faculty of Medicine, University of Sakarya, The neighborhood of Korucuk, The Campus of Korucuk, Adapazarı, Sakarya, TURKEY
T: **+90 264 295 31 36** E-mail **: kkaracan@sakarya.edu.tr**

Geliş Tarihi / Received : **25.11.2020** Kabul Tarihi / Accepted : **05.01.2021**

Orcid :

Keziban Karacan https://orcid.org/0000-0001-8861-1647
Alper Karacan https://orcid.org/0000-0001-8930-9546

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):91-96) DOI: 10.31832 smj.831560

Abstract

Objective The study was aimed to predict the COVID 19 prognosis using a semi-quantitative scoring method with computed tomography (CT).

Materials and Methods From April 1 to June 25, 2020, 108 symptomatic COVID-19 patients were enrolled and followed up until they were discharged or died. CT scans were reviewed for the patterns and distribution of lung abnormalities, total CT scores and number of lobes involved. A semi-quantitative CT score was calculated based on the extent of lobar involvement (0:0%; 1:5-25%; 2:26-50%; 3:51-75%; 4, 76-100%; range 0-4; global score 0-20). The predictive role of the CT score on the prognosis of the patients was evaluated statistically.

Results The mean global CT score was 7.47±5.18. 12 patient did not show any parenchymal involvement at CT and was therefore scored as 0. Comparisons have been made between lobes for each lung. Regarding the right lung, mean CT score was significantly higher in right lower lobe than in middle lobe (p=0.001) and right upper lobe (p=0.001); mean CT score was significantly higher in right middle lobe than in upper lobe (p=0.001). Concerning the left lung, mean CT score was significantly higher in left lower lobe than in left upper lobe (p =0.001). Mean global CT score of survival group was 5.53±3.94, while mortal group was 9.40±5.57. The score of mortal group was significantly higher than survival group (p=0.001).

Conclusion The imaging features and dynamic changes could provide the most direct evidence for assessing the severity of the disease and the prognosis. Simple scoring method according to CT scans may help triage patients and screening patients who need more aggressive treatment and closely monitoring.

Keywords COVID-19; computed tomography; scoring methods; prognosis

Öz

Amaç *Çalışmamızda Bilgisayarlı tomografi (BT) ile yarı kantitatif bir puanlama yöntemi kullanarak COVID 19 prognozunu tahmin etmeyi amaçladık.*

Gereç ve Yöntemler *1 Nisan - 25 Haziran 2020 arasında 108 semptomatik COVID-19 hastası taburcu olana veya ölene kadar takip edildi. Akciğer anormalliklerinin paternleri ve dağılımı, toplam BT skorları ve tutulan lobların sayısı için BT görüntüleri değerlendirildi. Lober tutulumun kapsamına göre yarı kantitatif BT skoru hesaplandı (0: % 0; 1: % 5-25; 2: % 26-50; 3: % 51-75; 4: %76-100; aralık 0-4; toplam puan 0-20). BT skorunun hastaların prognozu üzerindeki prediktif rolü istatistiksel olarak değerlendirildi.*

Bulgular *Toplam BT skoru ortalama 7.47 ± 5.18'di. 12 hastada BT'de herhangi bir parankimal tutulum görülmedi ve bu nedenle 0 olarak skorlandı. Her akciğer için loblar arasında karşılaştırmalar yapıldı. Sağ akciğerle ilgili olarak, ortalama BT skoru sağ alt lobda orta lobdan (p =0.001) ve üst lobdan (p =0.001) anlamlı olarak yüksekti; ortalama BT skoru sağ orta lobda üst loba göre anlamlı olarak daha yüksekti (p =0.001). Sol akciğerle ilgili olarak ortalama BT skoru sol alt lobda üst lobdan anlamlı olarak yüksekti (p =0.001). Sağ kalanlar grubunun total BT skoru ortalama 5.53 ± 3.94 iken, mortalite grubunda 9.40 ± 5.57 olarak bulundu. Mortalite grubunun skoru sağ kalanlar grubuna göre anlamlı derecede yüksekti (p =0.001).*

Sonuç *Görüntüleme özellikleri ve dinamik değişiklikler, hastalığın ciddiyetini ve prognozunu hesaplamak için doğrudan bilgi sağlayabilir. BT görüntülemeleri ile yapılan basit puanlama yöntemi, hastaların yönlendirilmesine, yakından izlenmeye veya agresif tedaviye ihtiyaç duyan hastaların belirlenmesine yardımcı olabilir.*

Anahtar Kelimeler *COVID-19; bilgisayarlı tomografi; skorlama metodları; prognoz*

INTRODUCTION

The 2019 new coronavirus disease (COVID-19) continues as a pandemic, causing the death of more than 1 million people since December 12, 2020, when it was first seen. Early diagnosis of the disease is very important in terms of both treatment and prevention of its spread.[1,2] Treatment options vary depending on the severity of the patient's condition, and patients with severe and critical cases of COVID-19 have a poor survival prognosis.[3]

Diagnosis of COVID-19 is confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) test with high specificity but low sensitivity.[3,4] Computed Tomography (CT) is an important alternative to RT-PCR in the rapid diagnosis and monitoring of COVID-19 pneumonia. It has been reported that patients with negative RT-PCR results may have positive chest CT findings, and combining RT-PCR with CT scans is expected to improve the diagnosis of COVID-19.[4] CT imaging features of COVID-19 patients at admission included peripheral and bilateral ground glass opacities (GGO) were also often accompanied by consolidation.[5] A better understanding of the progression of CT findings in COVID-19 pneumonia may help facilitate accurate diagnosis and disease stage.[2] Some studies have estimated the severity of COVID-19 based on CT characteristics or semiquantitative visual CT scores.[5]

The purpose of this retrospective study is to predict short-term mortality with CT-based semi-quantitative scoring method.

MATERIALS and METHODS

This retrospective descriptive study was carried out among 108 patients who were admitted to Sakarya University Education and Research Hospital between 1 April and 25 June 2020 with suspicion of COVID-19. The study protocol was approved by the local ethics committee of Sakarya University, Faculty of Medicine (22/09/2020-E.8423 No:71522473/050.01.04/504).

Patients and Study Design

The data required for this retrospective study were obtained from medical records of the patients in the information system of our hospital. RT-PCR assay of nasopharyngeal swab samples and chest CT imaging data of 108 patients were recorded within the scope of the study. The exclusion criteria were as follows: (1) patients who recently experienced clinically defined pulmonary infection attributable to other pathogens, (2) patients with severe artifacts on CT images, and (3) patients whose age was less than 18 years.

CT Imaging Acquisition

All the patients underwent non-enhanced chest CT examinations for detecting COVID-19 pneumonia in the supine position during end-inspiration. The CT scans of patients were performed with a 64-section multi-detector CT scanner (Aquilion 64, Toshiba, Japan). The protocols were as follows. Tube voltage 120 kV, automatic tube current (120–380) mA, thickness 5 mm, slice interval 5 mm, rotation speed 0.5 s, and helical pitch 1.0875:1 or 1.375:1. The informed consents for CT examination were obtained from all patients or their parents.

CT Visual Quantitative Evaluation

The degree of pulmonary involvement of these abnormalities were evaluated by a semiquantitative scoring system. Percentage of involvement in each lobe was recorded as well as the overall lung "total severity score (TSS)". Each of the five lung lobes was assessed for percentage of the lobar involvement and classified as none (0%), minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (76–100%), with corresponded score as 0, 1, 2, 3 or 4. The TSS was reached by summing the five lobe scores (range from 0 to 20).

The distribution of lung abnormalities was recorded as predominantly subpleural (involving mainly the peripheral one-third of the lung), central (involving mainly the central two-third of the lung), both peripheral and central

or random (without predilection for subpleural or central regions).

Statistical Analysis

Data management and statistical analysis were performed by using the statistical package for social sciences (SPSS) version 18 for Microsoft Windows. After administrating descriptive statistical analyses (frequency, percentage distribution, mean ± standard deviation (SD)), normal distribution of continuous variables was assessed by Shapiro-Wilk and Kolmogorov Smirnov Tests. Chi-square test was conducted in order to evaluate the group difference in terms of discrete variables. Indipendent t-tests were administrated for the ones with continuous variables meeting parametric assumptions. The data obtained were compared by considering the gender difference. Statistical significance was indicated by a p value of less than 0.05.

RESULTS

A total of 108 patients, 51 men (47.2%) and 57 women (52.8%), were included in the study. The average age is 70.83±11.98 years (age range, 34–96 years). Peripheral lesions were more common than central lung lesions. The majority of patients had bilateral lung involvement during the course of the diease. (Table 1)

Pathological involvement was most common in the inferior lobes, right lower lobe (RLL) in 93 patients (86.1%), and left lower lobe (LLL) in 87 patients (80.6%). The mean CT scores were found as follows: 1.26±1.02 for the right upper lobe (RUL), 1.33±1.16 for the middle lobe (ML), 1.87±1.34 for the right lower lobe (RLL), 1.2±0.95 for the left upper lobe (LUL), and 1.79±1.39 for the left lower lobe (LLL) (Table 2). The mean global CT score was 7.47±5.18. 12 patient did not show any parenchymal involvement at CT and was therefore scored as 0. Comparisons have been made between lobes for each lung. Regarding the right lung, mean CT score was significantly higher in RLL than in ML (p= 0.001) and RUL (p=0.001); mean CT score was significantly higher in RML than in UL (p=0.001). Concerning the left lung, mean CT score was significantly higher in LLL than in LUL (p=0.001)

Table 1. CT features in mortality and survival groups.

CT Features	All patients (n=108)	Survival Group (n=54)	Mortality Group (n=54)	p
Predominant distribution				
Peripheral	37(34.3)	23(42.5)	14(25.9)	0,068
Peripheral + Central	31(28.7)	9(16.6)	22(40.7)	0,006*
Random	25(23.1)	13(24)	12(22.2)	0,082
Central	1(0.9)	1(1.8)	0	
Anatomic sides involved				
Left lung	1(0.9)	1(1.8)	0	
Right lung	7(6.4)	5(9.2)	2(3.7)	0,241
Both lung	88(81.4)	41(75.9)	47(87)	0,137

CT: Computed Tomography
*p<0,05 statistically significant

Table 2. CT scores in mortality and survival groups

CT Features	All patients (n=108) mean±SD	Survival Group (n=54) mean±SD	Mortality Group (n=54) mean±SD	p
Right upper lobe	1.26 ± 1.02	0.88 ± 0.71	1.64 ± 1.15	0.001*
Right middle lobe	1.33 ± 1.16	1.07 ± 0.98	1.59 ± 1.26	0.019*
Right lower lobe	1.87 ± 1.34	1.38 ± 1.07	2.37 ± 1.41	0.001*
Left upper lobe	1.2 ± 0.95	0.88 ± 0.74	1.54 ± 1.01	0.001*
Left lower lobe	1.79 ± 1.39	1.31 ± 1.12	2.27 ± 1.47	0.001*
Total CT score	7.47± 5.18	5.53 ± 3.94	9.40 ± 5.57	0.001*

CT: Computed Tomography SD: Standard Deviation
*p<0,05 statistically significant

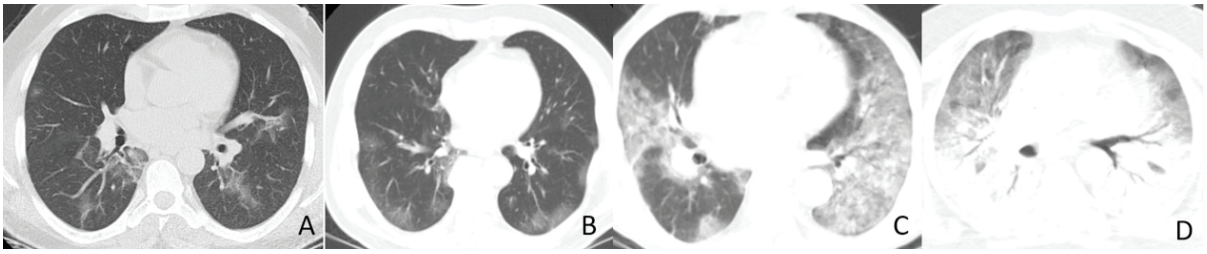


Figure 1. Representative computed tomography (CT) images of COVID-19 pneumonia. The CT images show multifocal bilateral ground-glass opacities (A, B, C) and ground-glass opacities with consolidations(D). Total CT score was A:3, B:6, C:15 and D:20

Mean global CT score of survival group was 5.53±3.94, while mortality group was 9.40±5.57. The score of mortality group was significantly higher than survival group (p=0.001).

DISCUSSION

COVID-19 pneumonia can cause respiratory failure and death, especially in elderly patients with comorbidities.[6,7] The treatment protocol is related the severity of the disease.[8] The fastest and most reliable method to determine the severity of the disease is CT.[9]

The average sensitivity of the diagnostic performance of CT for COVID-19 is 87.8% and the specificity is 66.4%.10 CT is widely used in the diagnosis of COVID-19, but is used in conjunction with PCR-RT to confirm the diagnosis.

There are different scoring methods used to determine the severity of the disease.[11,12] The CO-RADS classification, designed by the Dutch Radiology Association, has been described as simple and convenient, but has not yet been standardized.[10] CO-RADS assesses the suspicion for pulmonary involvement on CT. Accordingly, it has to be interpreted together with the duration and type of symptoms, as well as clinical and laboratory findings, when it comes to building a clinical diagnosis of COVID-19 with or without lung involvement. CO-RADS score, tested on a large sample of symptomatic patients, should be considered a valid tool for the identification of lung involvement in patients with suspected COVID-19. Moreover, the CO-RADS scheme has been developed specifically to be used in patients with moderate to severe symptoms.[13] But in CO-RADS a final diagnosis was not available for patients with false-positive CT findings.[14]

In a recent study by Michael et al., a scoring method used to show the severity of inflammation on CT images based on the degree of involvement of each lobe.[15] We used the same method to measure pulmonary inflammation and correlate it with disease prognosis.

Consistently with several recent reports regarding to CT findings of 2019-nCoV infected pneumonia (NCIP), our results showed that CT manifestations of NCIP were peripheral (34%), bilateral (81%) and lower lung zones (91%) being mostly involved.

Yiki H. et al. stated that 47-53% of patients who died from COVID-19 had GGO and consolidation and the total score average was 12.97 ± 5.87. The authors also showed that in patients who died from COVID-19, the total CT score increased significantly in follow-up imaging compared to the time of presentation. 16 In our study, the total CT score of mortality group was 9.40 ± 5.57 and survival group was 5.53 ± 3.94. The CT scores were significantly higher in mortality group compared to survival group.

As a conclusion,the imaging features and dynamic changes could provide the most direct evidence for assessing the

severity of the COVID-19 prognosis. We hope the simple scoring method according to CT scans may help triage patients and screening patients who need more aggressive treatment and closely monitoring. However, the efficacy of such approach to decrease mortality remains to be validated in future studies.

The study protocol was approved by the local ethics committee (Faculty of Medicine, Sakarya University, Date:22/09/2020-E.8423 No:71522473/050.01.04/504).

References

1. *Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol. 2020; 92(4): 401–402. https://doi.org/10.1002/jmv.25678 PMID: 31950516*
2. *Bogoch II, Watts A, Thomas-Bachli A, et al. Potential for global spread of a novel coronavirus from China. J Travel Med. 2020; 27(2), taaa011. https://doi.org/10.1093/jtm/taaa011 PMID: 31985790.*
3. *Xie X, Zhong Z, W Zhao, C Zheng, F Wang, J Liu. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. Radiology. 2020; 200343. Advance online publication. https://doi. org/10.1148/radiol.2020200343*
4. *Fang Y, Zhang H, Xie J, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiolog. 2020; 200432. Advance online publication. https://doi.org/10.1148/radiol.2020200432*
5. *Zhang B, Zhang J, Chen H, Chen L, Chen Q, Li M, et al. Novel coronavirus disease 2019 (COVID-19): relationship between chest CT scores and laboratory parameters. European Journal of Nuclear Medicine and Molecular Imaging, 2020; 1.*
6. *Xiong F, Tang H, Liu L, Tu C, Tian JB, Lei CT, Liu J, et al. Clinical characteristics of and medical interventions for COVID-19 in hemodialysis patients in Wuhan, China. J. Am. Soc. Nephrol. 2020; 31: 1387–1397.*
7. *Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized With COVID-19 in the New York city area. JAMA 2020; 323: 2052–2059.*
8. *HE, Yueyue. Translation: Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7): National Health Commission, National Administration of Traditional Chinese Medicine. Infectious Microbes & Diseases. Chin Med J 2020; 133:1087-1095.*
9. *Kim H. Outbreak of novel coronavirus (COVID-19): what is the role of radiologists? Eur Radiol 2020; Feb 18 [Epub]. https:// doi.org/10.1007/s00330-020-06748-2.*
10. *Fujioka T, Takahashi M, Mori M, Tsuchiya J, Yamaga E, Horii T, et al. Evaluation of the usefulness of CO-RADS for chest CT in patients suspected of having COVID-19. Diagnostics, 2020; 10(9): 608.*
11. *Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol 2020; Mar 25 [Epub]. https://doi.org/10.1007/s00330-020-06817-6.*
12. *Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Invest Radiol 2020; 55:327-331.*
13. *Prokop M, Van Everdingen W, Van Rees VT, Quarles UJ, Stöger L, Beenen L et al. CO-RADS–A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. Radiology, 2020; 201473.*
14. *Bellini D, Panvini N, Rengo M, Vicini S, Lichtner M, Tieghi T et al. Diagnostic accuracy and interobserver variability of CO-RADS in patients with suspected coronavirus disease-2019: a multireader validation study. European radiology, 2020; 1-9.*
15. *Chung M, Bernheim A, Mei X, et al CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology, 2020; 200230. https:// doi.org/10.1148/radiol.2020200230.*
16. *Hu Y, Zhan C, Chen C, Ai T, Xia L. Chest CT findings related to mortality of patients with COVID-19: A retrospective case-series study. Plos one, 2020; 15: 8 e0237302.*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Relations of Brugada ECG Pattern and Fraqmented QRS in Patient with Schizophrenia

Şizofreni Hastalarında Brugada EKG Paterni ve Fraqmente QRS İlişkisi

Osman Bektaş[1], Ahmet Kaya[1], Esra Yancar Demir[2], Seçkin Dereli[1]

[1] Department of Cardiology, Ordu University Medical School, Ordu, Turkey
[2] Department of Psychiatry, Ordu University Medical School, Ordu, Turkey

Yazışma Adresi / *Correspondence:*
Osman Bektaş

Ordu University Medical School, Department of Cardiology, 52000, Ordu, Turkey
T: **+90 452 225 23 42** E-mail **: bektas7960@gmail.com**

Geliş Tarihi / Received : **09.09.2020** Kabul Tarihi / Accepted : **06.01.2021**

Orcid :

Osman Bektaş https://orcid.org/0000-0002-6616-9891
Ahmet Kaya https://orcid.org/0000-0001-9845-7938
Esra Yancar Demir https://orcid.org/0000-0002-9639-6649
Seçkin Dereli https://orcid.org/0000-0003-0090-3835

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):97-102) DOI: 10.31832/smj.792890**

Abstract

Objective	Schizophrenia is a psychiatric disease with high risk of fatal rhythm disorders and sudden cardiac death. A previous study reported that Brugada syndrome was highly prevelant in patients with schizophrenia. In this study we aimed to investigate the prevelance of Brugada syndrome and fraqmanted QRS in patients with schizophrenia.
Materials and Methods	Two hundred and fifty patients with schizophrenia who were followed up in the psychiatry clinic, and 400 age- and sex-matched non schizophrenia controls were included. Standart ECGs and high intercostal ECGs with V1 and V2 derivation above two intercostal intervals were taken.
Results	In schizophrenia patients, Type 1 Brugada syndrome was not observed, Type 2 Brugada was identified in one subject and Type 3 Brugada was observed in two patients. In the control group, Type 2 Brugada pattern was identified in one subject and again one control had Type 3 Brugada pattern(p=0.320). The fragmented QRS (fQRS) incidence, QRS duration and corrected QT were observed to be higher in the schizophrenia group compared to the control group (p=0.001, p=0.003, p<0.001, respectively).
Conclusion	There is no increased prevalence of Brugada-ECG pattern in patients with schizophrenia. Importantly, the prevelance of fQRS was significantly higher in patients with schizophrenia compared to the control group. Fqrs can be used to estimate the frequency of cardiovascular events in patients with schizophrenia.
Keywords	Schizophrenia; Brugada Syndrome; fragmented QRS

Öz

Amaç	*Şizofreni, ölümcül ritim bozuklukları ve ani kardiyak ölüm riski yüksek olan psikiyatrik bir hastalıktır. Brugada sendromunun şizofreni hastalarında oldukça yaygın olduğunu düşünülmektedir. Bu çalışmada şizofreni hastalarında Brugada sendromu ve fraqmante QRS sıklığını araştırmayı amaçladık.*
Gereç ve Yöntemler	*Psikiyatri kliniğinde izlenen iki yüz elli şizofreni hastası ve 400 yaş ve cinsiyet uyumlu şizofreni olmayan kontrol grubu çalışmaya dahil edildi. Standart EKG'ler ve iki interkostal aralığın üzerinde V1 ve V2 derivasyonu olan yüksek interkostal EKG'ler alındı.*
Bulgular	*Şizofreni hastalarında Tip 1 Brugada sendromu gözlenmedi, bir hastada Tip 2 Brugada, iki hastada Tip 3 Brugada gözlendi. Kontrol grubunda bir hastada Tip 2 Brugada paterni belirlendi ve yine bir kontrol hastasında Tip 3 Brugada paterni vardı (p = 0.320). Fragmente QRS (fQRS) insidansı, QRS süresi ve düzeltilmiş QT'nin şizofreni grubunda kontrol grubuna göre daha yüksek olduğu gözlendi (sırasıyla p = 0.001, p = 0.003, p <0.001).*
Sonuç	*Şizofreni hastalarında Brugada EKG paterninin sıklığında artış yoktur. Şizofreni hastalarında fQRS sıklığı kontrol grubuna göre anlamlı olarak daha yüksekti. fQRS bulunan şizofreni hastalarının kardiyovasküler olay sıklığını öngörmede kullanılabilir.*
Anahtar Kelimeler	*Şizofreni; Brugada Sendromu; fragmente QRS*

INTRODUCTION

Brugada syndrome is an autosomal dominant inherited genetic syndrome and known to have an increased risk of sudden death linked to rapid polymorphic ventricular tachycardia or ventricular fibrillation.[1] Recent studies showed that fragmented QRS (fQRS) is a reliable electrocardiogram (ECG) finding with the importance of an indicator of myocardial fibrosis and scarring.[2]

One of the common causes of sudden cardiac death in schizophrenia is thought to be cardiac arrhythmia. Although the cause of the increase in the incidence of cardiac arrhythmia is uncertain, medications used or genetic variations identified in schizophrenia patients are thought to affect the electrophysiology of the heart through sodium channels.[3] A previous study reported that there was a very high rate (11.6%) of Brugada syndrome, which has a genetic inheritance and high risk of sudden cardiac death, in patients with schizophrenia.[4]

In this study we aimed to investigate the frequency of Brugada syndrome and fQRS in patients with schizophrenia.

MATERIALS and METHODS

This study is a descriptive study. Our study included a total of 250 patients being monitored in the psychiatry clinic for the diagnosis of schizophrenia according to the Diagnostic Statistical Manual of Mental Disorders – IV classification. Patients who did not give permission for electrocardiography (ECG), patients with advanced heart failure, valve disease and bundle branch block were excluded from the study. The study was approved by Ordu University ethic committee(03.06.2016, no:2016/54) and all participants provided written informed consent. The study also included an age- and sex-matched control group of 400 individuals applying to the psychiatry clinic without diagnosis of schizophrenia.

ECG Analysis

Standard ECGs and high intercostal ECGs with V1 and V2 derivations above two intercostal intervals were obtained from all participants. All ECGs were screened for Type 1 (At the end of QRS, an ascending and quick slope with a high take-off ≥2mm followed by concave or rectilinear downsloping ST), Type 2 and Type 3 Brugada syndrome ECG characteristics by a cardiologist blind to the patients' diagnoses .Fragmented QRS (fQRS) was defined as narrow QRS complex (duration <120 ms) with R wave notching, S wave notching, RSR' pattern or more than one R' in at least two consecutive derivations. The diagnosis of Brugada Syndrome requires typical ST-segment elevations in right precordial ECG leads and events suggestive of cardiac arrhythmia or a family history of Brugada.[1]

Statistical analysis

SPSS (SPSS 20.0 software) packet program was used for statistical analysis. Continuous variables were given as mean standard deviation (SD) and categorical variables were given as percentages. Pearson chi-square analysis and Fisher's Exact test were used to compare categorical variables. A p value <0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the groups included in our study are shown in Table 1. The ECG parameters of the groups are shown in Table 2. The fQRS frequency, QRS duration and QTc were observed to be higher in the schizophrenia group compared to the control group (p=0.001, p=0.003, p<0.001, respectively). Both mild and severe QTc prolongation were observed more often in the schizophrenia group (p<0.001, p<0.001, respectively). In subgroup analysis, fQRS (Fig.1) was found to be more common in male sex (p<0.011) and in those with fQRS, QTc was observed to be higher (425.7±42.4 vs. 397.6±25.4; p<0.001).

Table 1: Clinical and demographic characteristics of the study population

		Schizophrenia Group (n: 250)	Control Group (n: 400)	p
Age, mean±SD (years)		44.33 ± 14.7	45.6 ± 9.8	0.164
Male, n(%)		130(52)	230(57.5)	0.169
Diabetes Mellitus, n(%)		10(4)	30 (7.5)	0.070
Hypertension, n(%)		25(10)	45 (11.2)	0.616
Hyperlipidemia, n(%)		20(8)	41(10.1)	0.338
Heart Rate, mean± SD(beat/min.)		78.4± 14.1	77.6± 16.1	0.509
Sodium channel blockers, n(%)		85 (34)	-	-
QT-interval–prolonging drugs, n(%)		190 (76)	-	-
Selective serotonin reuptake inhibitors,n(%)		38 (15.2)	30 (7.5)	0.002
Tricyclic antidepressants, n(%)		40 (16)	25 (6.2)	<0.001
Antipsychotics	Clozapine, n(%)	150 (60)	-	-
	Olanzapine, n(%)	50 (20)		
	Aripiprazol, n(%)	15 (6)		
	Risperidon, n(%)	15 (6)		
	Quetiapine, n(%)	5 (2)		

Table 2: Comparison of ECG parameters between Schizophrenia and Control Group

		Schizophrenia Group (n:250)	Control Group (n:400)	p
Brugada	Type 1, n(%)	-	-	0.320
	Type 2, n(%)	1(0.4))	1(0.25)	
	Type 3, n(%)	2(0.8))	1(0.25)	
Mild Prolongation of QTc-interval, n(%)		31(12.4)	1(0.25)	<0.001
Severe Prolongation of QTc-interval, n(%)		21(8.4)	-	<0.001
QTc duration, mean±SD (ms)		413.0 ± 31.4	390.4 ± 23.1	<0.001
QRS duration, mean±SD (ms)		102.1 ± 24.1	92.3 ± 14.1	0.003
fQRS, n(%)		50(20)	39 (9.8)	0.001
Heart Rate, mean±SD(beat/min.)		78.4 ± 14.1	77.6 ± 16.1	0.509

QTc: Corrected QT, fQRS: Fragmented QRS

DISCUSSION

According to the results of our study; The Brugada ECG frequency was similar to schizophrenia patients and non-schizophrenia control group. Importantly, the prevalence of fQRS was significantly higher in patients with schizophrenia compared to the control group.

Previous studies have shown that schizophrenia patients have higher mortality secondary to sudden cardiac death and cardiac arrhythmia compared to the normal population.[5-6] The most important cause of this is considered to be the arrhythmogenic potential of the medications used and the possibility of genetic ion defects shown in this patient population that may affect cardiac electrophysiology.[3] Brugada syndrome is a rare clinical entity with high risk of sudden cardiac death1 and a study by Bloom et al. found high rates of Brugada syndrome among schizophrenia patients in their population (north Holland). They suggested that the higher prevalence of Brugada syndrome may be responsible for the increased mortality rate in schizophrenia patients.[4] Bloom et al. identified a higher incidence of sudden cardiac death in their study population. However the association between higher prevalence of Brugada syndrome and increased rate of sudden cardiac death was only an observation far from being just an established clinical cause-effect relationship.[4] Again, Bloom et al. proposed that the antipsychotics especially Na channel blockers used by schizophrenia patients may provoke Brugada syndrome.[4] Contrary to the results of the study of Bloom et al, schizophrenia patients using antipsychotics and Na channel blockers were not found to have a higher prevalence of Brugada syndrome in our study. However, in line with the previous studies the QTc prolongation was identified to be higher in our patient population.[7-8]

In the European countries such as Germany and Denmark, the prevalence of Brugada Pattern on ECG was low with the rates of <0.05% (<1 in 2000), while in Turkey it was reported to be ≥0.05% (≥1 in 2000) (Type 1 Brugada pattern 0.08%, Type 2-3 Brugada pattern 0.40%).[9] The study by

Bloom et al. revealed that the prevalence of Brugada syndrome among patients monitored for schizophrenia was higher than the control group (11.6% vs. 1.1% and 2.4%).[4] Although the prevalence of Brugada syndrome in Turkey is known to be higher compared to European countries[10], the present study demonstrated that the prevalence of Brugada syndrome was not higher among schizophrenia patients when compared to controls in Turkey (p:0.320) contrary to the results of the study of Bloom et al. which was conducted in north Holland. Although Brugada syndrome is an autosomal inherited disease, it is known to occur 8-10 times more often in men compared to women.[10] In our study 52% of the patiens were male, while in the study by Bloom et al. this rate was 70.9%. Consequently the Brugada prevalence found in the study by Bloom et al. was very high and we believe that larger prospective studies are required to explain this difference.

Yap et al. found a weak correlation between the manifestation of Brugada syndrome and increase in sudden cardiac death risk with the use of sodium channel blockers.[11] In our study the prevalence of Brugada was not increased among schizophrenia patients, leading to the consideration that there was no effect of the medications used. Previous studies of schizophrenia patients have focused on the fact that genetic variations in ion channels may affect cardiac electrophysiology and may trigger arrhythmic deaths.[1,3,4] Unfortunately we did not perform any genetic study in our research.

Many studies have shown that the presence of fQRS on ECG is related to myocardial fibrosis and and increases the risk of sudden cardiac death[12] Many causes including cardiac ischemia, myocarditis or increased sympathetic activity may cause development of myocardial fibrosis.[12-13] Myocardial fibrosis disrupts the electrical activity of the heart and increases the risk of arrhythmic death.[12-14] The antipsychotic medications used in the treatment of schizophrenia are known to cause myocarditis and increase sympathetic activity.[15-16] In our study we found that the frequency of fQRS, which is a strong predictor of cardiac fibrosis was significantly higher in patients with schizophrenia. We suggest that this may be due to the cardiac effects of medications used or the neurohormonal changes in schizophrenia. fQRS, which is easy to assess with surface ECG, shows electrical heterogeneity secondary to myocardial fibrosis[17] and may be beneficial to predict sudden cardiac arrhythmias. We believe that it will be valuable to determine whether there is a correlation between presence of fQRS on ECG and mortality in patients with schizophrenia with prospective studies.

Study Limitations

Our study had a cross-sectional design with no prospective monitoring of patients. Patients were not monitored to show the correlation between presence of fQRS and mortality. Lack of echocardiographic evaluation, magnetic resonance imaging or histological assessment in order to demonstrate myocardial fibrosis can also be considered as a limitation. Drug use of the patient group can also be considered as study limitations. However, the obligation of patients with schizophrenia to receive treatment is a part of their lives.

CONCLUSION

We found that the prevalence of Brugada ECG pattern was not higher in patients with schizophrenia. Many factors such as the low prevalence of Brugada syndrome in the general population, geography, genetics and sex may have affected the results of our study. The higher prevelance of fQRS in schizophrenia patients in our study leads to the consideration that myocardial involvement than the genetic transmission may be more frequent in these subjects. For the use of fQRS as a marker of cardiac risk in schizophrenia patients, there is a need for large scale studies in different geographical regions.

Disclosure statement

The authors declare that they have no competing interests.

Conflict of interest

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Ordu University ethic committee (03.06.2016, no:2016/54)

References

1. *Soylu M, Duran Demir AD, Korkmaz Ş. Brugada Syndrome. Turk Kardiyol Dern Ars. 2003; 31(4): 219-225.*
2. *Is Fragmented Qrs Associated with The Severity Of Carotid Artery Disease? Edem E. Reyhanoğlu H. Sakarya Med J. 2018;8(2):279-284*
3. *Emul M, Kalelioglu T. Etiology of cardiovascular disease in patients with schizophrenia: current perspectives. Neuropsychiatr Dis Treat 2015; 11: 2493–503.*
4. *Blom MT, Cohen D, Seldenrijk A, Penninx BW, Nijpels G, Stehouwer CD et al. Brugada syndrome ECG is highly prevalent in schizophrenia. Circ Arrhythm Electrophysiol 2014;7:384-91.*
5. *Saha S, Chant D, McGRath J. A systematic review of mortality in schizophrenia. Arch Gen Psychiatry. 2007;64:1123–31.*
6. *Appleby L, Thomas S, Ferrier N, G Lewis, J Shaw, T Amos. Sudden unexplained death in psychiatric in-patients. Br J Psychiatry 2000;176:405–06.*
7. *Timour Q, Frassati D, Descotes J, Chevalier P, Christé G, ChahineM. Sudden death of cardiac origin and psychotropic drugs. Front Pharmacol 2012;3: 76.*
8. *Ames D, Camm J, Cook P, P Falkai, C Gury, R Hurley, et al. Minimizing the risks associated with QTc prolongation in people with schizophrenia: A consensus statement by the Cardiac Safety in Schizophrenia Group. Australasian Psychiatry, 2002; 10: 2; 115-24*
9. *Postema PG. About Brugada syndrome and its prevalence. Europace 2012;14:925-8.*
10. *Alings M, Wilde A. Brugada syndrome: clinical data and suggested patho -physiological mechanism.Circulation 1999; 99: 666–73*
11. *Yap YG, Behr ER, Camm AJ. Drug-induced Brugada syndrome. Europace 2009;11:989–94*
12. *Pei J, Li N, Gao Y, Wang Z, Li X, Zhang Y et al. The J wave and fragmented QRS complexes in inferior leads associated with sudden cardiac death in patients with chronic heart failure. Europace 2012;14: 1180–87*
13. *O'Driscoll DM, Horne RS, Davey MJ, Sarah A Hope, Vicki Anderson, John Trinder, et al. Increased sympathetic activity in children with obstructive sleep apnea: cardiovascular implications. Sleep Med 2011;12: 483–88*
14. *Lecomte D, Fornes P, Fouret P, Nicolas G. Isolated myocardial fibrosis as a cause of sudden cardiac death and its possible relation to myocarditis. J Forensic Sci 1993; 3: 617-21*
15. *Li JK, Yeung VT, Leung CM, Chow CC, Ko GT, So WY et al. Clozapine : a mimicry of phaeochromocytoma. Aust N Z Y Psychiatry1997;6: 889-91*
16. *Ronaldson KJ.Cardiovascular Disease in Clozapine-Treated Patients: Evidence, Mechanismsm and Management. CNS Drugs 2017; doi: 10.1007/s40263-017-0461-9.*
17. *Sha, J, Zhang S, Tang M, Keping Chen, Xinran Zhao, Fangzheng Wang . Fragmented QRS is associated with all-cause mortality and ventricular arrhythmias in patient with idiopathic dilated cardiomyopathy. Ann Noninvasive Electrocardiol 2011; 16: 270-5*

ARAŞTIRMA MAKALESİ / *Research Article*

Obstrüktif Uyku Apne Sendromu Olan Hastalarda Klinik ve Demografik Verilerinin Değerlendirilmesi

Evaluation of Clinical and Demographic Data in Patients with Obstructive Sleep Apnea Syndrome

Ahmet Yıldırım[1], Aysel Tekeşin[2]

[1] Şanlıurfa Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, Şanlıurfa, Türkiye
[2] Sağlık Bilimleri Üniversitesi, İstanbul Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, İstanbul, Türkiye

Yazışma Adresi / *Correspondence:*
Ahmet Yıldırım

Şanlıurfa Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, 63250, Şanlıurfa, Türkiye
T: **+90 414 317 17 17** E-mail **: dr.ahmetyildirim@hotmail.com**

Geliş Tarihi / Received : **13.07.2020** Kabul Tarihi / Accepted : **07.01.2021**

Orcid :
Ahmet Yıldırım https://orcid.org/0000-0002-6644-9148
Aysel Tekeşin https://orcid.org/0000-0002-0856-9387

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):103-108) DOI: 10.31832/smj.768573

Öz

Amaç Çalışmanın amacı uykuda horlama ve/veya solunum durması şikayetleriyle başvuran hastalarda obstrüktif uyku apne sendromu (OUAS) varlığının değerlendirilmesi ve OUAS'lı hastaların demografik verilerini ve eşlik eden kronik hastalık birlikteliğini araştırmaktır.

Gereç ve Yöntem Bu çalışmada Ocak 2017- Haziran 2018 tarihleri arasında, uykuda horlama ve/veya solunum durması şikayetleriyle İstanbul Eğitim ve Araştırma Hastanesi uyku laboratuvarına yönlendirilen hastalar incelendi. Çalışmaya 385 hasta dahil edildi. Hastaların anamnezleri alınarak horlama ve/veya solunum durması şikayetlerinin yanı sıra kronik rahatsızlıklarının olup olmadığı sorgulanmış, alışkanlıkları ve demografik verileri kaydedilmiştir. Hastalarda OUAS varlığının tespiti için 1 gece süreyle polisomnografi (PSG) testi yapılmış ve Apne Hipopne İndeksine (AHİ) göre hastalar gruplandırılmıştır. Test sonucunda AHİ ≥ 5 olması OUAS olarak kabul edilmiştir. AHİ 5-14,9 arası hafif, 15-29,9 arası orta, 30 ve üzeri ağır olarak gruplandırılmıştır. Polisomnografi test sonucunda, AHİ 5'in altında olan ve horlaması olan hastalar basit horlama olarak gruplandırılmıştır. Hastaların ayrıca periyodik bacak hareket indeksi (PBHİ) değerlendirilmiştir.

Bulgular Polisomnografi test sonuçlarına göre hastaların 100'ü basit horlama (%26), 103'ü (%26,7) hafif derecede OUAS, 84'ü (%21,8) orta derecede OUAS ve 98'i (%25,4) ağır derecede OUAS olarak değerlendirilmiştir. OUAS hastalarında erkek cinsiyetin hakim olduğu, hipertansiyonun daha sık görüldüğü, daha yüksek VKİ'ye sahip oldukları ve ileri yaşın da OUAS için bir risk faktörü olduğu saptanmıştır.

Sonuç OUAS için risk faktörlerinin bilinmesi, OUAS komplikasyonlarına karşı erken önlem alınabilmesi adına yol gösterici olacaktır.

Anahtar Kelimeler Polisomnografi; horlama; obstrüktif uyku apne sendromu

Abstract

Objective *The aim of the study is to evaluate the presence of Obstructive Sleep Apnea Syndrome (OSAS) in patients presenting with snoring and/or apnea complaints and to investigate demographic data of patients with OSAS and the comorbid chronic disease.*

Materials and methods *In this study, patients who were referred to Istanbul Training and Research Hospital sleep laboratory between January 2017 and June 2018 with complaints of snoring and apnea during sleep were examined. 385 patients were included in the study.*
The anamnesis of the patients were taken, and the presence of chronic diseases as well as the complaints of snoring and/or apnea were questioned, and their habits and demographic data were recorded. One night polysomnography test was performed to determine the presence of OSAS in patients and the patients were grouped according to Apnea Hypopnea Index (AHI). Having AHI ≥ 5 was accepted as OSAS, AHI was included between 5-14.9 mild, moderate between 15.0-29.9, severe as 30 and higher. As a result of polysomnography test, patients with AHI below 5 and snoring were grouped as simple snoring. Periodic leg movement index (PLMI) of the patients were also evaluated.

Results *According to the polysomnography test results, 100 were evaluated as simple snoring (26%), 103 (26.7%) were mild OSAS, 84 (%21.8) were moderate OSAS, and 98 (25.4%) were severe OSAS. It was determined that male gender is dominant in OSAS patients, hypertension is more common, they have higher BMI and advanced age is a risk factor for OSAS.*

Conclusion *Determination of risk factors for OSAS, it will be a guide for taking early precautions against OSAS complications.*

Keywords *Polysomnography; snoring; obstructive sleep apnea syndrome*

GİRİŞ

Obstrüktif uyku apne sendromu (OUAS), uyku esnasında tekrarlayan üst solunum yolu obstruksiyonu epizotları ve beraberinde arteryel oksijen saturasyonunda azalma ile tanımlanan bir sendromdur. Bu durum basit horlamaya neden olan hava yolunun kısmi obstrüksiyonundan apne oluşumuna neden olan hava yolunun tam obstrüksiyonuna kadar değişebilir. Uyku esnasında üst hava yolu kapanmasının ana sebebi hava yolunu açık kalmasını sağlayan ve kollapsına neden olan güçlerin dengesinin bozulmasıdır.[1] OUAS'ın tipik bulguları, uykuda tekrarlayan üst solunum yolu tıkanmasına bağlı horlama, tanıklı apne ve gündüz aşırı uyku halidir. OUAS tanılı hastalarda sık uyanma ve sonuçta bölünmüş uyku nedeniyle gün içi yorgunluk, baş ağrısı, dikkat eksikliği, motorlu taşıt kazaları, cinsel isteksizlik ve iş performansında azalma görülmektedir. Sosyal ve nöropsikolojik sonuçlarının yanı sıra kardiyovasküler sonuçlarıyla da ciddi morbidite ve mortalite nedenidir.[2] OUAS tanısı için altın standart polisomnografidir (PSG)[3]. İleri yaş, VKİ'nin yüksek olması (obezite), alkol ve sigara kullanımı, erkek cinsiyet OUAS için risk faktörleridir.[4] Çalışmanın amacı uykuda horlama ve/veya solunum durması şikayetleriyle başvuran hastalarda obstrüktif uyku apnesi (OUAS) varlığının değerlendirilmesi ve OUAS'ı olan hastaların demografik verilerini ve eşlik eden kronik hastalık birlikteliğini araştırmaktır.

GEREÇ ve YÖNTEMLER

Ocak 2017- Haziran 2018 tarihleri arasında polikliniğimize gece uykuda horlama, gündüz aşırı uyku hali ve tanıklı apne belirtilerinden bir ya da daha fazlası ile başvuran 392 hasta incelendi. Çalışmaya katılmaya engel teşkil eden nörolojik hastalığı olan 4, mental retardasyonu olan 2 ve son 6 ayda madde kullanım öyküsü olan 1 hasta olmak üzere toplam 7 hasta araştırma dışı bırakılarak toplam 385 hasta çalışmaya alındı. Hastaların anamnezleri alınarak horlama ve/veya uykuda solunum bozukluğu şikayetlerinin yanı sıra başka bir kronik rahatsızlıklarının olup olmadığı kalp yetmezliği, kalp ritim bozukluğu, kalp krizi hikayesi, şeker hastalığı, kronik obstrüktif akciğer hastalığı, hipertiroidi. hipotiroidi, hipertansiyon öyküsü sorgulandı ve bunların dışında rahatsızlıkları olanların belirtmesi istendi. Hastaların alışkanlıkları, demografik verileri ve VKİ'leri kaydedildi. Hastalarda OUAS varlığının tespiti için 1 gece süreyle PSG testi yapıldı ve Apne Hipopne İndeksine (AHİ) göre hastalar gruplandırıldı. AHİ ≥5 olması OUAS olarak kabul edildi. PSG test sonucunda AHİ<5 ve horlaması olan hastalar, basit horlama olarak gruplandırıldı.

1) Apne-hipopne indeksi (AHİ) 5–14,9 olan; hafif OUAS
2) AHİ: 15-29,9 olan; orta düzey OUAS
3) AHİ ≥30 olan; ağır OUAS kabul edildi.
4- AHİ<5 ve horlaması olan hastalar, basit horlama olarak gruplandırıldı.

Hastalar PSG testi ile değerlendirildi. PSG'de; elektroensefalografi, elektrookülografi, çene ve bacak elektromiyelografisi, elektrokardiografi, oro-nazal termistor ile hava akımı, göğüs ve karın solunum hareketleri, parmak ucu pulse oksimetre ile oksijen saturasyonu, boyuna yerleştirilen trakeal mikrofon ile horlama ve vücut pozisyonu kaydedildi.

Etik kurul onayı Sağlık Bilimleri Üniversitesi İstanbul Eğitim ve Araştırma Hastanesi etik kurulundan 26/10/2018 tarihinde alınmıştır (Karar no:1478).

İstatistiksel verilerin analizinde IBM SPSS forwindows 20 istatistik paket programı kullanıldı. Niteliksel verlerin değerlendirilmesinde Ki-kare ve Fisherexact test, 2 grup arasındaki nicel verilerin karşılaştırılmasında student's t test ve Mann whitney u testleri, OUAS dereceleri arasındaki karşılaştırmalarda ANOVA ve Kruskalwallis testleri kullanıldı. P<0,05 anlamlı kabul edildi.

BULGULAR

Hastaların 239'u erkek 146'sı kadındı. PSG test sonuçlarında AHİ'ye göre hastaların 100'ü basit horlama (%26), 285'i (%74) OUAS hastası olarak değerlendirilmiştir.

Çalışmamızda OUAS tanılı nefes alamama şikayetleri ve HT'nin varlığı, basit horlaması olan hastalara göre anlamlı derecede fazlaydı (p<0,05). DM varlığı ile OUAS arasında ise ile anlamlı bir ilişki saptanmamıştır (Tablo-1).

Tablo 1: Basit horlaması olan ve OUAS'ı olan hastaların demografik verileri, klinik özellikleri ve eşlik eden hastalıkların karşılaştırılması

	OUAS tanılı hastalar		Basit horlaması olan hastalar		Ki-kare	p
	n	%	n	%		
Cins						
E	192	67,4	47	47,0		
K	93	32,6	53	53,0	13,04	0,0001
Uykuda Nefes Durması						
Yok	35	12,3	25	25,0		
Var	250	87,7	75	75,0	9,10	0,003
Ek Hastalık						
Yok	253	88,8	92	92,0		
Var	32	11,2	8	8,0	0,83	0,363
DM						
Yok	275	96,5	96	96,0		
Var	10	3,5	4	4,0	0,05	0,821
HT						
Yok	258	90,5	97	97,0		
Var	27	9,5	3	3,0	4,31	0,038

DM: Diabetes mellitus, HT: Hipertansiyon, OUAS: obstrüktif uyku apne sendromu

Çalışmamızda 103 hasta (%26,7) hafif derecede OUAS, 84 (%21,8) orta derecede OUAS ve 98'i (%25,4) ağır derecede OUAS olarak değerlendirilmiştir. OUAS derecesine göre risk faktörleri incelendiğinde; orta ve ağır OUAS'ı olan hastalarda erkek oranı ve uykuda nefes durması sıklığı hafif olgulara göre anlamlı derecede fazla bulunurken (p<0,01), OUAS derece grupları arasında ek hastalık, DM ve HT varlığı bakımından istatistiksel olarak anlamlı bir farklılık saptanmadı (Tablo 2).

Tablo 2: OUAS'ı olan hastalarda hastalığın şiddeti ile demografik verilerin, klinik özelliklerin ve eşlik eden hastalıkların karşılaştırılması

	AĞIR		ORTA		HAFİF		Ki-kare	p
	n	%	n	%	n	%		
Cins								
E	75	76,5	59	70,2	58	56,3		
K	23	23,5	25	29,8	45	43,7	9,78	0,007
Horlama								
Yok	1	1,0	3	3,6	8	7,8		
Var	97	99,0	81	96,4	95	92,2	5,78	0,055
Uykuda nefes durması								
Yok	5	5,1	10	11,9	20	19,4		
Var	93	94,9	74	88,1	83	80,6	9,56	0,008
Ek hastalık								
Yok	87	88,8	72	85,7	94	91,3		
Var	11	11,2	12	14,3	9	8,7	1,42	0,490
DM								
Yok	96	98,0	78	92,9	101	98,1		
Var	2	2,0	6	7,1	2	1,9	4,64	0,098
HT								
Yok	90	91,8	74	88,1	94	91,3		
Var	8	8,2	10	11,9	9	8,7	0,84	0,657

DM: Diabetes Mellitus, HT: Hipertansiyon, OUAS: Obstrüktif uyku apne sendromu

OUAS derecesi ile PSG verileri arasındaki ilişki incelendiğinde; Orta ve ağır OUAS saptanan hastalarda uyku süresi hafif olgulara göre anlamlı dercede fazla bulunmuştur (p<0,01). Ağır OUAS saptanan hastalarda Rem uyku yüzdesi hafif ve orta OUAS saptanan hastalara göre anlamlı derecede azalmıştır. Ağır OUAS saptanan hastalarda AHİ değerleri, orta ve hafif olgulara göre anlamlı derecede fazladır (p<0,001). Orta ve hafif olgularda ise PBHİ değerleri ağır olgulara göre anlamlı derecede fazladır (p<0,01). OUAS derece grupları arasında yaş ve VKİ değerleri bakımından istatistiksel olarak anlamlı bir farklılık saptanmadı (Tablo 3).

Tablo 3: OUAS'ı olan hastalarda hastalığın şiddeti ile demografik ve PSG verilerinin karşılaştırılması

	AĞIR		ORTA		HAFİF		
	ORT	SS	ORT	SS	ORT	SS	P
Yaş	48,97	12,26	51,90	10,87	47,64	12,35	,059
VKİ	32,76	6,53	31,09	5,67	30,50	5,16	,068
Uyku süresi	406,69	83,98	394,74	73,90	372,95	87,46	,009
REM uyku %	10,88	6,58	13,12	5,5337	14,09	6,44	,002
AHİ	54,26	20,15	21,58	4,29	10,22	2,83	,0001
PBHİ	0,13	0,87	1,97	8,38	,92	6,63	,027

VKİ: Vücut kitle indeksi, AHİ: Apne hipopne indeksi, PBHİ: Periyodik bacak hareketleri İndeksi, OUAS: Obstrüktif uyku apne sendromu, ORT: Ortalama, SS: Standart sapma

TARTIŞMA

Bu çalışmada OUAS tanısı olan hastaların demografik verileri ve komorbid hastalıkları incelendi ve OUAS şiddeti ile korelasyonları araştırıldı. Basit horlama şikayeti olan hastalara göre OUAS hastalarının daha ileri yaşta olduğu, VKİ'nin daha yüksek olduğu, erkek cinsiyet dominansı ve daha yüksek oranda HT varlığı saptandı. Ayrıca OUAS şiddeti arttıkça hastalarda uyku etkinliği yüzdesi ile REM uyku yüzdesinin azaldığı, uyku süresinin ise arttığı saptandı.

OUAS toplumda sık görülen, işgücü kaybına ve kronik hastalıkların oluşumuna neden olabilen üst solunum yolu obstrüksiyonu ile giden bir sendromdur. Üst solunum yollarında obstrüksiyon ve kollapsın gelişiminde 3 önemli fizyopatolojik neden vardır. Bunlar; üst solunum yollarının anatomisi, inspirasyon sırasında oluşan negatif basınç ve farengeal hava yolunu dilate eden kaslarda aktivite kaybıdır.[5,6] Yaş, cinsiyet, obezite, boyun çevresi, sigara, alkol ve sedatif kullanımı ile eşlik eden bazı sistemik hastalıklar ileri sürülen başlıca risk faktörleridir.[7]

OUAS'ın en sık 40-65 yaş grubunda görüldüğü ve 65 yaşından sonra prevalansının azaldığı kabul edilmektedir. Yaşın OUAS için belirgin bir risk faktörü olduğunu gösteren çalışmalar mevcuttur.[8] Bizim çalışmamızda olgularımızın yaş ortalaması 49,35±11,99'du ve OUAS'ı olan grupta yaş ortalaması, basit horlaması olan gruba göre anlamlı derecede yüksek bulundu. OUAS derecesi ile yaş ortalaması arasında anlamlı ilişki saptanmadı.

Erkek cinsiyeti OUAS için önemli bir risk faktörü olarak kabul edilse de son yıllarda yapılan çalışmalarda, kadınlarda da OUAS'ın azımsanmayacak kadar yüksek oranda görülebildiği ve her yaş grubu için kadın/erkek oranının yaklaşık 1/3 olduğu bildirilmiştir. Nieto ve ark. tarafından 6132 kişi üzerinde yapılan tarama çalışmasında, OUAS tanısı konulan olguların %37 kadarının kadın olduğu bildirilmiştir.[9] Bizim çalışmamızda OUAS'lı olguların %67,4'ü erkek, %32,6'sı kadındı. Erkek cinsiyet ile OUAS arasında anlamlı bir ilişki saptandı. Ayrıca OUAS şiddeti ile erkek cinsiyet arasında da anlamlı bir ilişki saptandı.

OUAS fizyopatolojisinde obezite önemli bir yer tutmaktadır.[10] Yapılan çalışmalar obezitenin varlığı nedeniyle; farengeal yağ pedleri, dil, lateralfarengeal duvarlar ve yumuşak damak gibi dokulardaki yağ depolarının artması sonucunda üst havayolu enine kesit alanında azalma ve havayolunda kollaps olabilme yatkınlığında artma ile OUAS arasındaki ilişki gösterilmiştir.[11-14] Obezite derecesini değerlendirmek için en sık kullanılan parametre vücut kitle indeksidir (VKİ). Bizim çalışmamızda VKİ ile OUAS arasında anlamlı ilişki saptandı. Ancak OUAS şiddeti ile VKİ arası anlamlı ilişki saptanmadı.

Normal kişilerde sistemik kan basıncı uyku esnasında % 20-23 oranında azalır ve uyanma ile birlikte normal günlük olan seviyesine tekrar gelmesine rağmen, şiddetli

horlama ve OUAS'ı olan hastalarda gün içerisinde ve uyku esnasında sistemik kan basıncında progresif artış olduğu saptanmıştır.[15] Uykuda apne ve hipopne atakları arterial kan basıncında 30 mm-Hg veya daha fazla artışı da içeren geçici kan basıncı değişikliklerine sebep olur. Renin-anjiyotensin ve vazoaktifpeptidlerdeki değişiklikler ve özellikle kilolu uyku apneli hastalarda görülen insülin rezistans sendromuda hipertansiyon oluşumunu artırabilir.[16] Bazı çalışmalarda uykuda solunum bozukluğu ve horlama ile şeker hastalığı (DM) gelişimi arasında bir ilişki bulunduğu gösterilmiştir.[17,18] Bizim çalışmamızda OUAS sendromu ile HT arasında anlamlı ilişki saptanırken DM ile belirgin bir ilişki saptanmamıştır.

OUAS'lı olgularda aşırı uyku hali sık karşılaşılan bir durumdur. Uykularının büyük kısmını yüzeyel uykuda geçiririler ve derin uyku periyodu sıklıkla yetersizdir. Ayrıca apne epizodları ve sık tekrarlayan arousallar ile kalitesiz bir gece uykusu geçirirler. Bu konuda yapılan bir çalışmada hafif dereceli OUAS'lıların %51,9'u, ağır dereceli OUAS'lıların ise %88,6'sı sabahları yorgunluk hissi ile uyandıklarını, sırasıyla %61,5 ve %75'i de yetersiz uyku uyuduklarını bildirmişlerdir[17]. Çalışmamızda da OUAS ile basit horlama arasında uyku etkinliği yüzdesi, uyku süresi ve REM uyku süresi bakımından istatistiksel olarak anlamlı bir farklılık saptanmazken, ağır evre OUAS saptanan hastalarda REM uyku süresinde azalma istatistiksel olarak anlamlı bulunmuştur.

Periyodik bacak hareketleri (PBH) uykuda istemsiz, tekrarlayıcı, stereotipik, kısa süreli, segmental ve sıklıkla alt ekstremitelerin etkilendiği bir tablodur. Al-Alawi ve ark. tarafından yapılan 798 hastanın incelendiği retrospektif bir çalışmada OUAS hastalarının yarısında PBH varlığı saptanmış, PBH varlığı ileri yaş ve kilo artışı ile ilişkili bulunmuştur. Aynı çalışmada, OUAS ile birlikte görülen PBH'nın gün içi uyku hali ve kan basıncı üzerinde etkisi olmadığı bildirilmiştir.[20] Manconi ve arkadaşlarının yaptığı çalışma yüksek AHİ değerlerinin PBH ile ilişkili olduğunu göstermiştir,[21] ancak bizim çalışmamızda hafif ve orta evre OUAS'lı olgularda PBH varlığı ağır olgulara göre anlamlı derecede fazlaydı.

Sonuç olarak çalışmamız, OUAS hastalarında erkek cinsiyetin hakim olduğunu ve hipertansiyonun daha sık görüldüğünü göstermiş, bunun yanında daha yüksek VKİ'ye sahip olduklarını ve ileri yaşın da bir risk faktörü olduğunu göstermiştir. Ek olarak OUAS şiddeti arttıkça hastalarda uyku etkinliği yüzdesi ile REM uyku yüzdesinin azaldığı, uyku süresinin ise arttığı saptanmıştır. Bulgularımız, horlama şikayeti ile başvuran hastalarda ileri tetkik için hasta seçimi konusunda yol gösterici olup, OUAS'ın bilinen komplikasyonlarına karşı erken önlem alabilmek adına da önemli veriler sunmaktadır.

Çıkar ilişkisi

Yazarların herhangi bir çıkar dayalı bir ilişkisi bulunmamaktadır.

Etik kurul onayı Sağlık Bilimleri Üniversitesi İstanbul Eğitim ve Araştırma Hastanesi etik kurulundan 26/10/2018 tarihinde alınmıştır (Karar no:1478).

Kaynaklar

1. *Coleman JA. Pathophyology of snoring and sleep apnea: airway dynamics. In Snoring and Obsturictive Sleep Apnea. Ed. Fairbanks D, Mickelson S, Woodson T. Lippincot Williams &Wilkins .Philadelphia 2003; 2:19-25.*
2. *Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin Sleep Med 2009; 5: 573-581*
3. *Loadsman JA, Hillman DR. Anaesthesia and sleep apnoea. Br J Anaesth 2001; 86: 254-266.*
4. *Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365:1046-53.*
5. *Köktürk O, Köktürk N. Obstrüktif uyku apne sendromu fizyopotolojisi. Tüberküloz ve Toraks 1998; 46: 288-300.*
6. *Papilla İ, Acıoğlu E. Obstrüktif Uyku Apne Sendromu. Klinik Gelişim 2005; 18: 42-50.*
7. *Köktürk O. Obstrüktif uyku apne sendromu epidemiyolojisi. Tüberküloz ve Toraks 1998; 46: 193-201*
8. *McNamara SG, Grunstein RR, Sullivan CE. Obstructive sleep apnea. Thorax 1993; 48: 754-63.*
9. *Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in large community based study. JAMA 2000; 283: 1829-36.*
10. *Wittels E, Thompson S. Obstructive sleep apnea and obesity. Otolaryngol Clin North Am 1990; 23; 751-60.*
11. *Schwab RJ. Upper airway imaging. Clinics in chestmedicine. 1998;19(1):33-54.*
12. *Stauffer JL, Buick MK, Bixler EO, Sharkey FE, Abt AB, Manders EK, et al. Morphology of the Uvula in Obstructive Sleep Apnea1-3. The American review of respiratory disease. 1989;140:724.*
13. *Zohar Y, Schwartz A, Sabo R, Gal R, Strauss M, Oksenberg A. Oropharyngeal fatty infltration in obstructive sleep apnea patients: a histologicstudy. Annals of Otology, Rhinology&-Laryngology. 1998;107(2):170-4.*
14. *Nashi N, Kang S, Barkdull GC, Lucas J, Davidson TM. Lingualfat at autopsy. The Laryngoscope. 2007;117(8):1467-73.*
15. *Fletcher EC, De Behnke RD, Lovoi MS, Gorin AB. Undiagnosed sleep apnea in patients with essential hypertension. Ann Intern Med. 1985;103(2):190-5.*
16. *Sharabi Y, Dagan Y, Grossman E. Sleep apnea as a risk factor for hypertension. Curr Opin Nephrol Hypertens. 2004;13(3):359-64.*
17. *Al-Delaimy WK, Manson JE, Willlett WC, Stampfer MJ, Hu FB. Snoring as a risk factor for type II diabetes mellitus: a prospective study. Am J Epidemiol. 2002;155(5):387-93.*
18. *Meslier N, Gagnadoux F, Giraud P, Person C, Ouksel H, Urban T, Racineux JL. Impaired glucose-insulin metabolism in males with obstructive sleep apnea syndrome. EurRespir J. 2003;22(1):156-60.*
19. *Guilleminault C. Clinical features and evaluation of obstructive sleep apnea. In: Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine. Philadelphia : W.B. Saunders Company, 1994; 667-77.*
20. *Al-Alawi A, Mulgrew A, Tench E, Ryan CF. Prevalence, risk factors and impact on day time sleepiness and hypertension of periodic leg movements with arousals in patients with obstructive sleep apnea. J Clin Sleep Med 2006;15:2:281-7.*
21. *Manconi M, Zavalko I, Bassetti CL, Colamartino E, Pons M, Ferri R. Respiratory-related leg movements and their relationship with periodic leg movements during sleep. Sleep 2014;37:494-504.*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Effects of Myricetin Against Testicular and Lung Injury Induced by Testicular Ischemia Reperfusion Model

Mirisetinin Testiküler İskemi Reperfüzyon ile İndüklenen Testis ve Akciğer Hasarına Karşı Etkileri

Deniz Öztürk[1], Ayhan Tanyeli[2], Derya Güzel Erdoğan[3], Mustafa Can Güler[2], Ersen Eraslan[4], Hüseyin Baylan[5]

[1] Medical Services and Techniques/Dialysis, Atatürk University Health Services Vocational School, Erzurum, Turkey
[2] Department of Physiology, Faculty of Medicine, Atatürk University, Erzurum, Turkey
[3] Department of Physiology, Faculty of Medicine, Sakarya University, Sakarya, Turkey
[4] Department of Physiology, Faculty of Medicine, Yozgat Bozok University, Yozgat, Turkey
[5] Department of Anatomy, Faculty of Medicine, Sakarya University, Sakarya, Turkey

Yazışma Adresi / *Correspondence:*
Ayhan Tanyeli

Department of Physiology, Faculty of Medicine, Atatürk University, Erzurum, 25240, Turkey
T: **+90 507 363 16 54** E-mail **: ayhan.tanyeli@atauni.edu.tr**

Geliş Tarihi / Received : **21.08.2020** Kabul Tarihi / Accepted : **07.01.2021**

Orcid :

Deniz Öztürk https://orcid.org/0000-0002-9939-5895
Ayhan Tanyeli https://orcid.org/0000-0002-0095-0917
Derya Güzel Erdoğan https://orcid.org/0000-0002-7618-5043
Mustafa Can Güler https://orcid.org/0000-0001-8588-1035
Ersen Eraslan https://orcid.org/0000-0003-2424-2269
Hüseyin Baylan https://orcid.org/0000-0002-9150-9210

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):109-114) DOI: 10.31832 smj.783480**

Abstract

Objective	Testicular torsion may lead to testicular atrophy and male infertility if untreated within some hours. Since ischemia reperfusion (I/R) injury is a reason for the harmful effects during testicular torsion, antioxidant agents are among the targets of science to deal with reactive oxygen species (ROS). As a flavonoid member, myricetin (3, 3, 4, 5, 5, 7-hexahydroxyflavone, MYR) has antioxidant, anticancer, anti-inflammatory, antiviral, and antidiabetic activities.
Materials and Methods	In this experiment 32 Wistar albino male rats were randomly divided into 4 groups (n=8). Group I was defined as the sham group. In group II, I/R group, testicular torsion detorsion was performed. In group III (MYR 25) and group IV (MYR 50), MYR was administrated intraperitoneally at 25 and 50 mg/kg doses, 30 minutes before detorsion. The testicular and lung tissue samples were examined biochemically.
Results	In both testis and lung tissues, MYR decreased TOS, MDA, and MPO levels at both high and low doses compared to the I/R group. Besides, SOD values increased in MYR treatment groups compared to the I/R group.
Conclusion	MYR performed promising effects on testicular and lung tissues following testicular I/R injury according to biochemical parameters.
Keywords	myricetin; torsion detorsion; ischemia reperfusion; testis; lung.

Öz

Amaç	*Testis torsiyonu birkaç saat içinde tedavi edilmezse erkeklerde testis atrofisine ve kısırlığa neden olabilir. Antioksidan ajanlar testis torsiyonu ile baş etmede hedefler arasındadır. Mirisetin (myricetin, 3, 3, 4, 5, 5, 7-hekzahidroksiflavon, MYR), antioksidan, antikanser, anti-inflamatuar, antiviral ve antidiyabetik aktivitelere sahiptir.*
Gereç ve Yöntemler	*32 adet Wistar albino erkek sıçan rastgele 4 gruba (n=8) ayrıldı. Grup I sham grup olarak tanımlandı. Grup II, I/R grubunda testis torsiyonu yapıldı. Grup III (MYR 25) ve grup IV'te (MYR 50), detorsiyondan 30 dakika önce 25 ve 50 mg/kg dozlarda MYR intraperitoneal olarak uygulandı. Testis ve akciğer doku örnekleri biyokimyasal olarak incelendi.*
Bulgular	*Testis ve akciğer dokularında MYR, I/R grubuna kıyasla hem yüksek hem de düşük dozlarda TOS, MPO ve MDA seviyelerini azaltmıştır. Ayrıca MYR uygulanan gruplarda I/R grubuna kıyasla SOD değerleri artmıştır.*
Sonuç	*Biyokimyasal parametreler değerlendirildiğinde, MYR testis I/R hasarını takiben testis ve akciğer dokuları üzerinde olumlu etkiler gösterdi.*
Anahtar Kelimeler	*mirisetin; torsiyon detorsiyon; iskemi reperfüzyon; testis; akciğer.*

INTRODUCTION

Testicular torsion is an emergency urological condition that often affects newborns, children, and adolescents, leading to infertility.[1,2] Testicular rotation decreases blood flow to the testicle and venous drainage is interrupted. This situation leads to ischemia and necrosis. The consequences of this injury depend on the duration and extent of the torsion.[3] Reperfusion therapy is required to repair ischemic tissue. However, reactive oxygen species (ROS) overproduction-related ischemia reperfusion (I/R) injury may occur during reperfusion, contributing to infertility.[4] I/R damage occurs due to the stimulation of an intracellular cascade involving the activation of neutrophils, inflammatory cytokines, and free oxygen radicals.[5] Moreover, during testicular I/R injury, newly arrived oxygen becomes toxic to testicular tissue due to ROS accumulation, testicular oxidative damage, changes in seminiferous tubule structure and function, germ cell apoptosis, and spermatogenesis damage. One of the main causes of excessive ROS accumulation in testicular tissue is the inequality in oxidation/antioxidant balance. Testicles contain powerful and complex antioxidant enzyme systems and ROS scavengers to ensure that the functions of spermatogenesis and steroidogenesis are not hampered by oxidative stress.[6] Clinicians widely recommend medications such as dexmedetomidine, morphine agonists, dimethyl sulfoxide, and antioxidants such as zinc, vitamin E, melatonin, and plant antioxidant extracts for I/R injury therapy.[7] The testicular I/R injury model is widely used in experimental animals to test various agents in testicular torsion/detorsion (TD) researches.[1,3,8,9]

Antioxidant mechanisms act by enzymatic or non-enzymatic pathways. Among the non-enzymatic parts of those mechanisms, flavonoids directly neutralize ROS through the donation of hydrogen (H), inducing antioxidant enzymes or affecting cell signaling.[10] As a member of flavonoids, myricetin (MYR) (3, 3, 4, 5, 5, 7-hexahydroxyflavone), has antioxidant[11], anticancer[12], anti-inflammatory,[13] and antiviral[14] activities.

MYR, present in some vegetables, fruits, and plants,[15,16] is mainly in the form of glycosides.[17] It is absorbed by the gastrointestinal tract and mostly metabolized by the liver. The metabolite of MYR is excreted into urine as 3,5-dihydroxyphenylacetic acid.[11]

Here, it was planned to determine the possible beneficial effects of MYR against testicular I/R-induced testicular and lung injuries.

MATERIALS AND METHODS

Animals and Ethics

All procedures performed in this study were approved by Atatürk University Animal Experiments Local Ethics Committee (protocol no: 28.06.2018/146). The study was performed at the Experimental Animals Research and Application Center, Atatürk University (August, 2019). All animal experiments were carried out in accordance with the guidelines on human's animal use and care for laboratory animals for biomedical research published by the National Institutes of Health (8th education, 2011), and the Helsinki Declaration was followed. 32 male Wistar albino rats were randomly divided into 4 groups (n=8). Rats were kept at a 12-hour dark-light cycle at 22°C. Before the experimental process, animals were debarred from food and allowed free access to water. All surgical interventions to animals were performed under anesthesia as 10 mg/kg, intraperitoneal (i.p.) xylazine hydrochloride (Rompun, Bayer, Istanbul), and 60 mg/kg, i.p. ketamine (Ketas, Pfizer, Istanbul). The scrotum regions of the animals were shaved and disinfected with 10% povidone-iodine.

Group I (sham group): The testicles were dissected through a longitudinal scrotal incision, and then the incision was sutured without any intervention.

Group II (I/R group): Scrotal incision was performed, and testicles were rotated clockwise 720 degrees to form bilateral testicular torsion. After 2 hours of torsion, 2 hours of detorsion was performed.[9,18,19]

Group III (MYR 25) and Group IV (MYR 50): Same procedures were carried out with the I/R group. MYR was administered i.p. 30 minutes before detorsion at 25 mg/kg and 50 mg/kg doses as described in a previous I/R study.

The testicular tissue samples were removed following the experimental process and stored at 80°C until analysis.

Evaluation of Biochemical Parameters in Testicular Tissues

Each tissue sample was weighed as 100 mg and homogenized in 2 ml phosphate buffer. Following the homogenization, they were centrifuged at 5000 rpm for 20 minutes at +4°C and transferred to the tubes to be stored at -80°C. Measurement of malondialdehyde (MDA), the final product of lipid peroxidation, was performed using the method of Ohkawa et al.[20] Myeloperoxidase (MPO) activity was evaluated using the technique used by Bradley et al.[21] Superoxide dismutase (SOD) level was determined using the method of Sun et al.[22] MDA, MPO, and SOD levels were measured using a spectrophotometer. The measurements of total antioxidant status (TAS) and total oxidant status (TOS) were determined with the commercial kit (Rel Assay Diagnostics). TOS to TAS ratio was admitted as the oxidative stress index (OSI).

Statistical analysis

SPSS 20 (SPSS Corporation, Chicago, IL, USA) statistics program was preferred for data analysis. Results were presented as Mean±Standard Error (SE), and $p<0.05$ was considered statistically significant. Statistical analysis was performed via One-way analysis of variance, and the difference between groups was determined by Tukey post hoc test.

RESULTS

In table 1, several parameters were evaluated for the testis tissues. TOS value increased in the I/R group compared to the sham group. When it was compared to the I/R group, MYR prevented the increase of TOS levels at both high and low doses. In terms of SOD, I/R reduced SOD value (a). However, both doses of MYR administration elevated the SOD levels compared to the I/R group (b) even the high dose of MYR administration made SOD levels slightly higher than the sham group did. As an indicator of neutrophil recruitment, MPO increased in the I/R group compared to the sham group (a). High dose of MYR administration prevented (b) neutrophil recruitment more than the low dose MYR did (c). The increase in MDA in the I/R group compared to the sham group indicates that there is an increase in lipid peroxidation in the I/R group (a). Both doses of MYR administration prevented lipid peroxidation (b), but the high dose of MYR prevented more than the low dose of MYR did.

In table 2, various parameters were evaluated for the lung tissues. TOS values in the I/R group increased compared to the sham group. Compared to the I/R group, high dose of MYR administration prevented the increase in TOS levels ($p<0.001$) more than the low dose of MYR did ($p<0.05$). I/R reduced the SOD value. However, both doses of MYR administration elevated the SOD value compared to the

Table 1. Results of Testicular I/R-induced Testis Tissues

Experimental Groups (n=8)	TAS (mmol/L)	TOS (µmol/L)	OSI (arbitrary unit)	SOD (U/mg protein	MPO (U/g protein)	MDA (µmol/g tissue)
Sham	0,02±0,10	7,31±1,13	0,71±0,10	375,58±68,28	50391,47±9741,38	267,19±43,98
I/R	0,58±0,09 [a]	10,51±7,05 [a]	1,85±0,43 [a]	171,09±25,18 [a]	89859,19±8358,07 [a]	456,20±88,81 [a]
MYR 25	0,85±0,09 [b]	8,35±1,22 [b]	0,98±0,18 [b]	315,07±34,56 [b]	60641,02±6288,59 [c]	316,49±38,75 [b]
MYR 50	0,98±0,07 [b]	7,63±0,86 [b]	0,78±0,11 [b]	403,83±87,61 [b]	54818,35±5590,98 [b]	274,47±29,52 [b]

[a]$p<0.001$ compared to the sham group. [b]$p<0.001$ and [c]$p<0.05$ compared to the I/R group
TAS= Total antioxidant status, TOS= Total oxidant status, OSI= Oxidative stress index, SOD= Superoxide dismutase, MPO= Myeloperoxidase, MDA= Malondialdehyde

Table 2. Results of Testicular I/R-induced Lung Tissues

Experimental Groups (n=8)	TAS (mmol/L)	TOS (μmol/L)	OSI (arbitrary unit)	SOD (U/mg protein	MPO (U/g protein)	MDA (μmol/g tissue)
Sham	0.75±0.05	11.13±1.14	1.46±0.07	299.24±59.37	408782.88±82459.90	129.07±22.52
I/R	0.49±0.03 [a]	15.52±1.68 [a]	3.15±0.50 [a]	144.18±23.91 [a]	671658.51±80920.84 [a]	231.53±7.73 [a]
MYR 25	0.73±0.04 [b]	13.27±1.44 [c]	1.81±0.10 [b]	261.87±31.31 [b]	448455.66±59076.16 [b]	149.09±13.28 [c]
MYR 50	0.77±0.09 [b]	11.74±1.16 [b]	1.52±0.13 [b]	284.74±34.39 [b]	406572.89±28178.81 [b]	137.35±7.57 [b]

[a]p<0.001 compared to the sham group. bp<0.001 and cp<0.05 compared to the I/R group
TAS= Total antioxidant status, TOS= Total oxidant status, OSI= Oxidative stress index, SOD= Superoxide dismutase, MPO= Myeloperoxidase, MDA= Malondialdehyde

I/R group (p<0.001). MPO increased in the I/R group compared to the sham group. Both doses of MYR administration prevented neutrophil recruitment compared to the I/R group (p<0.001). An increase in MDA levels was observed in the I/R group compared to the sham group (p<0.001). High dose of MYR administration prevented lipid peroxidation (p<0.001) more than the low dose of MYR did (p<0.05).

DISCUSSION

The main pathophysiological mechanism of testicular T/D is ischemia, and subsequent reperfusion damages the testicle by twisting the spermatic cord.[23] These injuries are caused by the ROS produced during I/R injury. ROS causes DNA damage and apoptosis in testicular germ cells.[6,18,24-26] Excessive ROS production can also cause distant organ failure. ROS can cause acute respiratory failure by causing capillary edema and blood-air barrier problems in the lungs.[27,28] Antioxidant defense mechanisms develop in tissues to reduce this damage[29,30], but tissue damage can occur if these antioxidant defense mechanisms fail. Antioxidant therapy has been suggested to prevent I/R damage.[31] Various drugs, enzymes, and chemical agents have been suggested for therapeutic purposes as they inhibit oxidative stress by increasing the effectiveness of antioxidant enzymes. MYR is more potent in terms of antioxidant capacity than other flavonoid types due to having more phenolic hydroxyl groups, including quercetin, kaempferol, catechin, and rutin.[32] It has been stated that flavonoids can play protective roles in many pathological mechanisms due to their anti-inflammatory and antioxidant properties.[33-35] This study also proved antioxidant effects of MYR on both testes (Table 1) and lungs (Table 2) as a remote organ. MYR plays a protective role on cells through inhibiting ROS generation and activating several antioxidant enzymes.[36] However, a study implied the antioxidant activity of MYR as dose-dependent. While higher concentrations of MYR have prooxidant property, lower concentrations perform antioxidant activity.[37]

MDA is a stable end product of lipid peroxidative degradation produced by ROS.[38] Malondialdehyde (MDA) is an indicator of lipid peroxidation in I/R injury studies because the MDA level elevates parallel to both non-enzymatic lipid peroxidation and after testicular injury as well.[39] Similarly, MPO, which increases in the I/R process, is an enzyme with strong prooxidative and proinflammatory properties, released by activated neutrophils. MPO is basically an indicator of neutrophil infiltration into cells.[40,41] In preclinical studies, it has been reported that post-ischemia testicular reperfusion leads to lipid peroxidation and an increase in tissue MDA and MPO levels.[18,19,31] Different doses of MYR have been reported to reduce MDA and MPO levels in many different studies.[39,42,43]

Superoxide dismutase (SOD) exists in different parts of the cell, such as mitochondria, cytosol, or extracellular membranes, to reduce the superoxide radicals to hydrogen peroxide.[44] SOD decreases in case of I/R injury.[45] SOD, an essential active substrate in the cell growth and differentiation process, protects the cell from injury.[46] Chen et al. report that MYR can lower the ROS level and increase

SOD and GPX values.[47] Besides, MYR has been reported to have strong antioxidative stress properties by regulating the Nrf2/HO-1 signaling pathway.[47,48] Our study demonstrated the effects of MYR on some antioxidant enzymes in testicular and lung damage created with the testis I/R model. The balance between I/R and oxidant/antioxidant systems in testicular and lung tissues, which was disrupted, approached the baseline levels in the 25 mg/kg and 50 mg/kg MYR groups.

As a result, we found that 25 and 50 mg/kg MYR administration 30 minutes before detorsion protected the testicle and lung against I/R damage caused by oxidative stress in rats. MYR's protective effect appears to be due to its antioxidant and anti-inflammatory properties. MYR may reduce testicular I/R damage in humans, but it is early to say this with the available data. Therefore, different studies are needed to obtain more and more detailed data.

Ethical Statement

All procedures performed in this study were approved by Atatürk University Animal Experiments Local Ethics Committee (protocol no: 28.06.2018/146).

References

1. *Kazaz IO, Demir S, Yulug E, Colak F, Bodur A, Yaman SO, et al. N-acetylcysteine protects testicular tissue against ischemia/reperfusion injury via inhibiting endoplasmic reticulum stress and apoptosis. J Pediatr Urol. 2019;15(3).*
2. *Parlaktas BS, Atilgan D, Ozyurt H, Gencten Y, Akbas A, Erdemir F, et al. The biochemical effects of ischemia-reperfusion injury in the ipsilateral and contralateral testes of rats and the protective role of melatonin. Asian J Androl. 2014;16(2):314-8.*
3. *Turkmen S, Gonenc OC, Karaca Y, Mentese A, Demir S, Beyhun E, et al. The effect of ethyl pyruvate and N-acetylcysteine on ischemia-reperfusion injury in an experimental model of ischemic stroke. American Journal of Emergency Medicine. 2016;34(9):1804-7.*
4. *Mete F, Tarhan H, Celik O, Akarken I, Vural K, Ekin RG, et al. Comparison of intraperitoneal and intratesticular ozone therapy for the treatment of testicular ischemia- reperfusion injury in rats. Asian J Androl. 2017;19(1):43-6.*
5. *Lysiak JJ, Nguyen QA, Turner TT. Peptide and nonpeptide reactive oxygen scavengers provide partial rescue of the testis after torsion. J Androl. 2002;23(3):400-9.*
6. *Aitken RJ, Roman SD. Antioxidant systems and oxidative stress in the testes. Adv Exp Med Biol. 2008;636:154-71.*
7. *Arena S, Iacona R, Antonuccio P, Russo T, Salvo V, Gitto E, et al. Medical perspective in testicular ischemia-reperfusion injury. Experimental and Therapeutic Medicine. 2017;13(5):2115-22.*
8. *Topdagi O, Tanyeli A, Akdemir FNE, Erdogan DG, Güler MC, Eraslan E. Higenamine decreases testicular damage injured by ischemia reperfusion: A biochemical study. Turkish Journal of Science. 2019;4(2):92-9.*
9. *Topdagi O, Tanyeli A, Akdemir FNE, Eraslan E, Guler MC. Barbaloin Attenuates Oxidative Testicular Injury Induced by Ischemia Reperfusion via Antioxidant Effects. Turkish Journal of Science. 2020;5(1):28-33.*
10. *Williams RJ, Spencer JPE, Rice-Evans C. Flavonoids: Antioxidants or signalling molecules? Free Radical Bio Med. 2004;36(7):838-49.*
11. *Ong KC, Khoo HE. Biological effects of myricetin. Gen Pharmacol-Vasc S. 1997;29(2):121-6.*
12. *Phillips PA, Sangwan V, Borja-Cacho D, Dudeja V, Vickers SM, Saluja AK. Myricetin induces pancreatic cancer cell death via the induction of apoptosis and inhibition of the phosphatidylinositol 3-kinase (PI3K) signaling pathway. Cancer Lett. 2011;308(2):181-8.*
13. *Tsai SH, Liang YC, Lin-Shiau SY, Lin JK. Suppression of TNF alpha-mediated NF kappa B activity by myricetin and other flavonoids through downregulating the activity of IKK in ECV304 cells. J Cell Biochem. 1999;74(4):606-15.*
14. *Yu MS, Lee J, Lee JM, Kim Y, Chin YW, Jee JG, et al. Identification of myricetin and scutellarein as novel chemical inhibitors of the SARS coronavirus helicase, nsP13. Bioorg Med Chem Lett. 2012;22(12):4049-54.*
15. *Ross JA, Kasum CM. Dietary flavonoids: bioavailability, metabolic effects, and safety. Annu Rev Nutr. 2002;22:19-34.*
16. *Miean KH, Mohamed S. Flavonoid (myricetin, quercetin, kaempferol, luteolin, and apigenin) content of edible tropical plants. J Agric Food Chem. 2001;49(6):3106-12.*
17. *Park KS, Chong Y, Kim MK. Myricetin: biological activity related to human health. Appl Biol Chem. 2016;59(2):259-69.*
18. *Tanyeli A, Eraslan E, Akdemir FNE, Güler MC , Erdoğan DG, Polat E, et al. Cryptotanshinone mitigates ischemia reperfusion-induced testicular damage: A experimental study. Annals of Medical Research. 2019;26(11):2549-52.*
19. *Güler MC, Tanyeli A, Eraslan E, Akdemir FNE. Lazaroid U-74389G Decreases Testis Tissue Injury Induced by Testicular Torsion Detorsion: An Experimental Study. International Journal of Academic Medicine and Pharmacy. 2020;2(2):96-100.*
20. *Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem. 1979;95(2):351-8.*
21. *Bradley PP, Priebat DA, Christensen RD, Rothstein G. Measurement of cutaneous inflammation: estimation of neutrophil content with an enzyme marker. J Invest Dermatol. 1982;78(3):206-9.*
22. *Sun Y, Oberley LW, Li Y. A simple method for clinical assay of superoxide dismutase. Clin Chem. 1988;34(3):497-500.*
23. *Zhang T, Li CY, Jia JJ, Chi JS, Zhou D, Li JZ, et al. Combination Therapy with LXW7 and Ceria Nanoparticles Protects against Acute Cerebral Ischemia/Reperfusion Injury in Rats. Curr Med Sci. 2018;38(1):144-52.*
24. *Ustun H, Akgul KT, Ayyildiz A, Yagmurdur H, Nuhoglu B, Karaguzel E, et al. Effect of phospodiesterase 5 inhibitors on apoptosis and nitric oxide synthases in testis torsion: an experimental study. Pediatr Surg Int. 2008;24(2):205-11.*
25. *Lysiak JJ, Turner SD, Nguyen QA, Singbartl K, Ley K, Turner TT. Essential role of neutrophils in germ cell-specific apoptosis following ischemia/reperfusion injury of the mouse testis. Biol Reprod. 2001;65(3):718-25.*
26. *Yulug E, Turedi S, Karaguzel E, Kutlu O, Mentese A, Alver A. The short term effects of resveratrol on ischemia-reperfusion injury in rat testis. J Pediatr Surg. 2014;49(3):484-9.*
27. *Ware LB, Matthay MA. Medical progress - The acute respiratory distress syndrome. New Engl J Med. 2000;342(18):1334-49.*
28. *Piantadosi CA, Schwartz DA. The acute respiratory distress syndrome. Ann Intern Med. 2004;141(6):460-70.*
29. *Kulkarni SK, Patil CS. Phosphodiesterase 5 enzyme and its inhibitors: update on pharmacological and therapeutical aspects. Methods Find Exp Clin Pharmacol. 2004;26(10):789-99.*
30. *Circu ML, Aw TY. Redox biology of the intestine. Free Radic Res. 2011;45(11-12):1245-66.*
31. *Keseroglu BB, Ozgur BC, Surer H, Ogus E, Hucemenoglu S, Ozer E, et al. Which agent should be used to reduce ischemia-reperfusion injury after testicular torsion: a comparative animal experiment. J Pediatr Urol. 2019;15(6):607 e1- e7.*
32. *Pekkarinen SS, Heinonen IM, Hopia AI. Flavonoids quercetin, myricetin, kaemferol and (+)-catechin as antioxidants in methyl linoleate. J Sci Food Agr. 1999;79(4):499-506.*
33. *Soobrattee MA, Neergheen VS, Luximon-Ramma A, Aruoma OI, Bahorun T. Phenolics as potential antioxidant therapeutic agents: Mechanism and actions. Mutat Res-Fund Mol M. 2005;579(1-2):200-13.*
34. *Zeka K, Marrazzo P, Micucci M, Ruparelia KC, Arroo RRJ, Macchiarelli G, et al. Activity of Antioxidants from Crocus sativus L. Petals: Potential Preventive Effects towards Cardiovascular System. Antioxidants (Basel). 2020;9(11).*
35. *Yavtushenko IV, Nazarenko SM, Katrushov OV, Kostenko VO. Quercetin Limits the Progression of Oxidative and Nitrosative Stress in the Rats' Tissues after Experimental Traumatic Brain Injury. Wiad Lek. 2020;73(10):2127-32.*
36. *Semwal DK, Semwal RB, Combrinck S, Viljoen A. Myricetin: A Dietary Molecule with Diverse Biological Activities. Nutrients. 2016;8(2):90.*
37. *Laughton MJ, Halliwell B, Evans PJ, Hoult JR. Antioxidant and pro-oxidant actions of the plant phenolics quercetin, gossypol and myricetin. Effects on lipid peroxidation, hydroxyl radical generation and bleomycin-dependent damage to DNA. Biochem Pharmacol. 1989;38(17):2859-65.*
38. *Mertoglu C, Senel U, Cayli S, Tas U, Kusku Kiraz Z, Ozyurt H. Protective role of methylprednisolone and heparin in ischaemic-reperfusion injury of the rat testicle. Andrologia. 2016;48(7):737-44.*
39. *Eksi E, Yalcin Comert HS, Imamoglu M, Alver A, Aydin Mungan S, Sarihan H. Effects of myricetin on testicular torsion-detorsion injury in rats. Andrologia. 2020:e13775.*
40. *Grisham MB, Benoit JN, Granger DN. Assessment of Leukocyte Involvement during Ischemia and Reperfusion of Intestine. Method Enzymol. 1990;186:729-42.*
41. *Loria V, Dato I, Graziani F, Biasucci LM. Myeloperoxidase: a new biomarker of inflammation in ischemic heart disease and acute coronary syndromes. Mediators Inflamm. 2008;2008:135625.*
42. *Mao MT, Huang MY. Myricetin attenuates lung inflammation and provides protection against lipopolysaccharide-induced acute lung injury by inhibition of NF-kappa B pathway in rats. Trop J Pharm Res. 2017;16(11):2585-93.*
43. *Zhao J, Hong T, Dong M, Meng YX, Mu JY. Protective effect of myricetin in dextran sulphate sodium-induced murine ulcerative colitis. Mol Med Rep. 2013;7(2):565-70.*
44. *Majima HJ, Oberley TD, Furukawa K, Mattson MP, Yen HC, Szweda LI, et al. Prevention of mitochondrial injury by manganese superoxide dismutase reveals a primary mechanism for alkaline-induced cell death. Journal of Biological Chemistry. 1998;273(14):8217-24.*
45. *McCord JM, Edeas MA. SOD, oxidative stress and human pathologies: a brief history and a future vision. Biomedicine & Pharmacotherapy. 2005;59(4):139-42.*
46. *Takhtfooladi MA, Moayer F, Takhtfooladi HA. Beneficial effect of pentoxifylline into the testis of rats in an experimental model of unilateral hindlimb ischemia/reperfusion injury. Int Braz J Urol. 2015;41(3):576-83.*
47. *Chen S, Fan B. Myricetin protects cardiomyocytes from LPS-induced injury. Herz. 2018;43(3):265-74.*
48. *Wu S, Yue Y, Peng A, Zhang L, Xiang J, Cao X, et al. Myricetin ameliorates brain injury and neurological deficits via Nrf2 activation after experimental stroke in middle-aged rats. Food Funct. 2016;7(6):2624-34.*

ARAŞTIRMA MAKALESİ / *Research Article*

Tıbbi Biyokimya Laboratuvarı Yaz Stajı Öğrenim Düzeyi Değerlendirmesi: Bir Afiliye Hastane Örneği

Medical Biochemistry Laboratory Summer Practice Learning Level Assessment: An Affiliated Hospital Example

Erdem Çokluk[1], Selin Tunalı Çokluk[2], Fatma Betül Tuncer[1], M. Ramazan Şekeroğlu[1], Meltem Boz[1]

[1] Sakarya Üniversitesi Tıp Fakültesi, Sakarya
[2] Sakarya İl Sağlık Müdürlüğü, Sakarya

Yazışma Adresi / *Correspondence:*
Erdem Çokluk

İzmir Tınaztepe Üniversitesi Aydoğdu, 1267/1. Sk. No:4, 35400 Buca/İzmir
T: **+90 506 497 16 15** E-mail **: erdemcokluk205@hotmail.com**

Geliş Tarihi / Received : **28.11.2020** Kabul Tarihi / Accepted : **07.01.2021**

Orcid :
Erdem Çokluk https://orcid.org/0000-0002-6205-5109
Selin Tunalı Çokluk https://orcid.org/0000-0001-9159-1595
Fatıma Betül Tuncer https://orcid.org/0000-0002-4034-4188
M. Ramazan Şekeroğlu https://orcid.org/0000-0001-8383-6740
Meltem Boz https://orcid.org/0000-0002-7939-8503

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):115-121) DOI: 10.31832/smj.832765

Çalışmada herhangi bir finansal ya da materyal desteği alınmadığı ve herhangi bir çıkar çatışmasının olmadığını yazarlar beyan etmektedirler.

Öz

Amaç Bu çalışma, Tıbbi Biyokimya Laboratuvar Yaz Stajının; tıp fakültesi öğrencileri tarafından algılanma şekli ve öğrencilerin klinik biyokimya laboratuvarı ile ilgili pratik ve teorik bilgi düzeyine sağladığı katkıyı tespit etmek amacıyla planlandı.

Gereç ve Yöntem Tıbbi Biyokimya Laboratuvar Yaz Stajına katılan Sakarya Üniversitesi Tıp Fakültesi dönem 1(D-I) ve dönem 2(D-II) öğrencilerine staj başlangıcında ön test ve staj sonunda da son test uygulandı. Çalışmada 26 sorudan oluşan anket formu kullanıldı. Öğrencilere bireysel kod oluşturularak ön test ve son testte genel ve kişisel bilgi düzeylerinde meydana gelen değişiklikler tespit edildi.

Bulgular D-I ve D-II öğrencilerinin ön test puan ortalamaları sırasıyla 60±24,1 ile 70,3±24,6; son test puan ortalamaları ise 68±23,6 ve 78,8±25,2 bulundu. Ön test ve son test puanları karşılaştırıldığında son test puanlarının ön test puanlarından anlamlı derecede yüksek olduğu tespit edildi(p=0,009). Öğrenciler dönemlere göre ayrıldığında ise, D-II öğrencilerinin hem ön test hem de son test puanları, D-I öğrencilerinden anlamlı olarak yüksek saptandı(p<0,05).

Sonuç Ön test puanlarından daha yüksek son test puanları, staj eğitiminin öğrencilerin bilgilerini artırdığını göstermektedir. Derslerine ek olarak, seçmeli yaz stajları aktif öğrenmeleri için faydalı olacaktır. Böylece klinik laboratuvarın nasıl çalıştığını kolayca anlayabilirler. Bu tür aktif öğrenme programları, tıbbi yaşamlarında da etkilidir ve gelecekte uzmanlık seçimi için bir rehber niteliği taşıyabilir.

Anahtar Kelimeler Tıbbi Biyokimya Eğitimi; Yaz Stajı; Öğrenim Düzeyi Değerlendirmesi

Abstract

Objective *This study was planned to determine the Medical Biochemistry Laboratory Summer Internship how perceived by the students of the medical faculty and its contribution to the level of practical and theoretical knowledge of the clinical biochemistry laboratory.*

Materials and methods *Participating of the Medical Biochemistry Laboratory Summer Internship, Sakarya University Faculty of Medicine term 1(D-I) and term 2(D-II) students were pre-tested at the beginning of the internship and post-test at the end of the internship.A questionnaire form consisting of 26 questions was used in the study. Changes of general and personal knowledge levels were determined in pretest and posttest by creating individual code for all the students,*

Results *The pre-test and ppost test mean scores of D-I and D-II students were 60±24.1, 70.3±24.6, and 68±23.6, 78.8±25.2 respectively. Posttest scores were significantly higher than the pretest scores(p=0,009) in all groups.When students were separated by terms , the pre-test and post-test scores of D-II students were significantly higher than the D-I students.*

Conclusion *Higher post-test scores than the pre-test scores show that, internship education increases the knowledge of students. In addition to their lectures, elective summer internships would be beneficial for their active learning. So they can easily understand that, how does clinical laboratory work. This type of active learning programmes also be efficient in their medical life and would be a guide to the speciality choice in future.*

Keywords *Medical Biochemistry Education; Summer internship; Educational Level Assessment*

GİRİŞ

Geçmişten günümüze tıp biliminin ve eğitiminin dinamik değişimi düşünüldüğünde, tıp eğitiminin en iyi nasıl sunulacağına dair sürekli bir arayış durumu söz konusudur. Bu arayışlar doğrultusunda birçok tıp fakültesinde farklı eğitim modelleri uygulanmaktadır.[1]

1998 yılında Dünya Tıp Eğitimi Federasyonu tıp eğitiminde uluslararası standartlar programını başlatmış ve her hekim adayının minimum alması gereken eğitimi belirtmiştir.[2] Ancak standartların olması tek tip eğitim anlamına da gelmemektedir. Her fakülte, mezunlarının minimum çekirdek eğitim programındaki yeterliliğe sahip olmasını sağlamalı, buna ek olarak kaliteli bir ortamda öğrencilerini meslek yaşamlarına hazırlamak için kendi müfredat programlarını belirlemelidir.[1]

Bu kapsamda fakültemizde öğrencilere Ulusal Çekirdek Eğitim Programı (ÇEP) kapsamında temel tıbbi eğitim verilmekte, hekimliğin teknik ve prosedürel yönü geliştirilmektedir. Buna ek olarak mesleki davranış yetkinliğine sahip birinci basamakta koruyucu ve tedavi edici sağlık hizmeti verebilen hekimler mezun edebilmek için teorik eğitim ile birlikte pratik donanım kazandırmak için uygulamalı eğitimler de sunulmaktadır.[3,4]

Bu amaçla yapılan çalışmalardan bir tanesi de mezuniyet öncesi eğitim döneminde öğrencilere yaz staj programları sunarak, hekimlik hayatlarında gerekli pratik donanımları kazandırmaktır. Bu kapsamda öğrencilere içerisinde Tıbbi Biyokimya birimini de içeren yaz stajı imkânı sunulmuştur. Bu yaz stajı programının Tıbbi Biyokimya bölümünde staj süresince öğrencilere rutin laboratuvar işleyişi hakkında yerinde gözlem ve uygulamalı eğitim imkânı verilmiştir. Ayrıca her birinci basamak hekiminin bilmesi gereken biyokimya test parametreleri ile ilgili öğrencilerin seviyelerine uygun şekilde temel bilgilendirmelerde bulunulmuştur.

Bu çalışma Fakültemizde uygulanan Tıbbi Biyokimya Laboratuvar Yaz Stajının; staja katılan tıp fakültesi öğrencileri tarafından ne şekilde algılandığını öğrenmek ve bu stajın öğrencilerin klinik biyokimya laboratuvarı ile ilgili pratik ve teorik bilgi düzeyine katkısını tespit etmek amacıyla planlandı.

GEREÇ ve YÖNTEMLER

1. Evren ve Çalışma Grubu

Araştırmamız 16 - 26 Temmuz 2019 tarihleri arasında Tıbbi Biyokimya Laboratuvar Yaz Stajına katılan Sakarya Üniversitesi Tıp Fakültesi dönem 1 (D-I) ve dönem 2 (D-II) öğrencilerinde yapılmış tanımlayıcı bir araştırmadır. Bu kapsamda seçmeli olan Tıbbi Biyokimya laboratuvarı stajına devamlılık gösteren ve çalışmayı kabul eden tüm öğrencilere (26 öğrenci) anket uygulandı. Bu öğrenciler araştırmanın evreni olarak kabul edildi.

Çalışma için Sakarya Üniversitesi Tıp Fakültesi girişimsel olmayan etik kurulundan 02/10/2019 tarih ve 105 sayılı karar ile etik kurul onayı alınmıştır.

2. Veri Toplama Araçları

Çalışma kapsamında öğrenciler staj başlangıç tarihinde ön test, bitiş tarihinde ise son test uygulamasına tabi tutuldu. Uygulama için sosyo-demografik ve mesleki bilgileri içeren 6 (altı) ve biyokimya konusunda bilgiyi sorgulayan 20 (yirmi) sorudan oluşan anket formu kullanıldı. Formda 1, 4, 6, 7, 8, 11, 14, 16, 17 ve 20. maddeler olumlu, 2, 3, 5, 9, 10, 12, 13, 15, 18 ve 19. ise maddeler olumsuz ifadelerden oluşmaktaydı. Olumlu ifadelerde Doğru=5, Yanlış=0 puan; olumsuz ifadelerde ise Doğru=0, Yanlış=5 puan olarak puanlandı. Ankette minimum puan 0 iken, maksimum puan 100'dür. Anket soruları iki değerli ölçümlenmiş maddeler için iç tutarlılık güvenirlik kestirimlerinde kullanılan Kuder Richardson 20 (KR 20) katsayısı ile değerlendirilmiştir.[5] Testin yapı geçerliliği açısından değerlendirilmesi sonucunda KR 20 değeri sırasıyla 0,67 ve 0,69 dır. Çalışmaya katılan öğrencilere araştırmacılar tarafından anket formlarının nasıl uygulanacağı açıklandı ve formlar araştırmacılar gözetiminde öğrenciler tarafından doldurduldu.

Öğrenciler doğum tarihi ve spesifik numara ile kodlanarak genel ve kişisel bilgi düzeylerinde meydana gelen değişiklik tespit edildi. Staj süresince öğrencilere; numune alımından hasta sonucu elde edilene kadarki süreçte laboratuvar işleyişi, preanalitik/analitik/postanalitik hata kaynakları, numune reddi, laboratuvarda otomasyon ve kalite uygulamalarından bahsedildi. Ek olarak rutin biyokimya testleri ve hemogram sonuçlarının yorumlanması, tiroid fonksiyon testleri, kardiyak belirteçler ve HbA1c testi ve bunların klinik kullanımlarından bahsedildi.

3. Verilerin analizi

Elde edilen verilerin değerlendirilmesi bilgisayar ortamında SPSS 20.0 (IBM Statistical Packages for the Social Sciences; Armonk, NY, ABD) istatistik programı kullanılarak yapıldı. Verilerin tanımlayıcı istatistikleri olarak ortalama, standart sapma, medyan ve frekans değerleri incelendi. Nicel verilerin normal dağılıma uygunluğu Shapiro-Wilk testi ile tespit edildi. Ölçüm değerlerinin analizinde iki bağımsız değişkenin olduğu gruplarda parametrik test koşulları sağlandığında bağımsız gruplarda t testi, sağlanmadığında ise Mann-Whitney U testi uygulandı. Ön test ve son test puanları arasında karşılaştırma yaparken; normal dağılıma uyan değişkenlerde bağımlı gruplar için t testi; normal dağılıma uymayan değişkenlerde ise Wilcoxon testi kullanıldı. Anlamlılık düzeyi $p<0.05$ olarak alındı.

BULGULAR

Anket çalışmasına katılan 26 öğrencinin (13 D-I, 13 DII) dönemlere göre sosyodemografik özellikleri ve biyokimya eğitimine yönelik düşünceleri Tablo 1'de verilmiştir.

''Okulda tıbbi biyokimya dersinde yeterli teorik bilgiyi aldığınızı düşünüyor musunuz?" sorusuna D-I ve D-II öğrencileri sırasıyla %100, %92,3 evet cevabı verirken; ''Okulda tıbbi biyokimya dersinde yeterli pratik bilgiyi aldığınızı düşünüyor musunuz?" sorusuna sırasıyla %69,2, %46,2 evet cevabı vermişlerdir.

D-I ve D-II öğrencileri staj başlangıcında ''Stajda öğreneceğiniz bilgilerin tıp eğitiminize katkısının olacağını düşünüyor musunuz?" sorusuna sırasıyla %69,2, %84,6 evet cevabını verirlerken, Staj sonunda yapılan son testte ''Stajda öğrendiğiniz bilgilerin tıp eğitiminize katkısı olduğunu düşünüyor musunuz?" sorusuna ise öğrencilerin tamamı evet cevabını vermişlerdir (%100).

Tablo 1. Tıbbi Biyokimya Laboratuvar Stajına Katılan Öğrencilerin Sosyodemografik Özellikleri ve Eğitimle İlgili Düşünceleri

	DEĞİŞKEN		**DÖNEM 1 n (%)**	**DÖNEM 2 n (%)**
1	Cinsiyet	Kadın	8 (%61,5)	4 (%30,8)
		Erkek	5 (%38,5)	9 (%69,2)
2	Yaşanılan Yer	Ailesinin Yanında ya da Öğrenci Evinde	9 (% 69,2)	8 (% 61,5)
		Devlet Yurdunda ya da Özel Yurtta	4 (% 30,8)	5 (% 38,5)
3	Okulda tıbbi biyokimya dersinde yeterli teorik bilgiyi aldığınızı düşünüyor musunuz?	Evet	13 (%100)	12 (% 92,3)
		Hayır	0 (%0)	1 (% 7,7)
4	Okulda tıbbi biyokimya dersinde yeterli pratik bilgiyi aldığınızı düşünüyor musunuz?	Evet	9 (%69,2)	6 (% 46,2)
		Hayır	4 (% 30,8)	7 (% 53,8)
5*	Stajda öğreneceğiniz bilgilerin tıp eğitiminize katkısı olacağını düşünüyor musunuz?	Evet	9 (%69,2)	11 (%84,6)
		Hayır	4 (%30,8)	2 (%15,4)
6**	Stajda öğrendiğiniz bilgilerin tıp eğitiminize katkısı olduğunu düşünüyor musunuz?	Evet	13 (%100)	13(%100)
		Hayır	0 (%0)	0 (%0)

*5. soru Ön test sırasında **6. Soru son test sırasında sorulmuştur

Tablo 2. Tıbbi Biyokimya Laboratuvar Stajına Katılan Öğrencileri Tarafından Ön Test ve Son Test Sorularına Verilen Doğru Cevapların Sayı ve Frekansları

SORU SIRASI	SORULAR	ÖN TEST		SON TEST	
		D-I	D-II	D-I	D-II
1	Laboratuvar hataları preanalitik, analitik ve postanalitik olarak 3 ana gruba ayrılabilir.	12(%92,3)	13(%100)	13(%100)	13(%100)
2	Hastadan kan alınırken turnike kullanmak zorunludur.	7(%53,8)	4(%30,8)	5(%38,5)	6(%46,2)
3	Kan alınan iğnelerin kapakları kapatılmadan delici kesici alet kutusuna kesinlikle atılmamalıdır.	4(%30,8)	8(%61,5)	3(%23,1)	12(%92,3)
4	Kan alınırken önce koagülasyon tüpüne (mavi kapaklı) sonra sarı jelli tüpe alınmalıdır.	6(%46,2)	8(%61,5)	6(%46,2)	9(%69,2)
5	Biyokimya laboratuvarında her gün analiz başlangıcında dış kalite kontrol çalışması yapılması zorunludur.	3(%23,1)	6(%46,2)	3(%23,1)	7(%53,8)
6	Hemolizli numune bazı kan parametrelerinin ölçümünde hatalı sonuçlara neden olabilir.	12(%92,3)	13(%100)	13(%100)	13(%100)
7	Böbreklerin birim zamanda bir maddeden tamamen temizlediği plazma volumü o maddenin renal klirensi olarak tarif edilir.	9(%69,2)	13(%100)	9(%69,2)	13(%100)
8	Protrombin zamanı ve albumin karaciğerin sentez fonksiyonunu gösteren parametrelerdir.	9(%69,2)	7(%53,8)	13(%100)	9(%69,2)
9	GFR ölçümünde altın standart madde kreatinindir.	5(%38,5)	4(%30,8)	3(%23,1)	4(%30,8)
10	CK-MM kalbe en spesifik olan CK izoenzimidir.	4(%30,8)	7(%53,8)	6(%46,2)	9(%69,2)
11	HbA1c 'nin %6.5 dan büyük olması diyabet tanısında anlamlıdır.	10(%76,9)	12(%92,3)	13(%100)	13(%100)
12	Hba1c, anlık kan glukoz seviyesinin ortalamasını gösterir.	6(%46,2)	10(%76,9)	5(%38,5)	12(%92,3)
13	Etanol numunesi alınırken alkollü dezenfektan kullanmaya özen gösterilmelidir.	4(%30,8)	8(%61,5)	3(%23,1)	8(%61,5)
14	Panik/kritik değer: Hastalar için hayatı tehdit eden durumu gösteren, acil tedavi gerektiren sonuçlardır.	12(%92,3)	10(%76,9)	12(%92,3)	12(%92,3)
15	Hemogram paremetrelerindeki WBC eritrositlerin hareket hızını gösterir.	5(%38,5)	9(%69,2)	10(%76,9)	12(%92,3)
16	Hemogram paremetrelerindeki MCV ortalama eritrosit hacmini gösterir.	9(%69,2)	11(%84,6)	13(%100)	12(%92,3)
17	Akut miyokard infarktüsü tanısı koymada troponin yüksekliği önemli bir parametredir.	13(%100)	12(%92,3)	13(%100)	11(%84,6)
18	AST düzeyi ALT den daha fazla karaciğere spesifiktir.	7(%53,8)	6(%46,2)	9(%69,2)	9(%69,2)
19	Sağlıklı bir insanda glomerüler filtrasyon hızının 60'dan küçük olması beklenir. 60'ın üzerinde ise hasta acilen diyalize alınmalıdır.	6(%46,2)	10(%76,9)	10(%76,9)	8(%61,5)
20	Santrifüj cihazları tüpleri yüksek hızda çevirmek suretiyle farklı yoğunluktaki sıvıları birbirinden ayırmaya yarayan cihazlardır.	13(%100)	13(%100)	13(%100)	13(%100)

D-I: Dönem 1 i bitirmiş, D-II Dönem 2 yi bitirmiş

Anket formunda yer alan ön test ve son test sorularına verilen doğru cevapların sayı ve frekansları Tablo 2'de özetlenmiştir. Ön test ve son test uygulamasından elde edilen toplam test puanları ise Tablo 3 'de gösterilmiştir.

Çalışmaya katılan öğrencilerin ön test ve son test puanları incelendiğinde son test puanlarının ön test puanlarından anlamlı derecede yüksek olduğu belirlendi (p=0,009). Öğrenciler dönemlere göre ayrıldığında ise, D-II öğrencilerinin hem ön test hem de son test puanları D-I öğrencilerinden anlamlı olarak yüksekti (p<0,05). Öğrenciler cinsiyet, yaşanılan yere gruplandırıldığında ya da okulda tıbbi biyokimya dersinde yeterli teorik bilgiyi/pratik bilgiyi aldığınızı düşünüyor musunuz? sorusuna verdikleri cevaplara

Tablo 3. Tıbbi Biyokimya Laboratuvar Stajına Katılan Öğrencilerin Ön Test ve Son Test Puanları						
	ÖN TEST			**SON TEST**		
	D-I	**D-II**	**Toplam**	**D-I**	**D-II**	**Toplam**
Ort±SD	60±24,14	70,38±24,64	65,19±26,14	68,08±23,64	78,85±25,20	71,73±28,40
Min	45	50	45	45	55	45
Max	95	90	95	100	100	100
Ort: ortalama, SD:standart sapma, Min: Minimum puan, Max: Maksimum puan						

göre (evet/hayır diyenler) gruplara ayrıldığında ise gruplar arasında ön test son test puanlarında anlamlı fark saptanmadı (p>0,05).

TARTIŞMA

Ülkemizde ve dünyada toplumun sağlık gereksinimlerini karşılayabilecek bilgi, beceri ve tutuma sahip, sürekli öğrenen ve kendini geliştiren hekimler yetiştirme amacıyla tıp eğitimini geliştirme çalışmaları yapılmakta ve bu çalışmaların eğitime ve öğrenci tutumuna katkısı incelenmektedir.[6-8]

Bu kapsamda Dong ve ark[9] biyokimya dersi ile ilgili yaptıkları çalışmalarında deneysel öğretimi geleneksel öğretim ile karşılaştırmışlar ve deneysel/vaka kontrollü öğrenimin biyokimya dersine ilgi ve isteği arttırdığını göstermişlerdir. Ayar ve ark[10] da tıp fakültesi öğrencilerinde geleneksel öğrenme ve probleme dayalı öğrenmeyi (PDÖ) karşılaştırdıkları çalışmalarında; iki farklı öğrenim türü uyguladıkları öğrencilere eğitim sonunda başarı testi ve tutum ölçeği uygulamışlardır. PDÖ uygulanarak konuyu öğrenen grubun geleneksel yöntem grubuna göre hem konuya hem de biyokimya dersine karşı tutumlarında olumlu artış saptanmıştır. Eskiocak ve ark[11] ise rutin biyokimya eğitimini geliştirmek için D-II tıbbi biyokimya eğitimi içeriğine mesleki beceri eğitimi ve biyokimya laboratuvarlarının tanıtılması gibi eğitimleri eklemişler ve eğitim sonunda öğrencilerin memnuniyetini değerlendirmek için 5'li Likert tipi anket uygulamışlardır. Anket sonucunda biyokimya uygulamalarında farklı eğitim yöntemlerinin kullanılmasının öğrencilerin mesleki bilgi ve beceri kazanımlarına katkıda bulunacağını belirtmişlerdir. Benzer olarak Kohler ve ark[12] da 150 preklinik tıp öğrencisi ile yaptıkları çalışmalarında öğrencilerin klinik ve hasta odaklı eğitim talep ettiklerini, eğitim aşamasında klinik konulara atıfta bulunulmamasının öğrencilerde memnuniyetsizliğe neden olduğunu belirtmişlerdir. Yapılan çalışmalar tıp eğitiminde geleneksel eğitimin yanı sıra uygulama alanında yapılan katkıların öğrencilerin derslere karşı olan tutumuna pozitif etki yaptığı ve hekimlik hayatında kendilerini yeterli hissetmelerini sağladığını göstermektedir.[10,11,13]

Alhan ve ark[14] ise Marmara üniversitesi tıp fakültesi öğrencilerine çeşitli bölümlerde yaz stajı imkanı tanımış ve staj sonunda öğrencilerin stajdan memnuniyeti, staj yapma nedenleri, stajların öğrenciye katkısına ilişkin görüşleri anket yoluyla sormuşlardır. Yaz stajlarının öğrencilerin temel bilimlere ilişkin bilgilerinin uygulamadaki kullanımını görmelerini, hastane ortamını tanımlarını sağladığını ve kariyer planlamada olumlu katkı oluşturduğunu belirtmişlerdir. Giray ve ark[15] ise tıp fakültesi dönem 1 öğrencilerine yaz tatili gözlem ziyareti kapsamında klinik bölümlerinin işleyişi hakkında bilgi sahibi olma imkânı tanımışlardır. Gözlem ziyaretleri sonrasında öğrencilerin görüşlerinin alınması için anket uygulanmıştır. Öğrenciler yaz staj gözleminin mezuniyet sonrası alan seçmeye, mesleki gelişimlerine katkısı olduğunu ve gelecek iş hayatı ile ilgili fikir sahibi olduklarını belirtmişlerdir. Literatürde erken dönemde hasta ile karşılaşan öğrencilerin öğrenmeye ilgilerinin arttığı ve kendilerini hekim gibi hissettiklerini gösteren başka çalışmalar da mevcuttur.[16]

Biz de yaz stajı öğrenim düzeyi değerlendirme çalışmamızda öğrencilere ön test ve son test soru formu uyguladık. Öğrencilerin ön test ve son testte aldıkları puanlar karşılaştırıldığında son test puanları ön test puanlarından

anlamlı olarak yüksek saptandı. Her ne kadar çalışmamızda hem soru hem de öğrenci sayısı az olsa da, bu farklılık pratik eğitimin öğrencilerin bilgi seviyesini arttırdığını açık bir şekilde göstermektedir. Öğrencilerin puanları; dönemlere göre ayrılarak incelendiğinde hem ön test hem de son testte D-II öğrencilerinin puanlarının D-I öğrencilerinden yüksek bulunmasının nedeni olarak; D-II öğrencilerin fakülte eğitiminde daha ileri bir seviyede oldukları, tıbbi biyokimya ders içeriği ve diğer ilişkili ders içerikleri hakkında daha fazla bilgi sahibi oldukları ve buna bağlı olarak da stajda öğrendikleri bilgileri daha kolay anlamlandırabildikleri söylenebilir.

Ayrıca öğrencilere staj başlangıcında "Stajda öğreneceğiniz bilgilerin tıp eğitiminize katkısının olacağını düşünüyor musunuz?" sorusunu yönelttiğimizde D-I öğrencilerinin %69,2'si D-II öğrencilerinin ise %84,6'sı evet cevabını vermişti. Staj sonunda ise "Stajda öğrendiğiniz bilgilerin tıp eğitiminize katkısı olduğunu düşünüyor musunuz?" sorusuna D-I ve D-II öğrencilerinin tamamından evet cevabı alındı. Bu veriler öğrencilerin staj boyunca edindikleri pratik bilgilerin tıp eğitimlerine ve gelecekteki hekimlik yaşamlarına önemli oranda katkısı olacağını düşündürmektedir.

Ek olarak Okulda tıbbi biyokimya dersinde yeterli teorik bilgiyi aldığınızı düşünüyor musunuz? sorusuna D-I öğrencilerinin % 100'ü, D-II'nin de %92 evet cevabını verirken; Okulda tıbbi biyokimya dersinde yeterli pratik bilgiyi aldığınızı düşünüyor musunuz? Sorusuna D-I'in %69,2'si; D-II'nin ise %46,2 'si evet cevabını vermiştir.

Çalışmanın Kısıtlılıkları

Tek bir tıp fakültesinde yaz stajına katılan öğrencilere uygulandığı için katılımcı sayısının az olması bu çalışmanın başlıca kısıtlılığıdır. Ancak çalışmanın diğer tıp fakülteleri ile yapılacak iş birlikleri ölçüsünde büyük ölçekli bir şekilde uygulanması ile tıbbi biyokimya pratik eğitiminin geliştirilmesine ve öğrenciler arasında tıbbi biyokimyanın daha iyi algılanarak tıpta uzmanlık tercihi yaparken de bilinçli tercih yapmalarına katkı sağlayacağı kanısındayız.

SONUÇ

Bu sonuçlar göz önüne alındığında tıbbi biyokimya dersinde mezuniyet öncesi dönemde öğrencilerinin teorik olarak gördükleri derslerin klinik hastalıklarla ilişkisine değinilmesinin ve pratik derslerin ağırlığının arttırılmasının derse ilgi ve memnuniyetlerinin artmasına katkı sağlayacağını düşünüyoruz. Bununla birlikte uygulama derslerinde, hastanelerde hizmet veren klinik rutin laboratuvarın ve diğer birimlerin işleyişini öğrenebilecekleri şekilde düzenlemeler yapılmasının öğrencilerin hekimlik mesleğini kavramaları ve gelecek hekimlik hayatı için kendilerini daha yeterli hissetmelerini sağlayabilecektir. Ayrıca klinik eğitimde rutin stajlar arasında bulunmayan Tıbbi Biyokimya, Tıbbi Mikrobiyoloji gibi bölümlerin işleyişinin bu şeklide gönüllü yaz stajı şeklinde planlanmasının öğrencilerin tıpta uzmanlık tercihi yaparken daha bilinçli tercih yapmalarında yol gösterici olacağını da ön görmekteyiz.

Çıkar Beyannamesi

Herhangi bir çıkar çatışmasının olmadığını yazarlar beyan etmektedirler.

Kaynaklar

1. *Turan Özdemir S. Tıp Eğitimi ve Standartlar. Uludağ Üniversitesi Tıp Fakültesi Dergisi 2005; 31(2): 137-133.*
2. *Lilley PM, Harden RM. Standards and Medical Education. Medical Teacher 2003; 25: 349-351.*
3. *Sayek Y, Kılıç B. Türkiye'de Tıp Eğitimi. Türk Tabipler Birliği Mezuniyet Öncesi Tıp Eğitimi Raporu 2002:7-32.*
4. *Yükseköğretim Kurulu. https://www.yok.gov.tr/Documents/Kurumsal/egitim_ogretim_dairesi/Ulusal-cekirdek-egitimi-programlari/tip_fakultesi_cep.pdf. Erişim tarihi 17 Temmuz 2020.*
5. *Bademci V. Kuder-Rıchardson 20, Cronbach'ın Alfası, Hoyt'un Varyans Analizi, Genellenirlik Kuramı Ve Ölçüm Güvenirliği Üzerine Bir Çalışma. Dicle University Journal of Ziya Gokalp Education Faculty, 2011;17:173-93.*
6. *Uskun E, Doğan M, Kişioğlu A, Baylan S, Uzun E, Akkaya V. Süleyman Demirel Üniversitesi Tıp Fakültesi Öğretim Üyelerinin Tıp eğitimi ile ilgili düşünce ve uygulamaları. SDÜ Tıp Fakültesi Dergisi 2009; 11(3): 19-24.*
7. *Özvarış ŞB, Dinçtürk AA, Akova M, Dalkara T, Sayek Y. Hacettepe Üniversitesi Tıp Fakültesi'nde tıp eğitimini geliştirme konusunda yapılan çalışmalar. Hacettepe Tıp Dergisi 2000; 31(4): 377-382*
8. *Edirne T, Deveci A, Kolusarı A, Can T. Tıp fakültesi dönem 2 öğrencileri ve tıp eğitimi. Van Tıp Dergisi 2008; 15(1):18-22.*
9. *Dong J, Zeng P. The Application of CBL Teaching Combined with PBL Teaching Method in Biochemistry Experiment Teaching. Advances in Intelligent Systems Research. 7th International Conference on Management, Education and Information (MEICI) 2017;156: 641-644.*
10. *Mutlu A, Ayar Kayalı H. Koenzimler Konusunda Probleme Dayalı Uygulaması Uygulamasının Öğrenci Başarısı ve Biyokimya Dersine Karşı Tutumlarına Etkisi. İnönü Üniversitesi Eğitim Fakültesi Dergisi (INUJFE) 2018;19(1):49-65.*
11. *Eskiocak S, Gökmen SS, Erbaş H, Çakır E, Gülen Ş, Kazezoğlu C. Dönem II Öğrencileri Trakya Üniversitesi Tıp Fakültesi Biyokimya Uygulama Eğitimini Değerlendiriyor. Türk Biyokimya Dergisi 2004; 29(3): 216-225.*
12. *Kohler N, van den Bussche H, Je Beliebter. Nutzen, didaktische Qualität und Schwierigkeitsgrad des vorklinischen Lehrangebots aus der Sicht von Hamburger Medizinstudenten. Annals of Anatomy-Anatomischer Anzeiger 2004;186(3):283-288.*
13. *Günay O. Erciyes Üniversitesi Tıp Fakültesi son sınıf öğrencilerinin tıp eğitimi hakkındaki düşünceleri. Tıp Eğitimi Dergisi 2002;7:49-55.*
14. *Alhan Ö, Tazegül G, Yavuz S, Er A, İnanıcı S, Yeğen B. Marmara Tıp Öğrenci Bilimsel Araştırma Kulübü (Öbak) Tarafından Düzenlenen Yaz Stajları Programı: Bir Memnuniyet Anketi Çalışması. Tıp Eğitimi Dünyası 2015;14(42), 15-26.*
15. *Kolcu G, Öngel K. Süleyman Demirel Üniversitesi Tıp Fakültesi Yaz Gözlem Ziyaretinin Değerlendirilmesi. Smyrna Tıp Dergisi 2018; 38-43.*
16. *Sakles JC, Maldonado RC, Kumari VG. Integration of Basic Sciences and Clinical Sciences in a Clerkship: A Pilot Study. Medical Science Educator 2006;16(1):4-9.*

ARAŞTIRMA MAKALESİ / *Research Article*

Bir Üniversite Hastanesine Başvuran Göçmen ve Mülteci Hastaların Değerlendirilmesi

Evaluation of Immigrant and Refugee Patients Applying to a University Hospital

Zerrin Gamsızkan[1], Attila Önmez[2]

[1] Düzce Üniversitesi Tıp Fakültesi Aile Hekimliği AD
[2] Düzce Üniversitesi Tıp Fakültesi, İç Hastalıkları AD

Yazışma Adresi / *Correspondence:*
Zerrin Gamsızkan
Konuralp, 81100 Düzce /Türkiye
T: **+90 532 723 02 32** E-mail **: zgamsizkan@yahoo.com**

Geliş Tarihi / Received : **26.09.2020** Kabul Tarihi / Accepted : **07.01.2020**

Orcid :
Zerrin Gamsızkan https://orcid.org/0000-0001-8677-4004
Attila Önmez https://orcid.org/0000-0002-7188-7388

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):122-128) DOI: 10.31832/smj.800498

Öz

Amaç Bu çalışmanın amacı, Düzce Üniversitesi Araştırma ve Uygulama Merkezi'ne başvuran göçmen hastaların başvuru tanılarını ve hasta özelliklerini değerlendirmektir.

Gereç ve Yöntem Çalışma retrospektif olarak hasta kayıtlarının incelenmesi şeklinde tasarlanmıştır. Çalışmada 2014-2019 yılları arasında Düzce Tıp Fakültesi Araştırma ve Uygulama Merkezi'ne başvuran göçmen ve mülteci hastaların kayıtları geriye dönük olarak incelenmiştir.

Bulgular Çalışma sonuçlarına göre son 5 yılda Düzce Üniversitesi Araştırma ve Uygulama Merkezi'ne 4754 göçmen ve mülteci hasta başvurusu olduğu belirlenmiştir. Mükerrer başvurular elendiğinde 834 göçmen ve mülteci hastanın beş yıl içinde ilimizdeki üçüncü basamak sağlık hizmetini kullandığı tespit edilmiştir. Hizmet alan 834 hastanın 440'ı kadın, 394'ü erkektir. Cinsiyete göre yaş grupları arasında anlamlı bir fark bulunmamıştır. En sık ziyaret edilen klinikler incelendiğinde başvuruların %15,6'sı (n=745) acil servis polikliniğine, %11,8'i (n=561) kadın hastalıkları ve doğum kliniğine, %9,7'si (n=464) çocuk sağlığı ve hastalıkları kliniğine olacak şekilde sıralandığı tespit edilmiştir.

Sonuç Çalışma Sonuçları ile Göçmen ve mülteci hastaların sağlık ihtiyaçlarının öncelikleri belirlenmiş olup, sağlık hizmetinin planlanmasına rehberlik etmektedir. Sağlık sisteminin tüm basamaklarında göçmen ve mülteci hastaların sağlık hizmeti kullanım verilerinin araştırılması ve değerlendirilmesi gerekmektedir.

Anahtar Kelimeler Mülteci hasta; Mülteci sağlık hizmeti; Mülteci sağlığı

Abstract

Objective *The aim of this study is to evaluate the diagnosis and patient characteristics of immigrant patients who applied to Düzce University Research and Application Center.*

Materials and methods *The study was designed as a retrospective review of patient records. In the study, the health records of the patients who applied to Düzce University Research and Application Center between 2014 and 2019 were retrospectively analyzed.*

Results *According to the results of the study, it was determined that there were 4754 immigrant patient applications to Düzce University Research and Application Center in the last 5 years. When the repeated applications were eliminated, it was determined that 834 immigrant patients used the tertiary health service in our city within five years. 440 of 834 patients receiving service are female and 394 are male. No significant difference was found between age groups according to gender. When the most frequently visited clinics were examined, 15.6% (n = 745) of the admissions went to the emergency service outpatient clinic, 11.8% (n = 561) to the gynecology and obstetrics clinic, 9.7% (n = 464) It was determined that they were listed in the order of the pediatric health and diseases clinic.*

Conclusion *With the Results of the Study, the priorities of the health needs of the immigrant and refugee patients were determined and guide the planning of the health service. It is necessary to research and evaluate the health service usage data of immigrant and refugee patients at all levels of the health system.*

Keywords *Refugee patients; Refugee health service; Refugee health.*

GİRİŞ

Göç olgusu sadece göç alan devletleri değil, küreselleşmenin baş döndürücü bir biçimde şekillendiği günümüzde tüm insanlığı etkilemektedir. Dünya'da yaşanan savaşlar, belirsizlikler ve kaos ortamı özellikle yirminci yüzyılın ikinci yarısından sonra göç hareketlerinin yoğunluğunu açıklamaktadır. Birleşmiş Milletler verilerine göre son 20 yıldaki hızıyla artmaya devam ederse, dünyadaki uluslararası göçmenlerin sayısının 2050'de 405 milyona ulaşması beklenmektedir.[1]

Türkiye, coğrafi yakınlığı itibariyle Ortadoğu'da yaşanan savaş ve kaostan uzaklaşmak isteyen göçmenlere kapılarını açan, ihtiyaç duyanları koruma altına alan, tarihiyle de bu çizgiyi devam ettiren bir ülke özelliğindedir. Ülkelerinden çeşitli sebeplerle uzaklaşmak durumunda kalan insanların tanımlanmasında gerek Birleşmiş Milletler (BM), gerekse ülkemiz kanun ve düzenlemelerinde bazı değişiklikler ve karmaşa mevcuttur. Göçmen tanımı, genel olarak ülkesinde kendi rızasıyla ve refah istemi nedeniyle başka bir ülkeye vatandaşlık talep etmesidir. Mülteci ise güvenlik gibi dış zorlayıcı faktörlerle komşu veya uzak ülkelerden sığınma talebi etme olarak tanımlanmaktadır.[2] Ülkemiz, dış ülkelerden gelen insanların ülkelerinde devam eden kaos ve düzensizlik nedeniyle geri dönemeyen, ülkemizin refahını talep ederek uzun yıllar ülkemizde yaşayan bireylere ev sahipliği yaptığı gibi başka ülkelere gitmek isteyen mültecilere de çeşitli sağlık ve sosyal hizmet vermektedir. Bu bağlamda ülkemizin birçok ilinde göçmen ve mülteci yaşamaktadır. Ülkemizin sınır komşularından önce Irak daha sonra Suriye'de meydana gelen ve 2011 yılından beri 10 milyon insanın komşu ülkelere göç etmelerine neden olan savaşla birlikte ülkemizde son verilere göre 4 milyon, Düzce ili Göç Dairesi Başkanlığından alınan bilgiye göre Düzce ili sınırlarında 10.000 civarında göçmen ve mülteci nüfusun yaşadığı bilgisi öğrenilmiştir.[3] Gerek ülkemizde gerekse yaşadığımız ilde göçmen ve mülteci bireylerin sağlık ihtiyaçları, 1966 yılında imzalanan BM Ekonomik, Sosyal ve Kültürel Haklar sözleşmesinin 12. Maddesinde değinilen sağlık hakkı kapsamında değerlendirilerek karşılanmaktadır.[4]

Ortadoğu'da devam eden kaos, insanların evlerine geri dönmelerini engelleyerek, sığındıkları ülke şartlarını ve elbette sağlık imkanlarını zorlamaktadır. Ülkemizde giderek geliştirilen göçmen ve mülteci hizmetleri, sağlık alanında da önce acil sağlık ihtiyaçları, daha sonra da tüm sağlık gereksinimlerini karşılanmak suretiyle devam etmiştir. Genel olarak göçmenler ve mülteciler, yetersiz barınma ve sağlık koşulları, yetersiz beslenme, artan fiziksel tükenme ve uygun sağlık hizmetine erişimin kısıtlı olması ile pek çok hastalığın oluşmasına neden olan koşullarla karşı karşıya kalmaktadır. Tüm Dünya'daki göçmen ve mülteci sayısının giderek artması sebebiyle göçmen hastalara dair sağlık izleme ve raporlama sistemlerinin oluşturulması tavsiye edilmektedir.[5] Durumun hassasiyeti ve insan üzerinde bıraktığı olumsuz etkiler dolayısıyla sağlık raporları ve araştırmaları genelde hastaların maruz kaldığı travma sonrası stres bozukluğu çocuklar ve kadınların sağlığı üzerindeki etkileri savaş ve savaştan kaçarken oluşan akut yaralanmaları veya acil servis başvuru sonuçları ile ilgili verilerdir.[6-10]

Göç eden insanların ülkemizde uzun süre ikamet etmesi acil sağlık ihtiyaçlarının ötesinde; koruyucu sağlık hizmetleri, danışmanlık hizmetleri ve kronik hastalıkların yönetimi gibi süreklilik ve planlama gerektiren sağlık ihtiyaçlarının karşılanmasını gündeme getirmiştir. Türkiye'de göçmen ve mülteci hastalarla ilgili yapılmış çalışmalar incelendiğinde, genelde akut rahatsızlıklar ve yaşadıkları travmanın kendilerinde yarattığı psikososyal sorunlar kapsamında yapılmış olup, göçmen ve sığınmacı hastaların sağlık sistemini kullanım alanlarını ele alan çalışma eksikliği gözlenmiştir.

Çalışmanın amacı; Türkiye'nin batı kesiminde bulunan Düzce kentindeki bir üniversite hastanesinde göçmen ve mülteci hastaların başvuruda bulundukları poliklinikleri, başvuru tanıları ve sağlık hizmetini kullanım sıklığını tespit etmektir.

GEREÇ ve YÖNTEMLER

Bu çalışmada hasta kayıtlarının incelenmesi için Düzce Üniversitesi Girişimsel olmayan Klinik Çalışmalar Etik Kurulu 2018/256 protokol no'lu 07.01.2019 tarihli çalışma izni alınmıştır. Hastaların özel ve kişisel bilgileri konusunda gerekli hassasiyet gösterilmiştir. Çalışma Helsinki Deklarasyonu prensipleri' ne uygun olarak yapılmıştır. Çalışma tanımlayıcı tipte bir araştırmadır, retrospektif olarak hasta kayıtlarının incelenmesi şeklinde tasarlanmıştır. Çalışmada 2014-2019 yılları arasında Düzce Tıp Fakültesi Araştırma ve Uygulama Hastanesine başvuruda bulunarak sağlık hizmeti talep eden göçmen ve mülteci hastaların sağlık kayıtları incelenmiştir.

İstatistiksel analiz

Veri girişleri ve analizler SPSS 21.0 istatistik programı (IBM Corp., Armonk, NY, USA) kullanılarak yapıldı. Verilerin normal dağılıp dağılmadığı Kolmogorov-Smirnov ve Shapiro-Wilk testleri ile analiz edildi. Anormal dağılım gösteren veriler ortanca (minumum-maksimum) olarak ifade edildi. Tanımlayıcı istatistikler frekans ve yüzde ile ifade edilmiştir. Normal dağılım göstermeyen cinsiyetlere göre yaş parametresi Mann Whitney U analizi ile karşılaştırıldı.

BULGULAR

Çalışmaya Düzce Üniversitesi Uygulama ve araştırma hastanesine son 5 yıl içinde göçmen hastalar tarafından yapılan 4754 başvuru verisi dahil edilmiştir. 5 yıllık başvuru verileri incelendiğinde, mükerrer başvuruların olduğu gözlenmiş, mükerrer başvurular elendiğinde 834 göçmen hastanın beş yıl içinde ilimizdeki üçüncü basamak sağlık hizmetini kullandığı tespit edilmiştir. Hizmet alan 834 hastanın 440'ı kadın, 394'ü erkektir. Yaş ve cinsiyete göre incelendiğinde, ortanca yaşın kadınlarda 30 (0-85), erkeklerde de 30 (0-78) olduğu görülmüştür. Hastaları yaş gruplarına göre incelediğimizde hastaların 116'sı 0-15 yaş arası, 550'si 16-44 yaş arası, 143'ü 45-65 yaş arası ve 25'i 65 yaş üstüydü. Cinsiyete göre yaş grupları arasında anlamlı bir fark bulunmamaktaydı (Tablo-1).

Tablo 1. Göçmen ve Mülteci Hastaların Yaş, Cinsiyet ve Doğum yeri dağılımları (n=834)

	n (Sayı)	% (Yüzde)
Yaş grupları		
0-15 yaş	116	13,90
16-44 yaş	550	65,94
45-65 yaş	143	17,14
66 ve üstü	25	2,99
Cinsiyet		
Erkek	394	47,25
Kadın	440	52,75
Doğum yeri		
Irak	704	84,41
Afganistan	66	7,91
Suriye	14	1,67
İran	35	4,19
Filistin	15	1,79

Başvuru poliklinikleri incelendiğinde başvuruların %15,67'sı (n=745) acil servis polikliniğine, %11,80'i (n=561) kadın hastalıkları ve doğum kliniğine, %9,76'sı (n=464) çocuk sağlığı ve hastalıkları kliniğine, 8,79'u (n=418) ortopedi kliniğine, %6,87'si (n=327) kulak burun boğaz kliniğine, %6,62'si (n=315) göz hastalıkları kliniğine, %5,49'u (n=261) Deri ve zührevi hastalıklar kliniğine, % 4,48'ü (n=213) Genel cerrahi Kliniğine, %8,35'ü (n=397) İç hastalıkları polikliniklerinin çeşitli bölümleri olduğu görülmüştür (Tablo-2).

Tablo 2. Göçmen ve sığınmacı Hastaların 5 yıl içinde Hizmet Aldıkları Klinik Bölümler (n=4754)

Hizmet Alınan Poliklinik	Başvuru sayısı (n)	Yüzde (%)
Acil Servis Polikliniği	745	15,67
Kadın Hast. ve Doğum Kliniği	561	11,80
Çocuk Sağlığı ve Hast. Kliniği	464	9,76
Ortopedi Kliniği	418	8,79
Kulak Burun Boğaz Kliniği	327	6,87
Göz Hastalıkları Kliniği	315	6,62
Deri ve Zührevi hastalıklar	261	5,49
Genel Cerrahi Kliniği	213	4,48
İç Hastalıkları Kliniği genel poliklinikler	166	3,49
Tıbbi Onkoloji Polikliniği	128	2,6
Gastroenteroloji	42	2,69
Hematoloji Polikliniği	26	0,54
Nefroloji Polikliniği	55	1,15
Erişkin Endokrinoloji ve Metabolizma Hastalıkları	22	0,46
Üroloji Polikliniği	207	4,35
Göğüs Hastalıkları Polikliniği	178	3,74
Kardiyoloji Polikliniği	126	2,65
Aile Hekimliği polikliniği	24	0,50
Beyin Cerrahisi Polikliniği	99	2,08
Çocuk Cerrahisi	41	0,86
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji	68	1,43
Fiziksel Tıp ve Rehabilitasyon	88	1,8
Göğüs Cerrahisi polikliniği	23	0,48
Kalp ve Damar Cerrahisi	16	0,33
Nöroloji Polikliniği	82	1,72
Psikiyatri Polikliniği	46	0,96
Çocuk Psikiyatrisi Polikliniği	13	9,27

Göçmen hastalara gerek acil gerekse elektif şartlarda uygulanan operasyon kayıtlarına göre; Genel Cerrahi kliniğinde 7 herni operasyonu, 2 tiroidektomi, 3 obezite cerrahisi, 3 kolesistektomi ve 1 mastetktomi olmak üzere toplam 16 operasyon, Ortopedi kliniğinde 2 Kalça eklem protezi, 3 Diz artroplasti, 3 Akromioplasti ve 3 Gelişimsel kalça displazisi redüksiyonu olmak üzere toplam 11 operasyon gerçekleştiği tespit edilmiştir. Yine retrospektif verilere göre Kadın Hastalıkları ve Doğum Kliniğinde 28 sezaryan ve 21 normal doğum eylemi gerçekleşmiş olup, 3 adet miyomektomi ve 1 adet histerektomi operasyonu bilgisi mevcuttu. Üroloji kliniğinde 3 adet prostatektomi ve 1 adet nefrolitotomi uygulanmıştır. Kardiyoloji kliniğinde 18 adet Koroner anjiyoplasti ve stent, ve 1 adet Kardioverter Defibrilatör takılması şeklinde girişimsel işlem uygulandığı tespit edilmiştir (Tablo-3).

Tablo 3. Göçmen ve Mülteci hastalara elektif ve acil şartlarda uygulanan girişimsel operasyonlar (n=103)

Klinik	**Girişim Sayısı**	**Yüzde**
Genel Cerrahi Kliniği		
Herni operasyonu	7	6,79
Tiroidektomi	2	1.94
Obezite cerrahisi	3	2,91
Kolesistektomi	3	2,91
Mastektomi	1	0,97
Ortopedi Kliniği		
Kalça eklem protezi	2	1,94
Diz artroplasti	3	2,91
Akromioplasti	3	2,91
Gelişimsel kalça displazisi redüksiyonu	3	2,91
Kardiyoloji Kliniği		
Koroner anjiyoplasti ve stent	18	17,47
Kardioverter Defibrilatör takılması	1	0,97
Kadın Hastalıkları ve Doğum Kliniği		
Sezaryen	28	27,18
Normal Doğum	21	20,38
Myomektomi	3	2,91
Histerektomi	1	0,97
Üroloji Kliniği		
Prostatektomi	3	2,91
Nefrolitotomi	1	0,97

Göçmen hastaların Düzce Üniversitesi Araştırma ve Uygulama Merkezine başvuru tanı ve yakınmaları incelendiğinde, 464 başvurunun çocuk hastaların çeşitli yakınmaları, 447 başvurunun kas ve iskelet sistemi yakınmaları, 323 başvurunun erişkin hastaların kronik hastalıklarla ilgili yakınmaları, 379 başvurunun gebelik izlemi ve gebelikle ilgili hastalıklar olduğu, 317 başvurunun göz hastalıkları

yakınmaları, 276 başvurunun cilt hastalıkları yakınmaları, 268 başvurunun üriner sistem yakınmaları olduğu tespit edilmiştir. Ayrıca 128 başvuru ile göçmen hastaların onkoloji kliniğinden hizmet aldıkları görülmüştür (Tablo-4).

Tablo 4. Göçmen ve Mülteci Hastaların İlk 10 Sıradaki Başvuru Tanıları

Hastalık Sistemleri ve Yakınmalar	ICD-10	n (sayı)	%(Yüzde)
Çocuk Hastalıkları	A09, J20, Z00.1, J39.9, R05	464	9,76
Üst Solunum yolu enfeksiyonları	J01, J02, J03, J39	462	9,71
Kas-İskelet sistemi Hastalıkları	M13, M16, M17, M54, M51	447	9,40
Gebelik Gözlemi	Z33, Z34	379	7,97
Kronik Hastalıklar	I10, E03, E04, E10, I25, N18	323	6,79
Kadın Hastalıkları	Z01.4, N91, N77.1, N95	318	6,68
Göz Hastalıkları	H35, H52, H25, H10, H40	317	6,66
Cilt Hastalıkları	L20, L70, L50, L30, L80	276	5,80
Üriner Sitem Hastalıklar	N39, N23, N40, N19	268	5,63
Onkolojik Hastalıklar	C50, C56, C85, C34	128	2,69

TARTIŞMA

Çalışmamızda Düzce Üniversitesi Araştırma ve Uygulama Merkezi'ne son 5 yıl verilerine göre göçmen ve mülteci hastaların Üniversite hastanesindeki çeşitli kliniklerden yararlandığı görülmüştür. Göçmen ve sığınmacı hastaların hizmet aldıkları kliniklerden en sık başvurduğu klinik acil servis hizmetleri olduğu görülmüştür. Adıyaman ilinde 2015 yılı içinde acil servise yapılan hasta başvuruların incelendiği bir çalışmada göçü takiben acil başvuru oranının %8 oranında arttığı tespit edilmiş olup en sık ilk beş başvuru sebebinin sırasıyla üst solunum yolları enfeksiyonu, myalji, karın ve pelvik ağrı, idrar yolu enfeksiyonu ve göğüs ağrısı tanıları olduğu belirtilmiştir.[11] Cerrahpaşa Tıp Fakültesi'nde yapılmış olan kesitsel bir araştırma sonuçlarına göre de; en sık başvuru departmanının acil servis olduğu belirtilmiştir.[12]

Çalışma sonuçlarımıza göre Düzce Üniversitesi Araştırma ve Uygulama Merkezi Kadın Doğum Kliniği'ne başvuru sayısı toplam başvurular arasında ikinci sırada yer almaktadır. Çeşitli jinekolojik problemlerin yanı sıra kadın göçmen hastaların obstetrik ihtiyaçlarının da karşılandığı görülmektedir. Benzer şekilde Şanlıurfa'da 2015 yılında göçmen kadınlarla yapılan çalışma da üreme sağlığı hizmetlerinin yoğun olarak kullanıldığını söylemektedir.[13]

Hastalık sistemleri ve rahatsızlıklar bakımından incelendiğinde çalışma sonuçları göçmen ve mülteci hastaların en sık çocuk hastalıklarının ve çocuklara özgü rahatsızlıklar için hastanemizden hizmet aldıklarını göstermektedir. Çocuk hastalıkları için olan başvurular sıklıkla akut hastalıklar ve acil servis hizmetleri olmakla beraber üçüncü basamak hastanesinin çocuk hastalıkları yan dal hizmetlerinden de yararlanıldığı belirlenmiştir. Bu durum ilimizde göçmen ve mülteci çocuk hastaların her türlü sağlık ihtiyaçlarının karşılandığını göstermektedir. Yapılan çalışmalar, bu çocukların fiziksel, gelişimsel ve davranışsal sağlık sorunları açısından yüksek risk altında olduğu belirtilmektedir.[14] Yeni bir ülkede yaşamaya çalışmanın zorluklarına dil ve iletişim sorunları eklendiğinde çocuk hastaların bağışıklama, gelişim basamakları gibi tıbbi geçmişlerinin kısıtlı olarak bilinmesine sebep olur. Bu problemler, sağlık çalışanlarını da zorlamaktadır.[15] Problemlerin en aza indirilmesi için göçmen ve mülteci çocuk hastaların sağlık bilgilerinin ayrıntılı bir şekilde sağlık veri sistemlerine aktarılması gerektiğini düşünüyoruz. Tüm sağlık basamaklarının ulaşabildiği veriler kişiye bütüncül yaklaşım sağlayabilmek adına etkili olacaktır.

Yapılan çalışma sonuçlarına göre; göçmen ve mülteci hastaların en yaygın tıbbi hizmet aldıkları hastalıklar, cilt hastalıkları, sindirim sistemi hastalıkları, solunum sistemi hastalıkları, travmaya bağlı hastalıklar, zihinsel hastalıklar, yetersiz beslenme ve diğer bulaşıcı hastalıklar olarak belirtilmiştir.[16-18] Bizim çalışmamızda da göçmen ve mülteci hastaların benzer hastalıklar için başvuruları üst sıralarda yer almaktadır.

Lübnanda da mülteci popülasyonunda kronik hastalıkların belirgin olduğu, özellikle tip 2 diyabet, kardiyovasküler hastalık, hipertansiyon, kronik obstrüktif akciğer hastalığı ve kas-iskelet sistemi ağrısı belirtilmiştir. Bununla birlikte, finansman durumu göz önüne alındığında, kronik durumları yeterince tedavi etmek veya kanseri olan insanlar için, hiçbir hizmet veya tedavi imkanlarının olmadığı belirtilmektedir. Halk sağlığı hizmetlerinde sürveyansın ayrıca kronik hastalıkları izlemek ve kronik hastalıkların takibini yapabilmek için güvenilir rakamlar üretmek için kurulması gerektiği vurgulamaktadır.[19] Gerek ilimizde gerekse ülkemizde uzun yıllardır yaşayan göçmen ve mülteci hastaların kronik hastalıklar, genetik yatkınlıklar ve özellikli sağlık durumlarının bilgisini oluşturmak için göçmen hasta verilerinin çeşitli çalışmalarla incelenmesi gerektiğini düşünmekteyiz.

Küresel göçler ile birlikte toplumların hastalık yükü değişebilmekte, sağlık hizmetlerinin yeterli erişilebilirliğini sağlamak ve bunun yanında mültecilerin sağlığını geliştirmek için yardım yöntemlerinin sistematik olarak yeniden tasarlanmasının gerektiği yine çalışmalarda vurgulanmaktadır.[20] Bu bağlamda ülkemizde yaşayan göçmen ve mülteci hastaların hastalık ve başvuru yükünün tespit edilmesi, önlenebilir hastalıkların yönetimi konusunda yol gösterici olabileceği gibi daha ileride göçmen ve mülteci hastaların değişebilecek hastalık profili bilgilerine de ışık tutacaktır.

Literatürde bildirilen çalışmaların sonuçlarının; çalışmanın yapıldığı ülkenin sağlık uygulamaları ve kanunlarına bağlı olduğu unutulmamalıdır. Avrupa'da yaşanan soykırım sonrası ülkelerinden kaçmak zorunda kalan sığınmacıların yaşadığı sağlık sorunlarını ve başvuru tanılarını inceleyen Bischoff ve arkadaşları, İsviçre'nin çeşitli bölgelerinde değişik sağlık kantonları kurulduğunu başvuru tanılarının oranlarının bölgeden bölgeye değişebileceğini vurgulamaktadır.[21] Ülkemizdeki genel sağlık sigortasının bölgeden bölgeye değişmemesi ve göçmen hastaların diğer vatandaşlar gibi sağlık haklarından yararlanabilme imkanı, göçmen ve mülteci hastaların başvuru tanıları ve hizmet kullanım alanlarını daha sistematik ve güvenilir verilerle tespit edebilme fırsatı sunmaktadır. Yapılacak daha geniş çaplı başka araştırmalarla da hem ülkemizde göçmen ve mülteci sağlığının geliştirilmesine hem de yüksek sayıda göçmen yaşayan ülkemiz verilerinin dünya literatürüne katkı sağlayacağı düşünülmektedir.

Çalışmanın Kısıtlılıkları

Çalışmamızın bazı kısıtlılıkları mevcuttu. Çalışma Düzce ilinde sadece üçüncü basamak göçmen ve mülteci hasta verilerini içerdiğinden tüm ildeki göçmen ve mülteci hasta sağlık hizmeti kullanım ve sağlık bilgilerine genellenemez. Göçmen ve mülteci hastaların birinci ve ikinci basamak sağlık kuruluşlarında aldıkları sağlık hizmeti ve talepleri ile karşılaştırma yapabilecek ileri araştırmalara ihtiyaç olduğu görülmektedir.

SONUÇ

Bu sonuçlar göçmen ve mülteci hastaların kronik hastalıklarının tedavi ve çözümü için de acil servisi kullanıyor olabileceğini düşündürmekte olup, göçmen hastaların kronik hastalıklarının ve elektif şartlarda uygulanacak hizmetlerin daha programlı bir şekilde yönetilmesi ihtiyacını doğurmaktadır. Sağlık hizmetinin tüm basamaklarının devamlılığı ve gelişimini sağlamak için göçmen hastaların hasta kayıtlarının gözden geçirilmesi ve göçmen ve mülteci hastaların sağlık hizmeti kullanım önceliklerinin belirlenmesi gerekmektedir. Üçüncü basamak sağlık hizmetlerinin hasta kayıtlarındaki verileri ile başvuruların genel dağılımı ve yoğunluğunun bilinmesi daha etkin bir hizmet sunumuna rehberlik edecektir.

Çalışma için Düzce Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 07.01.2019 tarihinde onay alınmıştır. (Protokol No: 2018/256)

Kaynaklar

1. *T.C. İçişleri Bakanlığı Göç İdaresi Genel Müdürlüğü. https://www.goc.gov.tr/files/files/2016_goc_raporu_.pdf). (Erişim tarihi: 10.06.2020)*
2. *Çakran Ş, Eren V. Mülteci politikası: Avrupa Birliği ve Türkiye karşılaştırması. Mustafa Kemal Üniversitesi Sosyal Bilimler Enstitüsü Dergisi 2017;14(39):1-30*
3. *T.C. İçişleri Bakanlığı Göç İdaresi Genel Müdürlüğü. https://www.goc.gov.tr/files/files/2016_goc_raporu_.pdf) duzce.goc.gov.tr/tr/page/iletisim-il-goc-idaresi-mudurlugu (Erişim tarihi: 15. 06.2020)*
4. *Birleşmiş Milletler. Ekonomik, Sosyal ve Kültürel Haklara İlişkin Uluslararası Sözleşme, 1966.*
5. *Efird JT, Bith-Melander P. Refugee Health: An Ongoing Commitment and Challenge. Int J Environ Res Public Health 2018;15(1):131. Published 2018 Jan 13. doi:10.3390/ijerph15010131*
6. *Kazour F, Zahreddine NR, Maragel MG, Almustafa MA, Soufia M, Haddad R, et al. Post-traumatic stress disorder in a sample of Syrian refugees in Lebanon. Compr Psychiatry 2017;72:41-47.*
7. *Kroening ALH, Dawson-Hahn E. Health Considerations for Immigrant and Refugee Children. Adv Pediatr 2019;66:87-110.*
8. *Liu C, Ahlberg M, Hjern A, Stephansson O. Perinatal health of refugee and asylum-seeking women in Sweden 2014-17: a register-based cohort study. Eur J Public Health 2019;4. pii: ckz120. doi: 10.1093/eurpub/ckz120.*
9. *Benov A, Shkolnik I, Glassberg E, Nadler R, Gendler S, Antebi B, et al. Prehospital trauma experience of the Israel defense forces on the Syrian border 2013-2017. J Trauma Acute Care Surg 2019;87(1S Suppl 1):165-171.*
10. *Karakuş A, Yengil E, Akkücük S, Cevik C, Zeren C, Uruc V. The reflection of the Syrian civil war on the emergency department and assessment of hospital costs. Ulus Travma Acil Cerrahi Derg 2013;19(5):429-433.*
11. *Gulacti U, Lok U, Polat H. Emergency department visits of Syrian refugees and the cost of their healthcare. Pathog Glob Health 2017;111(5):219-224.*
12. *Tahirbegolli B, Çavdar S, Çetinkaya Sümer E, Akdeniz SI, Vehid S. Outpatient admissions and hospital costs of Syrian refugees in a Turkish university hospital. Saudi Med J 2016;37(7):809-812.*
13. *Şimşek Z, Yentur Doni N, Gül Hilali N, Yildirimkaya G. A community-based survey on Syrian refugee women's health and its predictors in Şanliurfa, Turkey. Women Health 2018;58(6):617-631.*
14. *Kroening ALH, Dawson-Hahn E. Health Considerations for Immigrant and Refugee Children. Adv Pediatr 2019;66:87-110.*
15. *Baauw A, Rosiek S, Slattery B, Chinapaw M, van Hensbroek MB, van Goudoever JB, et al. Pediatrician-experienced barriers in the medical care for refugee children in the Netherlands. Eur J Pediatr 2018;177(7):995-1002.*
16. *Pavli A, Maltezou H. Health problems of newly arrived migrants and refugees in Europe. J Travel Med 2017;1:24.*
17. *Van Loenen T, Van den Muijsenbergh M, Hofmeester M, Dowrick C, Van Ginneken N, Mechili EA, et al. Primary care for refugees and newly arrived migrants in Europe: a qualitative study on health needs, barriers and wishes. Eur J Public Health 2018;28(1):82-87.*
18. *Lebano A, Hamed S, Bradby H, Gil-Salmerón A, Durá-Ferrandis E, Garcés-Ferrer J, et al. Migrants' and refugees' health status and healthcare in Europe: a scoping literature review. BMC Public Health 2020;20(1):1039.*
19. *Coutts A, Fouad FM, Batniji R. Assessing the Syrian health crisis: the case of Lebanon. Lancet 2013;381(9875):e9. PubMed PMID: 23610779.*
20. *El-Khatib Z, Scales D, Vearey J, Forsberg BC. Syrian refugees, between rocky crisis in Syria and hard inaccessibility to healthcare services in Lebanon and Jordan. Confl Health 2013;7:18. doi: 10.1186/1752-1505-7-18.*
21. *Bischoff A, Denhaerynck K, Schneider M, Battegay E. The cost of war and the cost of health care - an epidemiological study of asylum seekers. Swiss Med Wkly 2011;141:w13252. doi: 10.4414/smw.2011.13252..*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Evaluation of Clinical Characteristics and Treatment Results of Head and Neck Cancer Patients: Single Center Experience

Baş Boyun Kanseri Hastalarının Klinik Özellikleri ve Tedavi Sonuçlarının Değerlendirilmesi: Tek Merkez Deneyimi

Ayşe Demirci[1] , Ceyhun Varım[2], İbrahim Vedat Bayoglu[1] , Cemil Bilir[1] , İlhan Hacıbekiroğlu[1]

[1] Department of Medical Oncology, Sakarya University Training and Research Hospital, Sakarya, Turkey
[2] Department of Internal Medicine, Sakarya University Medicine Faculty, Sakarya, Turkey

Yazışma Adresi / *Correspondence:*
Ceyhun Varım

Adnan Menderes caddesi, Sağlık Sokak, No: 195-54000, Adapazarı/Sakarya
T: **+90 264 255 21 06** E-mail **: ceyhunvarim@sakarya.edu.tr**

Geliş Tarihi / Received : **24.08.2020** Kabul Tarihi / Accepted : **10.01.2021**

Orcid :

Ayse Demirci https://orcid.org/0000-0002-6291-7573
Ceyhun Varım https://orcid.org/0000-0002-8369-0857
İbrahim Vedat Bayoğlu https://orcid.org/0000-0002-0481-1084
Cemil Bilir https://orcid.org/0000-0002-1372-4791
İlhan Hacıbekiroğlu https://orcid.org/0000-0002-0333-7405

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):129-136) DOI: 10.31832/smj.784990**

Abstract

Objective	The purpose of this study was to review the general characteristics, risk factors, treatment modalities of our head and neck cancer (HNC) patients and to calculate survival of patients, to evaluate the factors affecting our treatment results and survival.
Materials and Methods	Sixty-seven eligible patients with HNC were evaluated. The study data were obtained from the files of patients diagnosed with HNC who were followed up in Sakarya University Training and Research Hospital between 2011 and 2020.
Results	The median age at diagnosis was 62 ± 11.40 (range: 19 to 82), 62 in men and 50 in women. The most common location was larynx with 55% frequency. Cigarette and alcohol use rates were 69% and 18%, respectively. Secondary malignancy was observed in 18% (n = 12) of the patients, with the most common secondary malignancy being lung cancer (9%, n = 6). The stages of the patients at the time of diagnosis were 13.45% (n = 9), 22.47% (n = 15), 50.77% (n = 34) and 11.93% (n = 8) stage 1,2,3 and 4, respectively. Forty two percent of the patients had metastases at the time of diagnosis or metastasis developed during follow-up. Metastatic sites were lung in 13 patients (19.45%), lymph node in 10 patients (15%), bone in 7 patients (10.56%), and liver in 1 (1.50%) patient. Local recurrence occurred in 27% (n = 18) of patients. Local recurrence and / or metastasis developed in 50% of 58 patients with stage 1, 2 or 3. The majority of these patients were stage 3 (n = 17 (59%)). While the median disease free survival (DFS) of stage 1-2 patients was 49 ± 29.65 months (range: 0-107 months), the median DFS of stage 3 patients was calculated as 19 ± 10.95 months (range: 0-40 months). Median Progression-free survival (PFS) after first line chemotherapy (CT) with metastatic HNC cancer was 8±3 months (range: 2-14 months). Median overall survival (OS) was calculated 192±83 months in all patients.
Conclusion	Secondary malignancy development rates were found to be slightly elevated in our study. The total dose of cisplatin concurrent with RT was slightly lower than the other similar studies. The most preferred combination of chemotherapy in metastatic patients was cisplatin/5Fluorouracil/cetuximab. Our PFS results were slightly higher than in the literature.
Keywords	Head and Neck Cancer; Chemotherapy; Treatment

Öz

Amaç	*Bu çalışmanın amacı baş boyun kanserli (BBK) hastalarımızın genel özelliklerini, risk faktörlerini, tedavi modalitelerini gözden geçirmek ve sağkalımlarını hesaplayıp sağkalımı ve tedavi sonuçlarını etkileyen faktörleri değerlendirmekti.*
Gereç ve Yöntemler	*Altmış yedi BBK tanılı hasta değerlendirildi. Çalışmanın verileri Sakarya Üniversitesi Eğitim ve Araştırma Hastanesinde 2011-2020 yılları arasında takipli hastaların dosyalarından elde edildi.*
Bulgular	*Tanı anındaki medyan yaş erkekler 62, kadınlar 50 olmak üzere tüm hastalarda 62 ± 11,42 (aralık: 19-82) idi. En sık yerleşim yeri %55 oranla larinks idi. Sigara ve alkol kullanım oranları sırasıyla %69 ve %18 idi. Sekonder malignite oranı %18 olup en sık görüleni akciğer kanseriydi (%9, n = 6). Hastaların tanı anındaki evreleri 1,2,3 ve 4 sırasıyla %13,45 (n = 9), %22,47 (n = 15), %50,77(n = 34) ve %11,93 (n = 8) idi. Hastaların tanı anında ya da takibi sırasında olmak üzere toplam %42'si metastatikti. Metastaz bölgeleri 13 hastada (%19,45) akciğer, 10 hastada (%15) lenf nodu, 7 hastada (%10,56) kemik, ve 1 hastada (%1,50) karaciğerdi. Lokal rekürrens %27 (n = 18) oranındaydı. Evre 1,2 ve 3 58 hastanın %50'sinde lokal rekürrens ve/ veya metastaz gelişmişti. Bu hastaların çoğunluğu evre 3 hastalardı (n = 17 (%59)). Evre 1-2 hastalarda medyan hastalıksız sağkalım 49 ± 29,65 ay (aralık: 0-107 ay) iken evre 3 hastalarda medyan hastalıksız sağkalım 19 ± 10,95 ay (aralık: 0-40 ay) idi. Metastatik birinci seri kemoterapi sonrası medyan progresyonsuz sağkalım 8±3 ay (aralık: 2-14 ay) ve tüm hastalarda medyan genel sağkalım 192±83 ay idi.*
Sonuç	*Çalışmamızda sekonder malignite gelişme oranı hafif yüksekti. Radyoterapi eş zamanlı sisplatin total dozları literatürdeki benzer diğer çalışmalara göre hafifçe düşüktü. En çok tercih edilen metastatik birinci seri kemoterapi kombinasyonu sisplatin/5Fluorourasil/setuximab'tı. Progresyonsuz sağkalım sonuçları literatüre göre hafif yüksekti.*
Anahtar Kelimeler	*Baş ve Boyun Kanseri; Kemoterapi; Tedavi*

INTRODUCTION

Head and neck cancers (HNC) are a heterogeneous group of malignancies with different tumor biology, prognosis, and therapeutic response, including oral and nasal cavities, pharynx, larynx, paranasal sinuses, thyroid and salivary glands.[1] HNC is the sixth most common cancer worldwide, with over half a million cases and 300,000 deaths in 2008.[2] Tobacco and alcohol consumption are the strongest risk factors for HNC, however passive smoking, human papillomavirus (HPV) infection, Ebstein-Barr virüs (EBV) infection, low body mass index, low physical activity, poor diet, low socioeconomic status, and having a family history of cancer affect the risk.[3]

The primary treatment in HNC is surgery with or without lymph node dissection, depending on the stage of the disease at the time of diagnosis.[3] Although primary treatment is surgery, other treatment modalities can be applied alone or in combination before or after surgery depending on the stage of the tumor and its anatomical location. Adjuvant radiotherapy (RT) is performed after surgery to decrease the risk of local recurrence and increase survival, especially in patients with unfavorable pathological features. Chemotherapy (CT) can be used as an adjuvant treatment after surgical resection or in combination with RT as a palliative treatment for advanced or recurrent cancers.[4]

The purpose of this study was to review the general characteristics, risk factors, treatment modalities of our HNC patients and to calculate survival of patients, to evaluate the factors affecting our treatment results and survival. Then, to compare the compatibility of our results with the literature and analyze the factors affecting mortality.

MATERIALS and METHODS

This is a cross sectional study using data from January 1, 2011 and December 31, 2019. Sixty seven patients diagnosed with HNC and followed up at Sakarya University Training and Research Hospital were included in this trial. Inclusion criteria:

1. Above 18 years of age
2. Diagnosed with HNC

Exclusion criteria

1. Sarcoma, lymphoma and melanoma subtypes
2. Thyroidal cancers
3. Under 18 years of age

Ethics Committee approval was obtained from Sakarya University Ethics Committee (13.02.2020) (Ref. No.: 71522473/050.01.04/36)

Statistical analyzes

SPSS 22 statistical package program was used to assess the data obtained in the study. Descriptive statistics, Fisher's exact test and Chi-square test and Kaplan–Meier test for survival analysis was used. The possible factors identified with univariate analysis were further entered into the Cox regression analysis, with backward selection, to determine independent predictors of survival. Among correlated factors with similar effects on survival, only those with clinical significance were included. The proportional hazards assumption and model fit was assessed by means of residual analysis. A P value <0.05 was considered to be significant.

RESULTS

In this study, 67 eligible patients with HNC who were followed up between 2011 and 2020 at Sakarya University Training and Research Hospital were evaluated. Seven patients who didn't come to the outpatient clinic follow-up were not included in some statistical calculations, since there was no recent status information.

Of the patients 84% (n = 56) of the patients were male and 16% (n = 11) were female. The median age at diagnosis in all patients was 62 ± 11.40 (range: 19 to 82), 62 in men and 50 in women. When evaluated according to localization, the most common location was larynx with 55% frequency. Distribution according to tumor localization is

summarized in Figure 1. The average age of the patients with nasopharyngeal and oral cavity-oropharyngeal tumor localization was youngest and the average age was 48. Cigarette and alcohol use rates were 69% and 18%, respectively. When evaluated according to tumor site, the highest rate of smoking was laryngeal cancer with 86.55%. The frequency of alcohol use in laryngeal cancer is 25% and the highest compared to other localizations. Sixteen percent (n = 11) of the patients had a family history of malignancy. Secondary malignancy was present in 18% (n = 12) of the patients, with the most common secondary malignancy was lung cancer (9%, n = 6). Demographic and baseline characteristics of the patients are summarized in table 1.

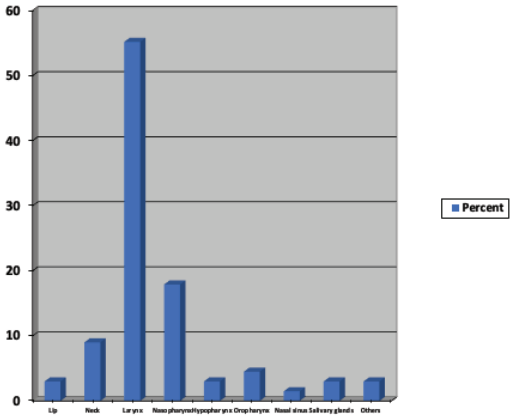


Figure 1. Distribution characteristics according to Tumor localization

Table 1. Demographic and baseline characteristics of patients (n=67)

Sex	
Male, n (%)	56 (84)
Female, n (%)	11 (16)
Median age	62 ± 11.40 (19-82)
Stage (at the time of diagnosis), n (%)	
1	9 (13.45)
2	15 (22.47)
3	34 (50.77)
4	8 (11.93)
Metastatic patients, n (%)	28 (42)
Local recurrence, n (%)	18 (27)
Metastatic sites, n (%)	
Lung	13 (19.45)
Lymph node	10 (15)
Bone	7 (10.56)
Liver	1 (1.50)
Cigarette use, n, (%)	46 (69)
Alcohol intake, n, (%)	12 (18)
Family history of malignancy, n (%)	11 (16)
Secondary malignancy, n (%)	12 (18)

Survival analyses

Whether variables such as age, gender, disease stage, smoking, alcohol consumption, tumor localization, presence of cancer history in the family and having at least 1 cardiovascular disease risk factor (acute coronary syndrome, cerebrovascular disease, diabetes mellitus, hypertension etc.) was evaluated by proportional hazard analysis. Although some variables had effects on survival, having only stage 4 disease had a statistically significant risk of mortality than reference stage-1 disease (hazard ratio [HR]= 69.65; 95% CI =5.30-899, p=0,001). The analysis results of all variables are summarized in table 2.

Eleven patients (16.50%) received neoadjuvant / induction CT or chemoradiotherapy (CRT). 41.80% (n = 28) of the patients had an operation to primary. Five (7.50%) patients had postoperative surgical margin positivity.

Table 2. Multivariate Cox regression analysis of the factors affecting overall survival

Variables	HR(95% Cl)	P Value
Age	1.04 (0.98-1.10)	0.190
Gender	2.52 (0.48-13.18)	0.275
AJCC Stage [stage I (Ref)]		
II	1.17 (0.19-6.97)	0.850
III	1.89 (0.41-8.78)	0.415
IV	69.6 (5.3-899.8)	0.001*
Tabocco Use [None (Ref)]		
Use	0.72 (0.15-3.31)	0.672
Smoking Pack Use	1.01 (0.98-1.03)	0.285
Alcohol Use	0.18 (0.02-1.46)	0.111
Localization [Laryngeal (Ref†)]		
Nasopharyngeal	0	0.982
Others	1.28 (0.48-3.38)	0.617
Family history of malignancy (positive)	0.03 (0.00-10.75)	0.255
Cardiovascular disease (positive)	1.28 (0.45-3.66)	0.641

Abbreviations: HR, hazard ratio; 95% CI, 95%confidence intervals; AJCC, American Joint Committee on Cancer.
* Significant at p<0.050.
† Reference group

Of the patients 46.50% (n = 31) had received CRT. Four patients (6%) who received CRT were diagnosed with larynx carcinoma who received CRT due to surgical margin positivity. Although 1 patient had positive surgical margin, she didn't receive any postoperative treatment because she didn't want CRT. Weekly cisplatin, weekly carboplatin, weekly cisplatin / docetaxel and weekly setuximab were administered while receiving CRT to 27 patients (40.35%), 2 patients (3%), 1 patient (1.50%), and 1 patient (1.50%), respectively. Radiotherapy was administered simultaneously for 6 weeks and the weekly dose of cisplatin was 20 mg / m2 in 1 patient, 35 mg / m2 in 1 patient and 30 mg / m2 in other 25 patients. Of the patients 20.85% (n = 14) received RT as curative (n = 8, 12.45%) or adjuvant (n = 6, 8.42%) treatment.

Local recurrence and / or metastasis developed in 50% of 58 patients who were stage 1, 2 or 3. Local recurrence and / or metastasis developed in 50% of 58 patients, the majority of whom were stage 3 (n = 17 [59%]). Median disease free survival (DFS) of patients with stage 1,2 or 3 was 33 ± 15.45 months (2.72-63.28 months). While the median DFS of stage 1-2 patients was 49 ± 29.65 months (range: 0-107 months), stage 3 patients was 19 ± 10.95 months (range: 0-40 months) (figure 2a,b)

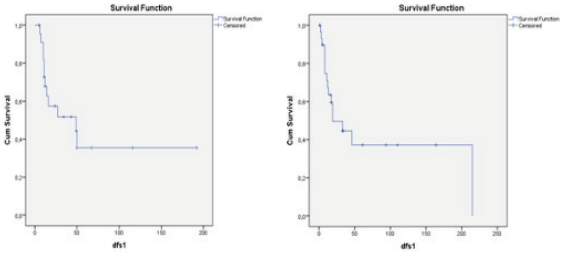


Figure 2.a: Disease free survival (DFS) curve of early-stage patients b: DFS curve of locally advanced stage patients

Chemotherapy agents administered to patients with metastatic stage is summarized in the table 3. Twenty-five of the patients who received CT as first line could be evaluated; data were not available for 3 patients because 2 patients left follow-up of outpatient and 1 patient did not accept CT. In patients with metastatic cancer median progression free

survival (PFS) after first line CT was 8±3 months (range: 2-14 months) (figure 3a), and 1 patient who received Cisplatin/5Fluorouracil (CF)/cetuximab was discontinued due to cetuximab allergy. One patient died due to sepsis whose median PFS was 6 months, while the patient had a CF-cetuximab response. One patient died after the first cycle of CT due to tracheosophageal fistula. Two patients died due to treatment-related (Docetaxel-CF and CF-cetuximab) side effects after first cycle of CT. Combinations with gemcytabine or docetaxel were often preferred as second line CT. Median OS was calculated 192±83 months in all patients (figure 3b)

Table 3: Chemotherapy agents administered to patients with metastatic stage

Treatments	Patient number (n)	Percent
CF	1	1.50
CF/Cetuximab	13	19.50
Cisplatin/Docetaxel	2	3
Cisplatin/Gemcytabin	1	1.50
Docetaxel/CF	5	7.50
Carboplatin/Paclitaxel	5	7.50
Abbreviation: CF: Cisplatin/5Fluorouracil		

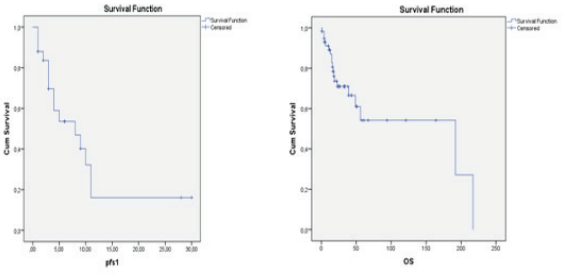


Figure 3, a: Progression free survival curve of first line treatment b: Overall survival curve of all patients

DISCUSSION

Head and neck cancers are a heterogeneous group of diseases and mostly originate from mucosal surfaces. A multidisciplinary approach is required in all stages of diagnosis and treatment, including head and neck surgeon, medical oncologist, radiation oncologist, dentist, pathologist, rehabilitation therapists, psychiatrist-psychologists and dieticians.[5]

Staging varies by region in HNC.[6] The tumor subtype is mostly squamous cell carcinoma, as in our patients. Apart from this, adenocarcinoma, lymphoma, melanoma and sarcoma types are also seen.[7] We excluded sarcoma, melanoma and lymphoma subtypes because patients with head and neck sarcoma and melanoma were evaluated separately and patients diagnosed with lymphoma are followed by hematology in our center. Head and neck squamous cell carcinomas represent approximately 3% of all human malignancies.[8]

The choice of treatment is based on the region, the stage of the tumor, and the functional, comorbid status of the patients. Approximately 30-40% of patients are stage I-II and these patients are usually treated with primary surgery or definitive RT.[7-9] Thirty six percent of our patients (n=24) were stage 1 and 2. Twelve of these patients were those who received adjuvant CT / CRT after the operation and 14 patients received definitive RT or CRT. Five-year survival in stage I-II patients usually reaches up to 70-90%.[7-9] Regularly follow-up of these patients after treatment is also very important because if there are cigarette and alcohol intake in etiology of HNC, the risk of secondary primary HNC and lung cancer are higher than others.[10] Some other studies have also shown that the risk of developing multiple primary malignancies is higher in oral cavity, pharynx, larynx, lungs, or esophagus tumors than others.[11-13] In our study, secondary malignancy was slightly higher than the other studies with the percent of 18 (n = 12) while in some studies with more patient series, the rate of secondary malignancy varies between 9% and 15.8%,[11,14] Cigarette and alcohol use rates were 69% and 18%, respectively and the highest rate of smoking and alcohol use was in laryngeal cancer patients with 86.55% and 25% respectively. So the highest rate of secondary malignancy was in laryngeal cancer. The most common secondary malignancy was lung cancer (9%, n = 6) in our study because in some patients, the distinction whether the mass in the lung is metastasis

could not be made exactly pathologically or radiologically. In other studies the most common secondary malignancy occured in the upper aerodigestive tract (40%–59%), lung (31%–37.5%), and esophagus (9%– 44%).8 Of the 12 patients with secondary malignancy were in 10 primary laryngeal carcinoma and 2 nasopharyngeal cancer.

Postoperative RT or CRT may be considered in early stage patients treated surgically if there is a surgical margin proximity or positivity, if the tumor is locally advanced, if there are risk factors such as perineural invasion, lymphovascular invasion, extranodal extension.[15] Postoperative treatments are also considered in patients who have malignant lymph node after lymph node dissection.[15-17] In our study, after surgery in early stage 8 patients received RT and 2 patients received CRT. One of these patients had surgical margin positivity and the other patients had one of the high risk factors.

In locally advanced disease, multimodal therapies are selected in which RT, CT and surgery are combined and organ preservation is aimed.[18] The rate of our locally advanced patients was 50.77 % (n=34) and was the highest. Options such as upfront surgery, then RT-CRT, induction CT, operation or only CRT are preferred according to the patient and tumor site. The majority of our locally advanced patients consisted of patients diagnosed with nasopharynx and larynx cancer. Surgical procedures were mostly performed in all but except nasopharyngeal cancer. Only one nasopharyngeal cancer patient underwent dissection to the neck lymph nodes remaining after CRT as a surgical procedure. Actually there are studies on open or endoscopic surgery in recurrent nasopharyngeal cancers.[19-20] Surgery is not preferred as the primary treatment method in nasopharengeal cancers. As concurrent CRT cisplatin is used weekly or tree weekly schedules with RT.[21] In our study none of the patients were given at a dose of 100 mg/m2 every 3 weeks of cisplatin simultaneously with RT due to potential toxicity concerns. Regardless of the primary site, the majority of our patients received 30 mg / m2 cisplatin weekly concurrent with RT. Moreover, 3-weekly cisplatin was not preferred in rural patients, considering that the risk of febrile neutropenia may increase due to their low socioeconomic level and low personal care. In a retrospective study Kose et al from Turkey, 3-weekly cisplatin and weekly cisplatin is compared in terms of survival and toxicity. While myelosuppression rates were higher in the 3-weekly cisplatin regimen, the mucositis rates were higher in the weekly regimen, but the difference was not statistically significant. Likewise, the majority of patients were in the weekly cisplatin regimen in Kose et al study.[22] Although 3 weekly 100 mg / m2 cisplatin is recommended as preferred regimen in our guidelines, it has been shown in other studies that it cannot be given due to increased myelotoxicity concerns in Turkey. In a meta-analysis comparing RT concurrent weekly and 3-weekly cisplatin regimens, the results of patients were evaluated according to who received definitive CRT and postoperative CRT.[21] In definitive treatment CRT setting, myelosuppression, nausea, vomiting and nephrotoxicity were found to be statistically significantly less in the weekly regimen compared to the 3-weekly regimen. However in the postoperative setting the two approaches were more equal with less differences in the cisplatin-induced toxicities, the weekly cisplatin induced more grade 3-4 dysphagia and weight loss.[21] Another noteworthy issue in our study was that patients received cisplatin at a maximum total dose of 180 mg from 30 mg /m2 weekly as a definitive or postoperative setting. This dose was lower than the total doses in other similar studies.[23-24]

Treatment options in recurrent and metastatic disease are cytotoxic CT, immunotherapy and molecular targeted agents.[25] Cisplatin-based chemotherapies are recommended as single agent or combination.[26-28] The KEYNOTE-048 study determined the use of pembrolizumab with or without CT as a first-line regimen metastatic or recurrent squamous cell carcinoma of head and neck.[29] This study showed that adding pembrolizumab to a combination of platinum and fluorouracil increases OS compared to a combination

of cetuximab plus a platinum and fluorouracil. Even for those with high PD-L1 expression (CPS ≥20), single agent pembrolizumab increases overall survival compared to a combination of cetuximab plus a platinum and fluorouracil.[29] There are studies in the literature with nivolumab as immunotherapy agent in metastatic HNC subsequent line, and a study with tremelimumab is also ongoing.[29-30] In our country since the reimbursement of immunotherapy drugs is not yet possible in HNC, none of our patients could be given immunotherapy agents. The majority of our patients received cisplatin-based chemotherapies. Cisplatin/Fluorouracil/Cetuximab combination was the most preferred agent, the other preferred regimens were cisplatin/fluorouracil/docetaxel, cisplatin/fluorouracil, carboplatin/paclitaxel and cisplatin/docetaxel. Median PFS was 8 ±3 months after first line treatment in metastatic HNC patients. In the EXTREME study, CF and CF-cetuximab chemotherapies were compared and median PFSs were found to be 3.30 and 5.60 months, respectively.[28] In KEYNOTE 048 trial pembrolizumab chemotherapy and cetuximab with chemotherapy were compared and median PFSs were 5.80 versus 5.20 months.[29] The reason we obtained higher results in terms of PFS is that our analyses includes nasopharyngeal and non-nasopharyngeal patients.

The most important limitations of our study; This study is single center study and the number of cases are low. Larger studies are needed on this subject

CONCLUSION

In conclusion, when we evaluated all our patients diagnosed with HNC, the most common histopathological subtype was squamous cell cancer as in the literature. Secondary malignancy development rates were found to be slightly elevated compared to other similar studies. Cisplatin was the most preferred CT agent at a weekly dose of 30 mg / m2 concurrent with RT. The total dose of cisplatin concurrent with RT was slightly lower. The most preferred combination of chemotherapy in metastatic patients was CF-cetuximab. Our PFS results were slightly higher than in the literature. We didn't have any patients receiving immunotherapy due to our health policies.

There is no conflict of interest between authors. No relationship has been established with pharmaceutical companies, biomedical device manufacturers or other companies that have a service or product related to the subject of the article.

References

1. *Emadzadeh M., Shahidsales S., Bajgiran AM., Salehi M., Massoudi T., Nikfarjam Z., & Salehi M. Head and neck cancers in North-east Iran: A 25 year survey. Iranian journal of otorhinolaryngology 2017; 29,92:137-145.*
2. *Ferlay J., Shin HR., Bray F., Forman D., Mathers C., Parkin DM. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008 International journal of cancer 2008;127,12:2893-2917.*
3. *Pezzuto F., Buonaguro L., Caponigro F., Ionna F., Starita N., Annunziata C., Tornesello ML. (2015). Update on head and neck cancer: current knowledge on epidemiology, risk factors, molecular features and novel therapies Oncology 2015;89,3:125-136.*
4. *Marur S., Forastiere AA. Head and neck squamous cell carcinoma: update on epidemiology, diagnosis, and treatment. In Mayo Clinic Proceedings 2016;91,3:386-396*
5. *Wheless SA., McKinney KA., Zanation AM. (2010). A prospective study of the clinical impact of a multidisciplinary head and neck tumor board. Otolaryngology—Head and Neck Surgery 2010;143,5:650-654.*
6. *Shah JP. Staging for Head and Neck Cancer: Purpose, Process and Progress. Indian journal of surgical oncology 2018;9,1:116-120.*
7. *Adeyemi BF., Adekunle LV., Kolude BM., Akang EE., Lawoyin JO. Head and neck cancer—a clinicopathological study in a tertiary care center. Journal of the National Medical Association 2008;100,6:690-697.*
8. *Priante AVM., Castilho EC., Kowalski LP. Second primary tumors in patients with head and neck cancer. Current oncology reports 2011;13,2:132-137.*
9. *Adoga AA., Kokong DD., Ma'an ND., Silas O A., Dauda AM., Yaro JP., Yabak CJ. The epidemiology, treatment, and determinants of outcome of primary head and neck cancers at the Jos University Teaching Hospital. South Asian journal of cancer 2018;7,3:183.*
10. *León X., del Prado Venegas M., Orús C., López M., García J.,Quer M. Influence of the persistence of tobacco and alcohol use in the appearance of second neoplasm in patients with a head and neck cancer. A case–control study. Cancer Causes & Control 2009;20,5:645-652.*
11. *Chuang SC., Scelo G., Tonita JM., Tamaro S., Jonasson JG., Kliewer EV., Friis S. (2008). Risk of second primary cancer among patients with head and neck cancers: a pooled analysis of 13 cancer registries. International journal of cancer 2008;123,10:2390-2396.*
12. *Di Martino E., Sellhaus B., Hausmann R., Minkenberg R. Survival in second primary malignancies of patient with head and neck cancer. The Journal of laryngology and otology 2002;116,10:831.*
13. *Lin K., Patel SG., Chu PY., Matsuo JM., Singh B., Wong RJ.,Boyle JO. Second primary malignancy of the aerodigestive tract in patients treated for cancer of the oral cavity and larynx. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck 2005;27,12: 1042-1048.*
14. *Haughey BH., Arfken CL., Gates GA., Harvey J. Meta-analysis of second malignant tumors in head and neck cancer: the case for an endoscopic screening protocol. Annals of Otology, Rhinology & Laryngology1992;101,2:105-112.*
15. *Cooper JS., Zhang Q., Pajak TF., Forastiere AA., Jacobs J., Saxman SB., Lustig R. (2012). Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. International Journal of Radiation Oncology* Biology* Physics 2012;84,5:1198-1205.*
16. *Mendenhall WM., Hinerman RW., Amdur RJ., Malyapa RS., Lansford CD., Werning JW., Villaret DB. (2006). Postoperative radiotherapy for squamous cell carcinoma of the head and neck. Clinical medicine & research 2006;4,3:200-208.*
17. *Cooper JS., Pajak TF., Forastiere AA., Jacobs J., Campbell BH., Saxman SB., Machtay M. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. New England Journal of Medicine 2004;350,19:1937-1944.*
18. *Aydil U. Recent Landmark Studies on Head and Neck Cancers: Evidence-Based Fundamentals of Modern Therapeutic Approaches. Turkish archives of otorhinolaryngology 2015;53,1:26.*
19. *Wang JQ., Han R., Li XP., Zhao YT., Yu XX., Wang XW., Li G. The efficacy and safety of salvage surgery for local recurrent nasopharyngeal carcinoma: a systematic review and Meta-analysis. Zhonghua er bi yan hou tou jing wai ke za zhi= Chinese journal of otorhinolaryngology head and neck surgery 2019;54,9:676-684.*
20. *Salom MC., López F., Pacheco E., Muñoz G., García-Cabo P., Fernández L., Llorente JL. Salvage surgery in the treatment of local recurrences of nasopharyngeal carcinomas. Acta Otorrinolaringologica (English Edition) 2018;69,6:339-344.*
21. *P. Szturz et al., "Weekly Low-Dose Versus Three-Weekly High-Dose Cisplatin for Concurrent Chemoradiation in Locoregionally Advanced Non-Nasopharyngeal Head and Neck Cancer: A Systematic Review and Meta-Analysis of Aggregate Data.Oncologist, vol. 22, no. 9, pp. 1056–1066, 2017.*
22. *Kose F., Besen A., Sumbul T., Sezer A., Karadeniz C., Disel U., Ozyilkan O. Weekly cisplatin versus standard three-weekly cisplatin in concurrent chemoradiotherapy of head and neck cancer: the Baskent University experience. Asian Pac J Cancer Prev 2011;12,12:1185-1188.*
23. *Espeli V., Zucca E., Ghielmini M., Giannini O., Salatino A., Martucci F., Richetti, A. Weekly and 3-weekly cisplatin concurrent with intensity-modulated radiotherapy in locally advanced head and neck squamous cell cancer. Oral oncology 2012;48,3;266-271.*
24. *Tsan DL., Lin CY., Kang CJ., Huang SF., Fan KH., Liao CT., Chang JTC. The comparison between weekly and three-weekly cisplatin delivered concurrently with radiotherapy for patients with postoperative high-risk squamous cell carcinoma of the oral cavity. Radiation Oncology 2012;7,1:215.*
25. *Marur S., Forastiere AA. Head and neck squamous cell carcinoma: update on epidemiology, diagnosis, and treatment. In Mayo Clinic Proceedings, 2016;91,3:386-396.*
26. *Clavel M., Vermorken JB., Cognetti F., Cappelaere P., De Mulder PHM., Schornagel JH., Dalesio O. (1994). Randomized comparison of cisplatin, methotrexate, bleomycin and vincristine (CABO) versus cisplatin and 5-fluorouracil (CF) versus cisplatin (C) in recurrent or metastatic squamous cell carcinoma of the head and neck: A phase III study of the EORTC Head and Neck Cancer Cooperative Group. Annals of oncology 1994;5,6:521-526*
27. *Veronesi A., Zagonel V., Tirelli U., Galligioni E., Tumolo S., Barzan L., Grigoletto E. (1985). High-dose versus low-dose cisplatin in advanced head and neck squamous carcinoma: a randomized study. Journal of Clinical Oncology 1985;3,8:1105-1108.*
28. *Vermorken JB., Mesia R., Rivera F., Remenar E., Kawecki A., Rottey S., Peyrade F. Platinum-based chemotherapy plus cetuximab in head and neck cancer. New England Journal of Medicine 2008;359,11:1116-1127.*
29. *Burtness B., Harrington KJ., Greil R., Soulières D., Tahara M., de Castro Jr G., Fuereder T. (2019). Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. The Lancet 2019; 394,10212:1915-1928.*
30. *Phase III Open Label Study of MEDI 4736 With/Without Tremelimumab Versus Standard of Care (SOC) in Recurrent/Metastatic Head and Neck Cancer - Full Text View - ClinicalTrials.gov. [Online]. 2020 Available: https://www.clinicaltrials.gov/ct2/show/NCT02551159?term=NCT02551159&rank=1*

RESEARCH ARTICLE / *Araştırma Makalesi*

Concomitant Ocular Diseases in Patients with SARS-CoV-2 Infection

SARS-CoV-2 Enfeksiyonlu Hastalarda Eşlik Eden Oküler Hastalıklar

Mahmut Atum, Ali Altan Ertan Boz, Burçin Çakır, Erkan Çelik, İsa Yuvacı

Department of Ophthalmology, Sakarya University Training and Research Hospital, Sakarya, Turkey

Yazışma Adresi / *Correspondence:*
Mahmut Atum

Department of Ophthalmology, Sakarya University Training and Research Hospital, Adnan Menderes Caddesi Sağlik Sok, Sakarya, Turkey
T: **+90 555 809 62 75** E-mail **: mahmutatum@gmail.com**

Geliş Tarihi / Received : **29.09.2020** Kabul Tarihi / Accepted : **10.01.2021**

Orcid :

Mahmut Atum https://orcid.org/0000-0001-7816-0627
Ali Altan Ertan Boz https://orcid.org/0000-0001-7740-5821
Burçin Çakır https://orcid.org/0000-0001-7816-0627
Erkan Çelik https://orcid.org/0000-0002-8681-7868
İsa Yuvacı https://orcid.org/0000-0003-0694-9009

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):137-141) DOI: 10.31832/smj.801248**

Abstract

Objective	To investigate the presence of chronic ocular diseases in patients who had a real-time reverse transcription-polymerase chain reaction (rRT-PCR) test of oropharyngeal/nasopharyngeal swabs for SARS-CoV-2 virus.
Materials and Methods	A retrospective chart review was conducted to determine all hospitalized patients who had a positive rRT-PCR test for SARS-CoV-2 virus. From these patients, who applied to eye polyclinics in the last one year were included and the diagnosis was investigated.
Results	This study investigated 1120 patients with a positive rRT-PCR test. Of these patients, 178 (15.8%) had applied to eye clinics previously. The most common diseases were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis.
Conclusion	The rate of concomitant ocular diseases in patients with confirmed SARS-CoV-2 was 15.8%. Avoiding touching the face and eyes and hand hygiene were the main prevention ways from SARS-CoV-2 infection. Concomitant ocular diseases might increase the risk of contact transmission routes.
Keywords	Eye disease; SARS-CoV-2; COVID-19

Öz

Amaç	*Nazofaringeal ve orofaringeal sürüntülerde SARS-CoV-2 virüsü için gerçek zamanlı ters transkripsiyon-polimeraz zincir reaksiyonu (rRT-PCR) testi pozitif olan hastalarda oküler hastalıkların varlığını araştırmak.*
Gereç ve Yöntemler	*SARS-CoV-2 virüsü açısından rRT-PCR testi pozitif olan hastanede yatan hastaların dosyaları geriye dönük tarandı. Bu hastalardan son bir yıl içinde göz polikliniğine başvuran hastalar çalışmaya dahil edildi ve almış oldukları tanılar kayıt edildi.*
Bulgular	*Bu çalışmada rRT-PCR testi pozitif olan 1120 hasta incelendi. Bu hastaların 178'i (% 15,8) daha önce göz kliniklerine başvurmuştu. En sık görülen hastalıklar kırma kusurları, kuru göz sendromu, blefarokonjonktivit ve alerjik konjonktivit idi.*
Sonuç	*SARS-CoV-2 varlığı doğrulanmış hastalarda eşlik eden oküler hastalık oranı % 15.8 idi. Kronik göz hastalıklarının, el-yüz teması nedeni ile SARS-CoV-2 enfeksiyonunun bulaştırıcılığı arttırabileceğini düşünüyoruz.*
Anahtar Kelimeler	*Göz hastalıkları; SARS-CoV-2; COVID-19*

INTRODUCTION

Coronaviruses (CoV) are RNA viruses that can cause a variety of diseases in humans. In humans, the diseases caused by CoV range from mild cold to fatal lower respiratory tract infections.[1] In late 2019, the pathogen of new pneumonia cases reported from China was determined to be a new coronavirus (2019-nCoV-COVID-19), and the virus spread to the whole world within months, causing a massive epidemic.[2] This new coronavirus was then named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) because of its close similarity to SARS-CoV-1.[2]

Human-to-human transmission of SARS-CoV-2 is usually via respiratory droplets. In addition, transmission may occur through hand-mouth, hand-nose or hand-eye contact.[3,4] The mucosa of the conjunctiva is linked to the upper respiratory tract, and one study reported that conjunctiva may be easily involved in SARS-CoV-2 infection and may act as a route of transmission.[5] Additionally, the angiotensin-converting enzyme 2 (ACE2) receptors found in the epithelium of the cornea and conjunctiva play a major role in the entry of viruses into host cell membranes.[6,7]

Relationships between SARS-CoV-2 infection and common systemic diseases, such as diabetes mellitus (DM) and essential hypertension (HT), have been established.[8] Based on the hypothesis that chronic eye diseases may increase the rate of getting the disease by increasing hand eye contact, this study was designed. The aim of the current study was to investigate the presence of chronic ocular diseases in patients who had a positive real-time reverse transcription-polymerase chain reaction (rRT-PCR) test of nasopharyngeal and oropharyngeal swabs.

MATERIALS and METHODS

The current study was designed as a retrospective descriptive study. Prior approval was received from the Institutional Review Board Sakarya University Faculty of Medicine Ethics Committee, 07/04/2020, IRB number:050.01.04/158), and written informed consent was obtained from each subject. The study was performed in adherence to the Declaration of Helsinki.

A retrospective chart review was conducted to determine all hospitalized patients who had a positive rRT-PCR test of nasopharyngeal and oropharyngeal swabs between March and April 2020. Patients who applied to eye polyclinics in the last one year were included in this study. The application information and diagnosis of the patients was obtained from the hospital information management system. Additionally, the presence of chronic systemic diseases, such as HT, DM, chronic obstructive pulmonary disease (COPD), and asthma, were noted. The results of blood tests and low-dose chest computerized tomography (CT) were also evaluated.

Patients with chronic ocular disease such as dry eye syndrome, refractive errors, blepharoconjunctivitis, glaucoma, and age-related macular degeneration were included in the study. Patients admitted for acute eye diseases, ocular trauma and eye surgery were not included in the study. Statistical analysis was performed using SPSS statistical software (IBM SPSS Statistics, Version 23.0. Armonk, NY: IBM Corp.). Descriptive analyses were performed to provide information on the general characteristics of the study population. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of the numerical variables was normal. The numeric variables were presented as mean ± standard deviation. An independent t-test or Mann-Whitney U test was used to compare parameters. The categorical variables were compared with a Chi-square test. A p-value < 0.05 was considered significant.

RESULTS

This study included 1120 patients with a positive rRT-PCR test. Of these patients, 178 (15.80%; 90 female, 88 male) had applied to eye clinics previously. The mean age of the patients was 55.82 ± 16.22 years. The chest CT results of 143 (80.30%) patients revealed findings compatible with SARS-CoV-2 infection. Table 1 shows the additional

chronic systemic diseases of these patients, and Table 2 summarizes the laboratory findings of the patients. The results of the blood tests were not different between the female and male patients, except those of blood urea tests. Table 3 shows the distribution of ocular diseases in patients. The most common diseases were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. Allergic conjunctivitis was more common in females ($p < 0.05$), while blepharoconjunctivitis was more common in males ($p < 0.05$).

Table 1: Chronic systemic diseases of patients with COVID-19	
Variable	N:178
Sex (M/F, %)	88/90 (49,40/50,60)
The mean age (mean±SD)	55,82± 16,22 years
Presence of HT (n, %)	30 (16,90)
Presence of DM (n, %)	8 (4,50)
Presence of asthma (n, %)	8 (4,50)
Presence of COPD (n, %)	4 (2,20)
M/F: male/female, SD: standard deviation HT: hypertension DM: diabetes mellitus COPD: chronic obstructive pulmonary disease	

Table 2: Laboratory findings of patients with COVID-19						
Variable	N	Mean	SD	Median	Min	Max
D-dimer (µg/L)	173	1769.11	5155.59	443.00	0.00	39300.00
CRP (mg/L)	155	53.63	68.83	36.40	1.00	570.00
Albumin (g/L)	136	34.54	6.17	34.10	19.50	47.90
Urea (mg/dL)	170	42.32	39.29	36.00	9.00	282.00
Creatinine (mg/dL)	172	0.99	1.11	0.76	0.39	9.19
Serum ferritin (ng/mL)	170	547.85	1742.91	275.63	5.22	20426.04
Lactate dehydrogenase (U/L)	168	296.11	170.68	286.00	138.00	1767.00
Lymphocyte count (109/L)	173	1.43	0.70	1.20	0.20	3.80
Neutrophil count (109/L)	150	4.49	3.60	3.70	0.89	20.70
SD: standard deviation, Min: minimum, Max: maximum						

Table 3: Distribution of chronic ocular diseases in patients with COVID-19	
Variable	N (%)
Refractive errors	104 (58,40)
Dry Eye Syndrome	64 (36,00)
Blepharoconjunctivitis	50 (28,00)
Allergic Conjunctivitis	26 (14,60)
Cataract	15 (8,40)
Glaucoma	9 (5,10)
Diabetic retinopathy	7 (3,90)
Age related macular degeneration	5 (2,80)
Pterygium	4 (2,20)

DISCUSSION

As mentioned previously, one of the main transmission routes of the SARS-CoV-2 virus is contact transmission: touching a contaminated surface or object and subsequently touching the mouth, nose, or eyes.[4,9] Thus, regular handwashing with soap or disinfection with hand sanitizer containing at least 60% alcohol (if soap and water are not available); avoidance of contact with infected people by maintaining an appropriate distance as much as possible; and refraining from touching the eyes, nose, and mouth with unwashed hands have been advised to all people for prevention.[10]

Ocular diseases frequently cause and increase the rate of hand-ocular surface contact time. The main symptoms of dry eye syndrome are itching, burning, stinging, and a sandy sensation.[10,11] Additionally, similar symptoms have been observed in patients with allergic conjunctivitis and blepharoconjunctivitis.[12,13] Furthermore, wearing glasses might prevent respiratory droplet transmission, but might also cause more contact with the face. There is a study showing that regular use of glasses due to refractive errors can reduce the likelihood of getting COVID-19 disease. Zeng et al.'s study found that in patients with COVID-19 were less likely to wear glasses than the general population, suggesting that daily use of glasses is associated with less susceptibility to COVID-19 infection.[14] In the current study, the most common ocular diseases were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. These diseases (especially ocular surface diseases) can cause severe hand-eye contact, thereby increasing the risk of transmission.

The current study aimed to identify concomitant ocular diseases in patients infected by the SARS-CoV-2 virus. Chen et al. retrospectively investigated 534 patients infected by the SARS-CoV-2 virus and found conjunctivitis, dry eye syndrome, keratitis, cataract, and diabetic retinopathy history in 85 patients; the rate of concomitant ocular disease was found to be 15.9%.[15] This rate was remarkably similar to the result found by the current study, which was 15.8%.

Other studies have investigated presumed ocular manifestations of SARS-CoV-2 virus infection.[15–18] For example, out of 72 patients with confirmed SARS-CoV-2 infection, Sun et al. found two patients with conjunctivitis and only one of them had a positive rRT-PCR test of a conjunctival swab.[19] Additionally, Chen et al. found a man with follicular conjunctivitis whose rRT-PCR test from conjunctival swab was positive.[20] Wu et al. found that a total of 12 of 38 patients (31.6%; 95% CI, 17.5-48.7) had ocular manifestations consistent with conjunctivitis, including conjunctival hyperemia, chemosis, epiphora, or increased secretion.[21] In the study conducted by Boz et al., anterior uveitis and acute follicular conjunctivitis were detected in patients with SARS-CoV-2 virus infection, but no fundus pathology was observed.[22] The study of Bozkurt et al. showed that COVID-19 patients may have pathological conjunctival changes without clinically significant ocular symptoms.[23] All these studies suggested a transmission route from conjunctiva and revealed the importance of prevention by washing hands, not touching eyes, and wearing protective goggles in hospitals.

CONCLUSIONS

In conclusion, the rate of previous ocular diseases in patients with a laboratory-confirmed SARS-CoV-2 was found to be 15.8%. The most common ocular disorders were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. Further studies with large samples should be performed to extend our information about ocular transmission routes of this highly contagious disease.

Sakarya University Faculty of Medicine Ethics Committee, 07/04/2020, IRB number:050.01.04/158

References

1. *Weiss SR, Navas-Martin S. Coronavirus Pathogenesis and the Emerging Pathogen Severe Acute Respiratory Syndrome Coronavirus. Microbiol Mol Biol Rev 2005;69:635–664.*
2. *Moorthy V, Henao Restrepo AM, Preziosi M-P, Swaminathan S. Data sharing for novel coronavirus (COVID-19). Bull World Health Organ 2020;98:150.*
3. *Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci 2020;12:9.*
4. *Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565–574.*
5. *Lu C-W, Liu X-F, Jia Z-F. 2019-nCoV transmission through the ocular surface must not be ignored. The Lancet 2020;395:e39*
6. *Ma D, Chen C-B, Jhanji V, Xu C, Yuan X-L, Liang J-J, et al. Expression of SARS-CoV-2 receptor ACE2 and TMPRSS2 in human primary conjunctival and pterygium cell lines and in mouse cornea. Eye 2020;34:1212–1219.*
7. *Leonardi A, Rosani U, Brun P. Ocular Surface Expression of SARS-CoV-2 Receptors. Ocul Immunol Inflamm 2020:1–4.*
8. *Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8:e21.*
9. *Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci 2020;12:9.*
10. *Adhikari SP, Meng S, Wu Y-J, Mao Y-P, Ye R-X, Wang Q-Z, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis Poverty 2020;9:29.*
11. *McGinnigle S, Naroo SA, Eperjesi F. Evaluation of dry eye. Surv Ophthalmol 2012;57:293–316.*
12. *Bernardes TF, Bonfioli AA. Blepharitis. Semin Ophthalmol 2010;25:79–83.*
13. *Kuruvilla M, Kalangara J, Lee FE-H. Neuropathic Pain and Itch Mechanisms Underlying Allergic Conjunctivitis. J Investig Allergol Clin Immunol 2019;29:349–356.*
14. *Zeng W, Wang X, Li J, Yang Y, Qiu X, Song P, et al. Association of Daily Wear of Eyeglasses With Susceptibility to Coronavirus Disease 2019 Infection. JAMA Ophthalmol 2020 2020;16:e203906*
15. *Chen L, Deng C, Chen X, Zhang X, Chen B, Yu H, et al. Ocular manifestations and clinical characteristics of 534 cases of COVID-19 in China: A cross-sectional study. Acta Ophthalmol 2020;10.1111/aos.14472.*
16. *Seah I, Agrawal R. Can the Coronavirus Disease 2019 (COVID-19) Affect the Eyes? A Review of Coronaviruses and Ocular Implications in Humans and Animals. Ocul Immunol Inflamm 2020;28:391–395.*
17. *Bostanci Ceran B, Ozates S. Ocular manifestations of coronavirus disease 2019. Graefes Arch Clin Exp Ophthalmol 2020;258:1959-1963.*
18. *Valente P, Iarossi G, Federici M, Petroni S, Palma P, Cotugno N, et al. Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report. J AAPOS 2020;S1091-8531(20)30115-4. doi: 10.1016/j.jaapos.2020.05.002.*
19. *Sun X, Zhang X, Chen X, Chen L, Deng C, Zou X, et al. The infection evidence of SARS-COV-2 in ocular surface a single-center cross-sectional study. Ocul Surf 2020;18:360-362.*
20. *Chen L, Liu M, Zhang Z, Qiao K, Huang T, Chen M, et al. Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease. Br J Ophthalmol 2020;104:748–751.*
21. *Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmol 2020;138:575-578.*
22. *Boz AAE, Atum M, Çakır B, Karabay O, Çelik E, Alagöz G. Outcomes of the Ophthalmic Examinations in Patients Infected by SARS-CoV-2. Ocul Immunol Inflamm. 2020 Nov 23:1-4. doi: 10.1080/09273948.2020.1844904. Epub ahead of print.*
23. *Bozkurt E, Özateş S, Muhafız E, Yılmaz F, Calıskan O. Ocular Surface and Conjunctival Cytology Findings in Patients with Confirmed COVID-19. Eye Contact Lens. 2020 Oct 13. doi: 10.1097/ICL.0000000000000752. Epub ahead of print.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Does Urapidil Alleviate Lung and Renal Injuries Induced by Cecal Ligation and Puncture?

Urapidil Çekal Ligasyon ve Delme ile İndüklenen Akciğer ve Böbrek Hasarını Hafifletir mi?

Derya Güzel Erdoğan[1], Ayhan Tanyeli[2*], Songül Doğanay[1], Mustafa Can Guler[2], Ersen Eraslan[3]

1Department of Physiology, Sakarya University, Faculty of Medicine, Sakarya, Turkey;
2Department of Physiology, Atatürk University, Faculty of Medicine, Erzurum, Turkey;
3Department of Physiology, Yozgat Bozok University, Faculty of Medicine, Yozgat, Turkey;

Yazışma Adresi / *Correspondence:*
Ayhan Tanyeli

Department of Physiology, Faculty of Medicine, Atatürk University, Erzurum, 25240, Turkey
T: **+90 507 363 16 54** E-mail **: ayhan.tanyeli@atauni.edu.tr**

Geliş Tarihi / Received : **28.08.2020** Kabul Tarihi / Accepted : **11.01.2020**

Orcid :

Derya Güzel Erdoğan https://orcid.org/0000-0002-7618-5043
Ayhan Tanyeli https://orcid.org/0000-0002-0095-0917
Songül Doğanay https://orcid.org/0000-0002-1730-1331
Mustafa Can Guler https://orcid.org/0000-0001-8588-1035
Ersen Eraslan https://orcid.org/0000-0003-2424-2269

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):142-147) DOI: 10.31832/smj.787082**

Abstract

Objective	Here, possible protective effects of Urapidil were investigated against lung and renal injuries induced by cecal ligation and puncture (CLP).
Materials and Methods	32 Sprague Dawley male rats were assigned to 4 groups as follows; sham, CLP, DMSO and Urapidil (URA) 0.5 mg/kg. Several oxidant, inflammatory and antioxidant parameters were determined in lung and renal tissues.
Results	Oxidant and inflammatory biomarkers increased while antioxidant biomarkers decreased in CLP and DMSO groups compared to sham group. Antioxidant parameters increased while oxidant and inflammatory biomarkers declined in treatment group compared to CLP and DMSO groups.
Conclusion	Present results have demonstrated that URA administration is effective against lung and renal injuries caused by CLP-related polymicrobial sepsis model.
Keywords	Urapidil; cecal ligation and puncture; lung; renal; rat.

Öz

Amaç	*Burada, çekal ligasyon ve ponksiyonun (CLP) neden olduğu akciğer ve böbrek yaralanmalarına karşı Urapidil'in olası koruyucu etkileri araştırıldı.*
Gereç ve Yöntemler	*32 Sprague Dawley erkek sıçan sham, CLP, Dimetil sülfoksit (DMSO) ve Urapidil (URA) 0.5 mg/kg şeklinde 4 gruba ayrıldı. Akciğer ve böbrek dokularında çeşitli oksidan, inflamatuvar ve antioksidan parametreler belirlendi.*
Bulgular	*CLP ve DMSO gruplarında sham grubuna göre oksidan ve inflamatuvar biyobelirteçler artarken antioksidan biyobelirteçler azalmıştır. Tedavi grubunda CLP ve DMSO gruplarına göre antioksidan parametreler artarken oksidan ve inflamatuvar biyobelirteçler azaldı.*
Sonuç	*Mevcut sonuçlar, URA uygulamasının CLP ile ilişkili polimikrobiyal sepsis modelinin neden olduğu akciğer ve böbrek hasarlarına karşı etkili olduğunu göstermiştir.*
Anahtar Kelimeler	*Urapidil; çekal ligasyon ve ponksiyon; akciğer; böbrek; sıçan.*

INTRODUCTION

Sepsis is a serious condition caused by bacterial infections. The inflammatory response of the organism intensifies over time due to sepsis causing multiple organ failure which often results in death.[1] According to a recent study, the incidence of sepsis ranged from 18% to 40%.[2] Intensive care unit patients face with death due to sepsis with a 30-70 % mortality rate.[3] The reason for this high mortality rate is that sepsis can cause impairment of vital organs such as lung, kidney, and liver. Traumatic injury or infection of these tissues activates the humoral system which causes the release of various cytokines and inflammation. Inflammatory response leads to hemostatic changes and organ dysfunction.[4] Sepsis is responsible on the formation of acute lung injury (ALI) and acute kidney injury (AKI) through oxidative stress.[5,6] Sepsis is a common and complex condition that generates excess free oxygen radicals that cause oxidative stress and multi-organ failure.[7] AKI is one of the primary complications observed during sepsis and it leads to death.[8] Oxidative stress occurs during sepsis and aggravates the harmful effects of oxidants.[9] High levels of reactive oxygen species (ROS) play role in sepsis formation through damage in lipid, carbohydrate and nucleic acid structures which may result in organ dysfunction in kidneys and lungs.[10,11] Malondialdehyde (MDA) is a lipid peroxidation metabolite and reflects severe tissue injury.[12] Total oxidant status (TOS) and total antioxidant status (TAS) values are used in the assessment of oxidative stress.[13,14] Proinflammatory cytokines including interleukin-1beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) are considered as pivotal mediators for sepsis-induced lung injury.[15,16] Cecal ligation and puncture (CLP) is used to compose a polymicrobial infection scene similar with human infections.[17-19] Drainage of primary focus of infection, antimicrobial therapy and symptomatic support underlie sepsis treatment.[20]

Several herbal and pharmacological agents have been examined to restrain oxidant damage.[19,21,22] Urapidil (URA) dilates arterioles and decreases the total peripheral resistance.[23] Here, the potential protective effects of URA against lung and renal injuries induced by CLP was investigated.

Ura is an antihypertensive and vasodilator agent.[24] The literature review revealed that it has not been investigated in terms of its effects on oxidative stress and inflammation in an experimental sepsis model. Therefore, the purpose of this study is to investigate the antioxidant and anti-inflammatory effects of URA in rats in a cecal ligation and puncture sepsis model.

MATERIALS and METHODS

Current study was carried out as an experimental animal research.

Animals, Drugs and Ethical Approval

During the study, animal rights were protected in accordance with Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) principles. Atatürk University Experimental Animal Ethics Committee admitted the study (date: 30.03.2018 protocol no:57). The animals were acquired from Experimental Animals Research and Application Center of Atatürk University and the experimental steps were carried out at the same center. The animals were caged in laboratory conditions such as appropriate humidity, temperature and light/darkness. Standard rat feed and tap water were provided to the animals.

Experimental Design, Drugs and Animals

This paper was based on our experimental study. Before the surgical steps, all rats were applied anesthesia, they were shaved, disinfected via %10 povidone-iodine and fixed in supine position. Thiopental sodium (Ulagay, İstanbul, Turkey) was preferred for anesthesia. URA and its solvent, Dimethyl Sulfoxide (DMSO), were purchased by Sigma-Aldrich Co.

32 Sprague Dawley male rats, weighing 240-270 g were used. They were randomized to 4 groups as: Group I (Sham

group, n=8): Abdominal area was incised to approach to the peritoneum and repaired with a 3.0 silk suture without any intervention. Group II (CLP group, n=8): All steps were performed as in group I.Then, cecum is tightly ligated to 2 cm distal and pierced via an 18-gauge needle (4 holes). [19] Afterwards, it is replaced to abdominal cavity and incisional space was sutured. Group III (CLP+DMSO group, n=8): 0.3 ml DMSO was administered intraperitoneally (i.p.) 30 minutes before the CLP model. Group IV (CLP+URA 0.5 mg/kg group, n=8): URA was given i.p. 30 minutes before the CLP model. The rats were fasted following surgical process, but water was allowed ad libitum for 18 hours until they were sacrificed.

Biochemical Analysis

Tissue samples were adjusted as each specimen weighing about 100 mg. They were homogenized via 2 mL of phosphate buffer solution (PBS). Centrifuge process was performed to obtain supernatant and kept in -80°C. MDA measurement is carried out through determination of the product level which occurs in case of MDA and thiobarbituric acid formation.[25] TAS and TOS parameters were evaluated by ELISA kits (Rel Assay Diagnostics). Oxidative stress index (OSI) demonstrates the ratio of TOS to TAS. Oxidation of MPO with 0-dianisidine composes a colored complex that is used for MPO measurement.[2]6 Formazan dye is the used to gauge superoxide dismutase (SOD) level.[27] TNF-α and IL-1β parameters were gauged with appropriate kits (Elabscience, Wuhan, China).

Statistical Analyses

One-way ANOVA test was chosen for biochemical data and then Tukey HSD test was used for multiple comparisons. The results were presented as Mean±Standard Deviation (SD). Statistical significance level was considered when p value below 0.05.

RESULTS

Lung Tissue Oxidative Stress Results

Table 1 shows the effects of URA on CLP-induced lung injury. While TAS and SOD levels declined in CLP and DMSO groups, they increased in URA treatment group. MDA, TOS and MPO levels elevated in CLP and DMSO groups but URA administration decreased those parameters.

Oxidative Stress Results of Kidney Tissue

Table 2 shows the effects of URA on CLP-induced kidney injury. A reduction in TAS and SOD values was observed in CLP and DMSO groups compared to sham group. Ura administration increased the current values. On the contrary, TOS, MDA and MPO levels were found to be higher in CLP and DMSO groups compared to sham group. Levels of these oxidant molecules decreased in the group treated with URA.

Proinflammatory Cytokine Results

Figure 1 and 2 show TNF-α and IL-1β values in CLP-induced lung and renal injuries, respectively. When CLP and

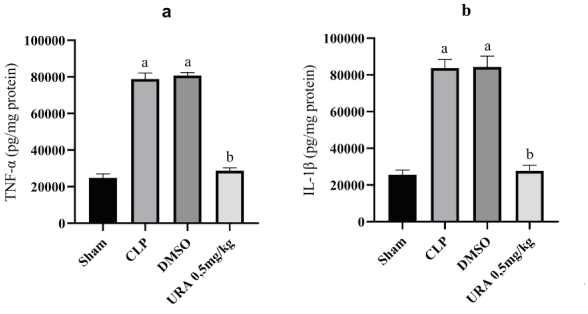
Table 1 Effects of URA treatment in CLP-induced lung injury.

Groups/Parameters (n=8)	Sham	CLP	DMSO	URA 0.5 mg/kg
TAS (mmol/L)	2,26±0,26	0,84±0,13[a]	0,83±0,09[a]	2,24±032[b]
TOS (µmol/L)	13,10±0,80	18,05±1,33[a]	18,96±0,95[a]	14,24±0,46[b]
OSI (arbitrary unit)	0,58±0,08	2,17±0,28[a]	2,24±0,30[a]	0,64±0,11[b]
SOD (U/mg protein)	399,01±24,59	226,95±20,49[a]	229,54±27,12[a]	393,32±11,77[b]
MPO (U/g protein)	309835,14±13303,41	480946,64±24113,50[a]	501102,50±17025,31[a]	319354,89±30266,51[b]
MDA (µmol/g tissue)	78,86±6,89	128,12±7,97[a]	132,15±9,15[a]	83,30±5,14[b]

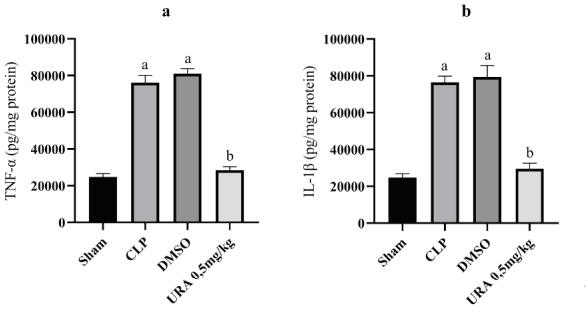
TAS; Total antioxidant status, TOS; Total oxidant status, OSI; Oxidative stress index, SOD; Superoxide dismutase, MPO; Myeloperoxidase, MDA; Malondialdehyde.
[a]p<0.001 compared to sham group. [b]p<0.001 compared to CLP group and DMSO group.

Table 2 Effects of URA treatment in CLP-induced kidney injury.				
Groups/Parameters (n=8)	Sham	CLP	DMSO	URA 0.5 mg/kg
TAS (mmol/L)	3,42±0,14	2,40±0,14[a]	2,31±0,25[a]	3,34±0,16[b]
TOS (μmol/L)	7,40±0,44	10,99±0,68[a]	11,35±0,75[a]	8,01±0,51[b]
OSI (arbitrary unit)	0,21±0,01	0,45±0,03[a]	0,49±0,07[a]	0,24±0,02[b]
SOD (U/mg protein)	350,59±51,99	202,33±13,71[a]	200,52±13,08[a]	358,78±67,75[b]
MPO (U/g protein)	16095,06±1586,52	35171,72±4819,18[a]	41903,66±2494,74[a]	16954,95±1484,18[b]
MDA (μmol/g tissue)	94,59±5,41	134,26±12,46[a]	142,75±10,35[a]	100,48±7,02[b]
TAS; Total antioxidant status, TOS; Total oxidant status, OSI; Oxidative stress index, SOD; Superoxide dismutase, MPO; Myeloperoxidase, MDA; Malondialdehyde. [a]p<0.001 compared to sham group. [b]p<0.001 compared to CLP group and DMSO group.				

DMSO groups were compared to sham group, TNF-α and IL-1β values elevated statistically in both tissues. In treatment group, TNF-α and IL-1β values diminished significantly when compared to CLP and DMSO groups.



compared with groups in rat lung tissues. [a]p<0.001 compared to sham group. [b]p<0.001 compared to CLP group.



compared with groups in rat renal tissues
[a]p<0.001 compared to sham group. [b]p<0.001 compared to CLP group.

DISCUSSION

Sepsis is a critical clinical condition with high mortality rates. Inflammation and weak immune response resulting from infections accompany to sepsis.[28] Sepsis leads to organ dysfunction and primarily affects the lungs.[29,30]. Sepsis induces acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).[31] It also causes acute kidney injury (AKI) which has a high mortality rate.[32] SOD scavenges reactive oxygen species (ROS) and thus eliminates superoxide radicals.[33] TAS and TOS are preferred to evaluate the oxidative stress.[13,14]

In severe sepsis cases, it is typically to observe increased inflammatory response to infection and imbalance between oxidants and antioxidants.[34,35] In CLP model, intestinal perforation is created to obtain abdominal sepsis.[36] Increased neutrophil activation enhances the production of ROS and proinflammatory cytokines.[37] Infections may result in inflammatory response including proinflammatory cytokine activation which may lead to multiple organ dysfunction.[38] During inflammatory response, TNF-α level increases and it induces cytokine release.[39] Excessive ROS level causes lipid peroxidation and increase MDA concentration. MDA is a toxic product produced during lipid peroxidation and indicates oxidative damage indirectly.[40-42] Oxidized lipids and proteins are associated with septic mortality.[43]

Here, MDA level increased in CLP and DMSO groups for

both tissues and treatment group decreased the MDA level. MPO activity elevates in case of intense infection as increased in CLP group of the current study.[44] URA treatment declined MPO activity. Oxidative stress demonstrates the supremacy of oxidant activity against antioxidant capacity. OSI represents the oxidative stress degree.[13,45] In current study, OSI levels diminished in treatment group compared to CLP and DMSO groups.

Although antibiotic treatment is effective to reduce mortality, resistance to these drugs is an inevitable result and thus new agents would be necessary.[46] URA binds the α1-adrenoceptor in the peripheral vascular system and the serotonin (1A) receptors of 5-hydroxytryptamine (5-HT1A) receptor in the central nervous system.[47,48] Thereby, URA reduces vascular tone which results in arterial and venous vasodilatation in the systemic and the pulmonary circulations.[49]

We assessed the renal and lung tissues for oxidative stress to find out the protective effect of URA against CLP-induced renal and lung injuries. It was observed that oxidative stress diminished with URA. Inflammation, oxidative stress pathways were inhibited by URA and this may a new agent in the treatment of CLP.

CONCLUSION

URA has protective effects against CLP-induced lung and renal injuries.

Ethical Committee and Protocol no

Atatürk University Experimental Animal Ethics Committee admitted the study (date: 30.03.2018 protocol no:57).

Conflict of interest

None

References

1. *Harasstani OA, Tham CL, Israf DA. Kaempferol and Chrysin Synergies to Improve Septic Mice Survival. Molecules 2017;22(1).*
2. *Kumar S, Gupta E, Kaushik S, Kumar Srivastava V, Mehta SK, Jyoti A. Evaluation of oxidative stress and antioxidant status: Correlation with the severity of sepsis. Scand J Immunol 2018;87(4):e12653.*
3. *Jawad I, Lukšić I, Rafnsson SB. Assessing available information on the burden of sepsis: global estimates of incidence, prevalence and mortality. J Glob Health 2012;2(1):010404.*
4. *Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. N Engl J Med 2003;348(2):138-150.*
5. *Wang Z, Holthoff JH, Seely KA, Pathak E, Spencer HJ, Gokden N, et al. Development of oxidative stress in the peritubular capillary microenvironment mediates sepsis-induced renal microcirculatory failure and acute kidney injury. Am J Pathol 2012;180(2):505-516.*
6. *Galley HF. Oxidative stress and mitochondrial dysfunction in sepsis. Br J Anaesth 2011;107(1):57-64.*
7. *Peralta JG, Llesuy S, Evelson P, Carreras MC, Flecha BG, Poderoso JJ. Oxidative stress in skeletal muscle during sepsis in rats. Circ Shock 1993;39(2):153-159.*
8. *Graziani G, Buskermolen M, Oldani S, Brambilla G. [Sepsis, acute renal failure and multiple organ dysfunction syndrome]. Giornale italiano di nefrologia : organo ufficiale della Societa italiana di nefrologia 2006;23 Suppl 36:S13-21.*
9. *Kaymak C, Basar H, Sardas S. Reactive oxygen species (ROS) generation in sepsis. FABAD J Pharm Sci 2011;36(1):41-47.*
10. *Dkhil MA, Kassab RB, Al-Quraishy S, Abdel-Daim MM, Zrieq R, Abdel Moneim AE. Ziziphus spina-christi (L.) leaf extract alleviates myocardial and renal dysfunction associated with sepsis in mice. Biomed Pharmacother 2018;102:64-75.*
11. *Wu GJ, Lin YW, Tsai HC, Lee YW, Chen JT, Chen RM. Sepsis-induced liver dysfunction was ameliorated by propofol via suppressing hepatic lipid peroxidation, inflammation, and drug interactions. Life sciences 2018;213:279-286.*
12. *Niki E, Yoshida Y, Saito Y, Noguchi N. Lipid peroxidation: mechanisms, inhibition, and biological effects. Biochem Biophys Res Commun 2005;338(1):668-676.*
13. *Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem 2005;38(12):1103-1111.*
14. *Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem 2004;37(4):277-285.*
15. *Goodman RB, Pugin J, Lee JS, Matthay MA. Cytokine-mediated inflammation in acute lung injury. Cytokine & growth factor reviews 2003;14(6):523-535.*
16. *Xiao XG, Zu HG, Li QG, Huang P. Sivelestat sodium hydrate attenuates acute lung injury by decreasing systemic inflammation in a rat model of severe burns. European review for medical and pharmacological sciences 2016;20(3):528-536.*
17. *Güzel Erdoğan D, Tanyeli A. Inhibition of NADPH oxidase attenuates sepsis induced acute lung oxidative damage in rats. Journal of Cellular Neuroscience & Oxidative Stress 2018;10(2).*
18. *Tanyeli A, Erdoğan Güzel D. Alliin mitigates Cecal Ligation Puncture (CLP)-induced lung injury through antioxidant and antiinflammatory effects. Turhish Journal of Sciences 2019;4(2):46-59.*
19. *Tanyeli A, Eraslan E, Güler MC, Şebin ÖS, Çelebi D, Özgeriş FB, et al. Investigation of biochemical and histopathological effects of tarantula cubensis D6 on lung tissue in cecal ligation and puncture-induced polymicrobial sepsis model in rats. Medicine Science International Medical Journal 2019;8(3):644-50.*
20. *dos Santos CC, Murthy S, Hu P, Shan Y, Haitsma JJ, Mei SH, et al. Network analysis of transcriptional responses induced by mesenchymal stem cell treatment of experimental sepsis. Am J Pathol 2012;181(5):1681-1692.*
21. *Öztürk D, Erdoğan Güzel D, Tanyeli A, Çomaklı S, Baylan H, Polat E. The protective effects of urapidil on lung tissue after intestinal ischemia-reperfusion injury. Turkish Journal of Biochemistry 2019;44(4):539-548.*
22. *Eraslan E, Tanyeli A, Polat E, Yetim Z. Evodiamine alleviates kidney ischemia reperfusion injury in rats: A biochemical and histopathological study. Journal of Cellular Biochemistry 2019;120(10):17159-166.*
23. *Bottorff MB, Hoon TJ, Rodman JH, Gerlach PA, Ramanathan KB. Pharmacokinetics and pharmacodynamics of urapidil in severe hypertension. J Clin Pharmacol 1988;28(5):420-426.*
24. *Shebuski RJ, Zimmerman BG. Suppression of reflex tachycardia following alpha-adrenoceptor blockade in conscious dogs: comparison of urapidil with prazosin. J Cardiovasc Pharmacol 1984;6(5):788-794.*
25. *Ohkawa H, Ohishi N, Yagi K. Assay for Lipid Peroxides in Animal-Tissues by Thiobarbituric Acid Reaction. Anal Biochem 1979;95(2):351-358.*
26. *Bradley PP, Priebat DA, Christensen RD, Rothstein G. Measurement of cutaneous inflammation: estimation of neutrophil content with an enzyme marker. J Invest Dermatol 1982;78(3):206-209.*
27. *Sun Y, Oberley LW, Li Y. A Simple Method for Clinical Assay of Superoxide-Dismutase. Clin Chem 1988;34(3):497-500.*
28. *Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. Jama 2009;302(21):2323-2329.*
29. *Hotchkiss RS, Monneret G, Payen D. Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy. Nat Rev Immunol 2013;13(12):862-874.*
30. *Nuytinck HK, Offermans XJ, Kubat K, Goris JA. Whole-body inflammation in trauma patients. An autopsy study. Arch Surg 1988;123(12):1519-1524.*
31. *Aziz M, Ode Y, Zhou M, Ochani M, Holodick NE, Rothstein TL, et al. B-1a cells protect mice from sepsis-induced acute lung injury. Mol Med 2018;24(1):26.*
32. *Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, et al. Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clin J Am Soc Nephrol 2007;2(3):431-439.*
33. *Pejić S, Todorović A, Stojiljković V, Kasapović J, Pajović SB. Antioxidant enzymes and lipid peroxidation in endometrium of patients with polyps, myoma, hyperplasia and adenocarcinoma. Reprod Biol Endocrinol 2009;7:149.*
34. *Tsiotou AG, Sakorafas GH, Anagnostopoulos G, Bramis J. Septic shock; current pathogenetic concepts from a clinical perspective. Med Sci Monit 2005;11(3):Ra76-85.*
35. *Mantzarlis K, Tsolaki V, Zakynthinos E. Role of Oxidative Stress and Mitochondrial Dysfunction in Sepsis and Potential Therapies. Oxid Med Cell Longev 2017;2017:5985209.*
36. *Walley KR, Lukacs NW, Standiford TJ, Strieter RM, Kunkel SL. Balance of inflammatory cytokines related to severity and mortality of murine sepsis. Infection and immunity 1996;64(11):4733-4738.*
37. *Bi J, Cui R, Li Z, Liu C, Zhang J. Astaxanthin alleviated acute lung injury by inhibiting oxidative/nitrative stress and the inflammatory response in mice. Biomed Pharmacother 2017;95:974-982.*
38. *Araújo CV, Estato V, Tibiriçá E, Bozza PT, Castro-Faria-Neto HC, Silva AR. PPAR gamma activation protects the brain against microvascular dysfunction in sepsis. Microvasc Res 2012;84(2):218-221.*
39. *Blackwell TS, Christman JW. Sepsis and cytokines: current status. Br J Anaesth 1996;77(1):110-117.*
40. *Yapca OE, Borekci B, Suleyman H. Ischemia-reperfusion damage. The Eurasian journal of medicine 2013;45(2):126-137.*
41. *Del Maestro RF. An approach to free radicals in medicine and biology. Acta physiologica Scandinavica Supplementum 1980;492:153-168.*
42. *Deng WS, Xu Q, Liu YE, Jiang CH, Zhou H, Gu L. Effects of melatonin on liver function and lipid peroxidation in a rat model of hepatic ischemia/reperfusion injury. Experimental and therapeutic medicine 2016;11(5):1955-1960.*
43. *Ozturk E, Demirbilek S, Begec Z, Surucu M, Fadillioglu E, Kirimlioglu H, et al. Does leflunomide attenuate the sepsis-induced acute lung injury? Pediatric surgery international 2008;24(8):899-905.*
44. *Gaut JP, Yeh GC, Tran HD, Byun J, Henderson JP, Richter GM, et al. Neutrophils employ the myeloperoxidase system to generate antimicrobial brominating and chlorinating oxidants during sepsis. Proceedings of the National Academy of Sciences of the United States of America 2001;98(21):11961-11966.*
45. *Rabus M, Demirbag R, Sezen Y, Konukoglu O, Yildiz A, Erel O, et al. Plasma and tissue oxidative stress index in patients with rheumatic and degenerative heart valve disease. Turk Kardiyoloji Dernegi arsivi : Turk Kardiyoloji Derneginin yayin organidir 2008;36(8):536-540.*
46. *Rangel-Frausto MS. The epidemiology of bacterial sepsis. Infect Dis Clin North Am 1999;13(2):299-312, vii.*
47. *Saxena PR, Villalon CM. Brain 5-HT1A receptor agonism: a novel mechanism for antihypertensive action. Trends Pharmacol Sci 1990;11(3):95-96.*
48. *Bopp C, Auger C, Diemunsch P, Schini-Kerth V. The effect of urapidil, an alpha-1 adrenoceptor antagonist and a 5-HT1A agonist, on the vascular tone of the porcine coronary and pulmonary arteries, the rat aorta and the human pulmonary artery. Eur J Pharmacol 2016;779:53-58.*
49. *Valenta B, Kotai E, Weisz E, Singer EA. Influence of urapidil and 8-OH-DPAT on brain 5-HT turnover and blood pressure in rats. J Cardiovasc Pharmacol 1990;15 Suppl 7:S68-74.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Influenza, Hepatitis B and Pneumococcal Vaccination Rates and Factors Influencing Vaccination Status in Patients with Diabetes

Diyabet Hastalarında İnfluenza, Hepatit B ve Pnömokok Aşılama Oranları ve Aşılanma Durumlarını Etkileyen Faktörler

Hasan Apaydın[1], Abdülkadir Aydın[2], Büşra Kanatsız[3], Seda Ahçı Yılmaz[4], Emin Pala[5], Sema Basat[6]

[1] Maltepe Üniversitesi Tıp Fakültesi, Aile Hekimliği, İstanbul, Türkiye.
[2] Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi, Aile Hekimliği, Sakarya, Türkiye;
[3] Şile Devlet Hastanesi, Aile Hekimliği, İstanbul, Türkiye.
[4] Sağlık Bilimler Üniversitesi Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi, Aile Hekimliği, İstanbul, Türkiye..
[5] Sağlık Bilimleri Üniversitesi Ümraniye Eğitim ve Araştırma Hastanesi, Aile Hekimliği, İstanbul, Türkiye.
[6] Sağlık Bilimleri Üniversitesi Ümraniye Eğitim ve Araştırma Hastanesi, İç Hastalıkları, İstanbul, Türkiye.

Yazışma Adresi / *Correspondence:*
Abdülkadir Aydın

Otuzikievler mh. 801. sk. No:3 D:2 Serdivan/Sakarya
T: **+90 532 430 86 24** E-mail **: drabkaay@gmail.com**

Geliş Tarihi / Received : **17.12.2020** Kabul Tarihi / Accepted : **18.01.2021**

Orcid :

Hasan Apaydın https://orcid.org/0000-0003-1367-1850
Abdülkadir Aydın https://orcid.org/0000-0003-0663-586X
Büşra Kanatsız https://orcid.org/0000-0003-1963-249X
Seda Ahçı Yılmaz https://orcid.org/0000-0002-4095-9887
Emin Pala https://orcid.org/0000-0001-9189-4342
Sema Basat https://orcid.org/0000-0002-6479-1644

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):148-154) DOI: 10.31832/smj.842236**

Abstract

Objective Diabetes Mellitus is a health problem that has increasingly become a worldwide concern due to its high frequency and complications. Infections in patients with diabetes are major cause of mortality and morbidity. The purpose of this study is to determine the rates of vaccination with influenza, pneumococcal, hepatitis B vaccine in diabetic patients, their awareness of the importance and necessity of vaccination, and how they reach on those awareness levels.

Materials and Methods This study was designed as a questionnaire based observational study. 504 patients aged 18 years and older who were admitted to Family Medicine and Diabetes Outpatient clinics, completed a questionnaire comprised of 15 questions regarding their socio-demographic profile, their awareness of higher risks of Influenza, Hepatitis B, Streptococcus infections in patients with diabetes, their knowledge about vaccinations for those infections, factors that encourage them to get vaccinated, other ways to protect themselves against vaccine-preventable diseases.

Results Of the patients who participated in the study, 76.4% were unvaccinated. The rates of patients vaccinated against Influenza, Hepatitis B, Pneumococcal, Pneumococcal+Influenza and Hepatitis B+Influenza were 10.1%, 6.9%, 5%, 1% and 0.6%, respectively. 22% of the patients had knowledge of governmental support for the vaccination of patients with Diabetes.

Conclusion As a result; it is seen that awareness of vaccination in both patients and health care providers are not enough. We reach the conclusion that those vaccination rates may increase with the cooperation between the Ministry of Health and the physicians by actively using visual, printed and social media and by broadcasting of public service announcements.

Keywords Diabetes Mellitus; Vaccination; Influenza; Pneumococcal; Hepatitis B

Öz

Amaç *Diyabet, tüm dünyada sıklığı ve neden olduğu komplikasyonlar nedeniyle önemi gitgide artan bir sağlık sorunudur. Diyabetik hastaların geçirmiş oldukları enfeksiyonlar ise önemli bir mortalite ve morbidite sebebidir. Çalışmamızda esas olarak; diyabetik hastaların influenza, pnömokok ve hepatit B aşılanma oranları, hastaların bu aşıların yapılmasının önemi ve gereklilikleri konusundaki farkındalıkları ve bu farkındalık seviyelerine hangi kanal yoluyla ulaştıkları incelenmiştir.*

Gereç ve Yöntemler *Çalışmamızda Aile Hekimliği ve Diyabet Polikliniğine başvuran 18 yaş ve üzeri 504 hastaya sosyodemografik profilleri, diyabetik hastalarda influenza, hepatit b, pnömokok enfeksiyonlarının daha ağır seyredebileceğinin farkındalığı, bu hastalıkların aşıları hakkında bilgi sahibi olup olmadıkları, onları aşılanmaya teşvik eden faktörleri, aşı ile önlenebilen hastalıklara karşı nasıl önlemler aldıklarını sorgulayan 15 soruluk bir anket uygulanmıştır.*

Bulgular *Çalışmamıza katılan hastaların %76,4'ü hiçbir aşı yaptırmamıştır. Veriler değerlendirildiğinde; diyabet tanısı aldıktan sonra influenza aşısı yaptıranların oranı %10,1, pnömokok aşısı yaptıranların oranı %5, Hepatit B aşısı yaptıranların oranının %6,9, pnömokok ve influenza aşılarını yaptıranların oranı %1, Hepatit B ve influenza aşılarını yaptıranların oranı ise %0,6 olarak bulunmuştur. Ayrıca hastaların yalnızca %22 kadarı diyabeti olan hastalarda devletin aşılanmayı desteklediğinin farkındaydı.*

Sonuç *Araştırmamız sonucunda; aşı farkındalığı ve aşılanma konusunda hem hasta, hem sağlık hizmeti sağlayıcıları kaynaklı eksikliklerimiz olduğu görülmektedir. Sağlık Bakanlığı ve hekimlerin ortak çalışmalarıyla ve görsel, yazılı, sosyal medyanın da aktif olarak kullanılması, gerekli kamu spotlarının yayınlanmasıyla bu aşılanma oranlarının artacağı kanaatine vardık.*

Anahtar Kelimeler *Diyabet; influenza aşısı; pnömokok aşısı; hepatit B aşısı*

INTRODUCTION

Diabetes Mellitus is a health problem that has increasingly become a worldwide concern due to its high frequency and complications. The number of people with diabetes has been rapidly increasing, especially in developed countries, due to unhealthy and poor eating habits, sedentary lifestyle, obesity and an aging population. While the number of individuals with diabetes in 2016 was around 415 million, including 193 million undiagnosed cases, it is estimated that 642 million people will have diabetes in 2040.[1,2]

Patients with diabetes have a higher risk of infections when compared with non-diabetic patients because an abnormal glucose metabolism leads to impairment of leucocyte function. Therefore, common infections such as Influenza, Hepatitis B and Streptococcus Pneumonia occur more frequently and are more severe in patients with diabetes.[3-5] In this way the infections increase mortality and morbidity rates in patients with diabetes. Immunization is one of the most effective methods for protection against the adverse effects of these infections.[6,7]

The Turkish Society of Endocrinology and Metabolism recommends a yearly influenza vaccine for diabetic patients of six months of age and older (especially in November), the Pneumococcal vaccine at least once in a lifetime for patients two years of age and older, and the Hepatitis B vaccine for patients between 19-59 years of age if not vaccinated before.[8]

In this study, we investigate whether patients with diabetes are aware of their higher risk of infections, the ways they can protect themselves against vaccine-preventible diseases, their vaccination rates, and the most important factors that encourage them to get vaccinated.

MATERIALS and METHODS

This study is a descriptive cross-sectional study. A total of 504 patients aged 18 years and older who were admitted to Family Medicine and Diabetes Outpatient Clinics from November 2014 to November 2017 were enrolled in the study. All eligible patients were informed about the study and written informed consent was obtained from the patients who agreed to participate. Patients completed a questionnaire comprised of 15 questions regarding their socio-demographic profile, their awareness of higher risks of Influenza, Hepatitis B and Streptococcus infections in patients with diabetes, their knowledge about vaccinations for those infections, factors that encourage them to get vaccinated, and other ways to protect themselves against vaccine-preventible diseases. The questionnaire lasted approximately ten minutes per patient under the supervision of a researcher.

Ethical approval for the study was obtained from the ethics committee of University of Health Sciences Umraniye Training and Research Hospital on 19.11.2014 with the decision case numbered 16709.

Data were analysed with the SPSS software package version 22.0 (IBM SPSS, Turkey). The Shapiro-Wilk test was used to evaluate whether the data were normally distributed. Data were expressed as mean ± standard deviation and frequency. To analyze qualitative data the Chi-square and Yates's correction for continuity tests were used. A p-value less than 5% was regarded as statistically significant.

RESULTS

Of the 504 patients that participated in the study, 191 (37.9%) were male and 313 (62.1%) were female. The mean age was 58.21±11.78 years. There was no statistically significant difference between vaccinated and unvaccinated patients according to educational level (Table 1). Most of the patients had diabetes for more than five years (Table 2). 67.9% of patients were not aware that individuals with diabetes could acquire more severe infections and 77.4% of the patients were not informed about vaccination by a physician after being diagnosed.

Table 1: Demographic characteristics and vaccination status of the diabetic patients

		Vaccination status		p
		Yes (n=119)	No (n=385)	
		Mean±SD	Mean±SD	
Age		59,5±12,55	57,81±11,53	**10,172**
Sex n (%)				
	Male	62 (52,1%)	129 (33,5%)	**2<0,001***
	Female	57 (47,9%)	256 (66,5%)	
Education level n (%)				
	Illiterate	16 (13,4%)	91 (23,6%)	**20,059**
	Primary school	81 (68,1%)	235 (61%)	
	Secondary school	9 (7,6%)	19 (4,9%)	
	High school	7 (5,9%)	31 (8,1%)	
	Graduate and more	6 (5%)	9 (2,3%)	

1Student t Test was used. 2Ki Kare Test was used.

Of the patients who participated in the study, 76.4% were unvaccinated. The proportion of patients vaccinated against Influenza, Hepatitis B, Pneumococcal, Pneumococcal+Influenza and Hepatitis B+Influenza were 10.1%, 6.9%, 5%, 1% and 0.6% respectively. 22% of patients had knowledge of governmental support for the vaccination of patients with chronic illnesses such as Diabetes.

Recommendations by their family physicians, awareness of higher risks of infections concerning them, and impact of television health programmes encouraged 39.1%, 16% and 16% of patients respectively to get vaccinated. Most of the patients were vaccinated in state hospitals and 65.5% of those vaccinated patients were informed about the duration of immunity (Table 2).

Table 2: Evaluation of vaccine and diabetes mellitus related factors

		n	%
Duration of diabetes (years)	0-5	181	35,9
	6-10	112	22,2
	11-15	101	20
	16-20	50	9,9
	More than 20 years	60	11,9
Past infections	None	52	10,3
	Influenza	434	86,1
	Pneumonia	15	3
	Hepatitis B+ Influenza	3	0,6
Are you aware of the higher severity of infections in diabetic patients?	Yes	162	32,1
	No	342	67,9
After being diagnosed have you received any physician recommendation for immunization?	Yes	114	22,6
	No	390	77,4
Vaccines received	Not vaccinated	385	76,4
	Influenza	51	10,1
	Pneumococcal vaccine	25	5
	Hepatitis B	35	6,9
	Pneumococcal+Influenza	5	1
	Hepatitis B+Influenza	3	0,6
Do you know the governmental support for the vaccines?	Yes	111	22
	No	393	78
Reasons to get vaccinated (n=119)	I heard from other vaccinated patients	14	11,8
	Diabetic patients could have more severe infections than healthy people	19	16
	A family physician recommended	47	39,5
	Health programmes on television	19	16
	Social and mass media	5	4,2
	Other reasons*	15	12,6
Place of vaccination (n=119)	Primary care center	40	33,6
	State hospital	49	41,2
	Private hospital	2	1,7
	Pharmacy	28	23,5
Do you know the duration of immunization? (n=119)	No	41	34,5
	Yes	78	65,5

*My children recommended, a pharmacist recommended, due to splenectomy operation, before going abroad or going on pilgrimage

Table 3 summarizes patients' reasons for not getting vaccinated and the the other ways patients protect themselves

against infections other than vaccination.

Table 2: Table3: Reasons for not receiving vaccination and precautions taken

		n	%
Reasons for not receiving vaccination (n=383)	Not recommended	308	80,4
	Concern about side effects	31	8,1
	I don't believe in immunization	40	10,4
	Cost of vaccines	3	0,8
	Other reasons	1	0,3
What kind of ways do you use for protection if you are not vaccinated?	pay attention to blood sugar control	78	20,3
	(n=385)	52	13,5
	pay attention to personal hygiene	38	9,9
	Wear mask	5	1,3
	any protection	202	52,5
	Other precautions	10	2,6

Correlations between each group of patients vaccinated for different types of infections and the impact of a physician's recommendation, reasons to get vaccinated and the rate of awareness of the higher severity of infections in patients with diabetes are shown in Table 4.

There was a statistically significant difference among sex distribution of vaccinated and unvaccinated patients (p:0.001; p<0.05). Among the vaccinated participants, the rate of men was higher and vaccinated females was significantly lower than the rate of unvaccinated females.

The rates of past infections, patients' awareness of the higher severity of infections in diabetic patients, being informed about vaccination by a physician after being diagnosed and having knowledge of governmental support for vaccinations, were significantly higher in vaccinated patients than unvaccinated ones (p: 0.001; p <0.05) (Table 5).

Table 4: Correlations between each group of patients vaccinated for different types of infections and the impact of a physician's recommendation, reasons to get vaccinated and the rate of awareness of the higher severity of infections in patients with diabetes.

		Vaccines					
		Not vaccinated	**Influenza**	**Pneumococcal vaccine**	**Hepatitis B**	**Pneumococcal+ Influenza**	**Hepatitis B+ Influenza**
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Are you aware of the higher severity of infections in diabetic patients?	Yes	75(19,5%)	34(66,7%)	19(76%)	27(77,1%)	5(100%)	2(66,7%)
	No	310(80,5%)	17(33,3%)	6(24%)	8(22,9%)	0(0%)	1(33,3%)
After being diagnosed have you received any physician recommendation for immunization?	Yes	23(6%)	30(58,8%)	23(92%)	31(88,6%)	5(100%)	2(66,7%)
	No	362(94%)	21(41,2%)	2(8%)	4(11,4%)	0(0%)	1(33,3%)
Reasons to get vaccinated (n=119)	I heard from other vaccinated patients	-	6(11,8%)	2(8%)	6(17,1%)	0(0%)	0(0%)
	Diabetic patients could have more severe infections than healthy people	-	9(17,6%)	5(20%)	4(11,4%)	1(20%)	0(0%)
	Family physician recommendation for vaccine	-	14(27,5%)	13(52%)	16(45,7%)	2(40%)	2(66,7%)
	Health programmes on television						
	Social and mass media	-	12(23,5%)	3(12%)	4(11,4%)	0(0%)	0(0%)
	Other reasons*	-	5(9,8%)	0(0%)	0(0%)	0(0%)	0(0%)

*My children recommended, a pharmacist recommended, due to splenectomy operation, before going abroad or going on pilgrimage

Tablo 5: Evaluation of vaccine and diabetes related factors among vaccinated and not vaccinated patients

		Vaccination status		p
		Yes (n=119)	No (n=385)	
		n (%)	n (%)	
Past infections	**Yes**	117 (98,3%)	335 (87%)	[2]**<0,001***
	No	2 (1,7%)	50 (13%)	
Are you aware of the higher severity of infections in diabetic patients?	**Yes**	87 (73,1%)	75 (19,5%)	[1]**<0,001***
	No	32 (26,9%)	310 (80,5%)	
After being diagnosed have you received any physician recommendation for immunization?	**Yes**	91 (76,5%)	23 (6%)	[1]**<0,001***
	No	28 (23,5%)	362 (94%)	
Do you know the governmental support for the vaccines?	**Yes**	90 (75,6%)	21 (5,5%)	[1]**<0,001***
	No	29 (24,4%)	364 (94,5%)	

[1]Pearson Chi-square Test
[2]Yate's Continuity for correction test
*p<0.05

DISCUSSION

In this study influenza, pneumococcal and hepatitis B vaccination rates of diabetic patients and patients' awareness of immunization were very low. Although childhood vaccination rates are quite high in our country[9], adult vaccination rates remain far behind the developed countries.

In a study conducted in the United States in 2012, vaccination rates in elderly age groups were 67%, whereas in a recent study in our country, adult vaccination rates were 27%.[10]

Results from this study concur with a study about vaccination in diabetic patients, conducted by Arslan et al. in 2016, in Turkey. In the study, the rate of influenza vaccination in diabetic patients was 14.6%5, whereas it was 10.1% and the rate of influenza vaccination both with hepatitis B or pneumococcal vaccine was 11,7% in our study. Influenza vaccination rate was 17.4% in a community-based study conducted by Asık et al. in 2013.[11] In a multicenter study conducted by Biberoğlu et al. in Aegean region of Turkey involving 11235 people, only 4.5% of participants received influenza vaccine.[12]

Pneumococcal vaccination rates vary between 1% and 4% in various studies conducted in different populations at different times in our country.[5,11,12] In our study, 5% of the patients were vaccinated only against pneumococcal diseases, while 6% of them were vaccinated against both influenza and pneumococcal diseases.

Among all the hepatitis B vaccinated diabetic patients (7,5%), 6,9% were vaccinated with hepatitis B vaccine alone, while 0,6% with both hepatitis B and influenza vaccines. Three previous studies in adults in different regions of Turkey determined hepatitis B vaccination rates as 15,5%, 10% and 4,1% respectively.[5,11,12]

In addition to low diabetic vaccination rates, the precautions patients took against vaccine-preventable diseases were insufficient. Most of the unvaccinated patients in this study had not taken any precautions against these diseases. Paying attention to blood sugar level, avoiding crowded places and sick individuals were the most commonly used ways for protection among unvaccinated patients.

In this study, vaccination rates of diabetic patients were less than rates in other studies. This may be due to differences in socioeconomic status of study groups, access to health care, and attitudes of health-care workers about vaccination. More comprehensive studies should be designed to better estimate the effects of these factors.

In this study the most important factor that encouraged all

groups of patients to get vaccinated was a physicians recommendation. After being diagnosed, 114 of the 504 diabetic patients were given information about one or more of the vaccinations. It appears that the rate of vaccination in diabetic patients is strongly affected by physicians' attitudes towards vaccination. Physicians neglect to provide this medical advice may be due to concerns about vaccine safety, lack of adequate knowledge of current recommendations for immunizations for adults and short doctor visit lengths. With increased efforts from the Ministry of Health, adult vaccination rates could be bettered with increased education of health-care workers about vaccination and active participation of primary care physicians in adult immunization.

Most of the patients received vaccines in state hospitals rather than at primary care centers, which are the cornerstones of preventive medicine in Turkey. Patients' preferences for the management of their chronic diseases by specialists in state hospitals might be a factor behind this. We believe that diabetic vaccination rates at primary care centers will increase if primary care physicians take an active role in chronic disease management through the implementation of the policies planned by the Ministry of Health.

In this study, 34.5% of vaccinated patients did not know the duration of their immunity. Patients' knowledge on the duration of immunity of Hepatitis B and Influenza vaccines was more than Pneumococcal vaccine. This might be due to inadequate information given to the patients by physicians and inefficient use of mass and social media by the Ministry of Health regarding the immunization schedules of the Pneumococcal vaccine.

80.4% of the 385 unvaccinated patients reported that they had not received any vaccinations due to not being informed about them. This supports our opinon that family physicians and The Ministry of Health were not efficiently involved in the vaccination process. 10.4% of the unvaccinated patients expressed that they did not believe in the benefits of vaccination. This points to the fact that patients might have other reasons, other than lack of information, that prevents them from getting vaccinated. As 8.1% of the patients stated their concern regarding side effects of vaccines, we think that anti-vaccination campaigns in social and mass media are strongly influential in this respect.

Patients awareness of the higher risk of infection in diabetic patients was very low in this study. We determined that television health programmes and a physician's recommendation for immunization were the most encouraging factors for receiving vaccinations in the few vaccinated diabetic patients.

It appears that there are deficiencies with both healthcare workers and patient regarding the awareness of immunization and getting vaccinated in Turkey. We concluded that in order to increase adult vaccination rates, healthcare workers should be educated about current recommendations for vaccinations, family physicians should take as active a role in adult vaccinations as in childhood vaccinations, and the use of public service announcements could be increased to inform patients of chronic diseases, higher risks of morbidity they face, and the importance of vaccination in preventing infections.

Acknowledgments

No conflict of interest was declared by the authors.

References

1. *International Diabetes Fedaration, IDF Diabetes Atlas. 7th edition. 2015.*
2. *Aydın A, Atadağ Y, Öksüz A, Kaya D, Aydın NE. Comparison of the effects of impaired fasting glucose and impaired glucose tolerance on diabetic development risks on Hba1c levels: A retrospective study. J Surg Med. 2017;1(1):1-4.*
3. *Wang IK, et al. Effectiveness of influenza vaccination in elderly diabetic patients: a retrospective cohort study. Vaccine. 2013;31:718-724.*
4. *Reilly ML, et al. Increased risk of acute hepatitis B among adults with diagnosed diabetes mellitus. J Diabetes Sci Technol. 2012;6:858-866.*
5. *Arslan İE, Altınova A, Törüner FB, et al. Awareness of hepatitis B, influenza and pneumococcal vaccine among diabetic patients. GMJ. 2016;27:115-117.*
6. *American Diabetes Association. Standards of medical care in diabetes 2013. Diabetes Care. 2013;36(1):11-66.*
7. *Bridges CB, Woods L, Coyne-Beasley T. Advisory committee on immunization practices (ACIP) recommended immunization schedule for adults aged 19 years and older - United States. MMWR Surveill Summ 62. suppl. 2013;62(1):9-19.*
8. *Türkiye Endokrinoloji ve Metabolizma Derneği, Diabetes Mellitus ve Komplikasyonlarının Tanı Tedavi ve İzlem Kılavuzu. 2016.*
9. *Sağlık İstatistikleri Yıllığı 2011. Sağlık Araştırmaları Genel Müdürlüğü. TC Sağlık Bakanlığı. 2012.*
10. *Recommendations from the National Vaccine Advisory Committee: Standards for Adult Immunization Practice. Public Health Rep 2014;129:115-123.*
11. *Aşık Z, Çakmak T, Bilgili P. Erişkinlerin erişkinlik dönemi aşıları hakkındaki bilgi, tutum ve davranışları. Türk Aile Hek Derg 2013;17:113–118.*
12. *Biberoğlu K, Biberoğlu S, Özbakkaloğlu M ve ark. Haydi büyükler aşıya! http://www.tihud.org.tr/main/content?ref=2&child=179. Citation date: 21.06.2017.*

RESEARCH ARTICLE / *Araştırma Makalesi*

Endocan As A Potential Marker of Early Endothelial Dysfunction In Polycystic Ovary Syndrome (PCOS)

Polikistik Over Sendromunda (PKOS) Erken Endotel Disfonksiyonunun Potansiyel Belirleyicisi Olarak Endocan

Mahmut Apaydın[1], Taner Demirci[2], Erman Çakal[3]

[1] Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, Endokrinoloji ve Metabolizma Hast. Bilim Dalı, Afyonkarahisar, Türkiye

[2] Sakarya Üniversitesi Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, Endokrinoloji ve Metabolizma Hast. Bilim Dalı, Sakarya, Türkiye

[3] Sağlık Bilimleri Üniversitesi Ankara Dışkapı Yıldırım Beyazıt SUAM, Endokrinoloji ve Metabolizma Hast. Kliniği, Ankara, Türkiye

Yazışma Adresi / *Correspondence:*
Mahmut Apaydın

Zafer Sağlık Külliyesi Dörtyol Mah. 2078 Sok. No:3, C.Blok, Endokrinoloji ve Metabolizma Hastalıkları B.D, Afyonkarahisar

T: **+90 0505 234 90 90** E-mail **: drmahmutapaydin@gmail.com**

Geliş Tarihi / Received : **06.01.2021** Kabul Tarihi / Accepted : **01.02.2021**

Orcid :

Mahmut Apaydın https://orcid.org/0000-0002-7533-7084
Taner Demirci https://orcid.org/0000-0002-9579-4530
Erman Çakal https://orcid.org/0000-0003-4455-7276

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):155-161) DOI: 10.31832 smj.855493**

Abstract

Objective	Polycystic ovary syndrome (PCOS) is a common endocrinological disease in women of reproductive age and has a wide range of metabolic effects. Chronic low-grade inflammation and endothelial dysfunction plays a key role in the pathogenesis of PCOS and they are associated with an increased risk of cardiovascular disease. Endocan, is an inflammatory marker showing endothelial dysfunction. The aim of our study, to compare serum endocan levels in PCOS and healthy control groups and to determine the relationship between some cardiovascular risk factors and serum endocan levels.
Materials and Methods	This case-control study included 52 PCOS patients and 59 age-matched healthy controls. Patients were diagnosed as PCOS based on 2003 Rotterdam criteria. Demographic data, history of menstrual irregularity and infertility, polycystic ovary appearance in ultrasonography and hirsutism status were recorded. Endocan levels of PCOS patients and controls were compared. Data analysis was performed by using SPSS-22 for Windows (Statistical Package for Social Science, SPSS Inc. Chicago IL, USA*Z).
Results	The median (IQR) value of serum endocan level was 420.7 ng/L (355.2-570.3) in the PCOS group and 320.0 ng/L (219.9-455.9) in the control group (p=0.003). While there was no significant correlation between serum endocan and some cardiovascular risk factors such as waist circumference, hip circumference, BMI, LDL, triglyceride, systolic and diastolic arterial tension but a positive correlation was found between homeostatic model assessment insulin resistance (HOMA-IR) (r= 0.276, p= 0.003).
Conclusion	Serum endocan levels are higher in PCOS patients, in line with the literature. Endocan level shows a significant correlation with insulin resistance, one of the metabolic parameters. This may be a sign of early endothelial dysfunction in PCOS.
Keywords	endocan; endothelial dysfunction; polycystic ovary syndrome; inflammation

Öz

Amaç	*Polikistik over sendromu (PKOS), üreme çağındaki kadınlarda sık görülen endokrinolojik hastalıktır. PKOS'ta izlenen kronik düşük dereceli inflamasyon ve endotel disfonksiyon artmış kardiyovasküler hastalık riski ile ilişkilidir. Endocan, endotel disfonksiyonunu gösteren inflamatuar bir belirteçtir. Çalışmamızda PKOS ve sağlıklı kontrol grubunu serum endocan düzeyleri açısından karşılaştırmayı ve kardiyovasküler risk faktörleri ile serum endocan düzeyleri arasındaki ilişkiyi belirlemeyi amaçladık.*
Gereç ve Yöntemler	*Bu vaka-kontrol çalışmasında, 52 PKOS hastası ve yaş eşleştirilmiş sağlıklı 59 bireyden oluşan kontrol grubu yer almaktadır. Hastalara, 2003 Rotterdam kriterlerine göre PCOS tanısı kondu. Demografik veriler, menstruel düzensizlikler, infertilite öyküsü, ultrasonografide polikistik over görünümü ve hirsutizm varlığı kaydedildi. PCOS hastaları ve kontrol grubunun serum Endocan düzeyleri karşılaştırıldı. Veri analizi Windows için SPSS-22 (Statistical Package for Social Science, SPSS Inc. Chicago IL, USA*Z) kullanılarak yapıldı.*
Bulgular	*Serum endocan düzeyi ortanca (IQR) değeri PKOS grubunda 420,7 ng / L (355,2-570,3), kontrol grubunda ise 320,0 ng / L (219,9-455,9) idi (p = 0,003). Serum endocan ile bel çevresi, kalça çevresi, BMI, LDL, trigliserit, sistolik ve diyastolik arteriyel basınç gibi bazı kardiyovasküler risk faktörleri arasında anlamlı bir ilişki bulunmazken, insülin direnci (HOMA-IR) ile arasında pozitif korelasyon saptandı (r = 0.276, p = 0,003).*
Sonuç	*Çalışmamızda, serum endocan düzeyleri literatürle uyumlu olarak PKOS hastalarında daha yüksek saptanmıştır. Endocan düzeyi, metabolik parametrelerden biri olan insülin direnci ile anlamlı bir korelasyon göstermektedir. Bu bulgular, PKOS' ta erken endotel disfonksiyonunun bir işareti olarak yorumlanabilir.*
Anahtar Kelimeler	*endocan; endotel disfonksiyonu; polikistik over sendromu; inflamasyon*

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrinological disease that affects 6-18% of women of reproductive age and has a wide range of metabolic effects.[1,2] It is the most common cause of infertility in women.[3] The main clinical features of PCOS are ovulatory dysfunction and hyperandrogenism, and these findings may persist throughout the reproductive period. Its etiology is unknown and causes long-term health problems. PCOS is associated with an increased risk of metabolic syndrome, type 2 diabetes, cardiovascular disease, and endometrial cancer.[2,4,5]

Because of these effects, the diagnosis of PCOS should not be ignored. Chronic low-grade inflammation is involved in the pathogenesis of obesity-related diseases. PCOS is also an obesity-related disease and is a proinflammatory condition. A great deal of literature has been published showing that many inflammatory cytokines or molecules such as interleukin-1, interleukin-6, C- reactive protein (CRP), and tumor necrosis factor- alpha (TNF-alfa) are altered in relation to PCOS.[6-10] Endothelial dysfunction is associated with an increased risk of cardiovascular disease, and there are many studies associated with this in PCOS.7,11-13 Although there are conflicting information about the definite increase in cardiovascular mortality in PCOS, which is a premenopausal disease, it is an indisputable fact that cardiovascular disease risk factors frequently accompany PCOS.[4,14]

Endocan (Endothelial cell Spesific Molecule-1; ESM-1), a proteoglycan found in serum and produced by the endothelium, is an inflammatory marker showing endothelial dysfunction.[15-17]

Endocan has been studied in many chronic inflammatory diseases and cancers, and similar studies have been conducted in PCOS. In these studies, endocan levels in PCOS, as in other chronic diseases, were found to be higher than healthy control groups.[1,13,16,18-20] The aim of this study is to compare the endocan level in PCOS patients with the healthy control group and to show the relationship between some cardiovascular risk indicators accompanying PCOS and endocan level.

MATERIALS and METHODS

Study design

This research is a case-control study conducted between January 01, 2017 and December 31, 2018. Our study was evaluated by the Clinical Research Ethics Committee of Health Sciences University Yıldırım Beyazıt Dışkapı Training and Research Hospital and ethics committee approval was obtained with the decision number 24/30, dated 30.06.2015. In addition, the research was carried out in accordance with the Declaration of Helsinki Principles (www.wma.net/e/policy/b3.htm). The study included 52 PCOS patients and 59 age-matched healthy controls. Between the two groups, some cardiovascular risk parameters such as insulin resistance and arterial blood pressure were compared, as well as age, anthropometic measurements, biochemical markers and hormones associated with hirsutism. In addition, to make a comparison according to their body mass index (BMI), both groups were subgrouped within themselves: normal (BMI <25 kg/m2), overweight (BMI = 25-29.9 kg/m2) and obese (BMI≥30 kg/m2). Since there were no obese patients in the control group, it was categorized only as normal and overweight. Serum endocan levels were compared both between groups and between BMI subgroups.

Diagnosis and case selection

Demographic data, history of menstrual irregularity and infertility, polycystic ovary appearance in ultrasonography and hirsutism status were recorded. Hirsutism scoring was done according to Modified Ferriman Gallwey Scoring System.[21] Oligomenorrhea is defined as menstrual intervals over 35 days, and amenorrhea is defined as not having periods for more than 6 consecutive months. PCOS diagnoses were made based on Rotterdam and Androgen Excess Society diagnostic criteria, if in the pelvic or transvaginal ultrasound, 2-9 mm twelve or more preantral

follicle appearance or ovarian volume was more than 10 ml and/or chronic oligo-anovulation (oligomenorrhea) and clinical and/or laboratory hyperandrogenism findings were detected.[22,23] Women under 18 years of age, pregnant women, postmenopausal women, other causes of ovarian and non-ovarian hyperandrogenism (congenital adrenal hyperplasia, idiopathic hyperandrogenism, adrenal and ovarian tumors, etc.), patients using drugs such as oral contraceptives, anti-androgen pills and synthetic steroids, and patients with acute or chronic inflammatory diseases were not included in the study. Those with known cardiovascular disease or predominant risk for cardiovascular disease were also excluded.

Laboratory parameters

Biochemistry and follicular phase hormonal parameters were taken in the follicular phase of the menstrual cycle (within the first 7 days of menstruation). It was sampled at any time in oligomenorrheic patients. All baseline blood tests were performed between 08:00 and 10:00 in the morning, following an 8-hour fasting period. Serum samples for the endocan were first stored for coagulation and then centrifuged at 4000 xg for 15 minutes at + 4 ° C. The serum samples obtained were divided into aliquots and stored in a freezer at -80˚C until analysis. Subsequently, endocan was studied with elisa method with "Human ESM1 / Endocan, PicoKine™, EK0752" kit belonging to "Boster Biological Technology USA". Its sensitivity is <10 pg/ml, the measurement range is 31.2pg / ml-2000pg / ml. Routine biochemistry, thyroid function tests, follicular phase hormonal panel, total testosterone, dehydroepiandosterone sulfate (DHEA-S) and basal 17 OH-P levels at diagnosis were also recorded.

Statistical Analysis

Data analysis was performed by using SPSS-22 for Windows (Statistical Package for Social Science, SPSS Inc. Chicago IL, USA®Z). The variables were investigated using visual (histograms, probability plot) and analytical methods (Kolmogorov-Simirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. We performed analyses to describe and summarize the distributions of variables. Continuous variables were reported as the median and interquartile range (IQR). We use the Mann-Whitney U test to compare continuous nonparametric variables. When investigating the changes in serum endocan by groups (PCOS or control), the effects of BMI was adjusted using ANCOVA tests. While investigating the associations between non-normally distributed and/or ordinal variables, the correlation coefficients and their significance were calculated using Spearman test. The statistically significant two tailed p-value was considered as <0,05.

RESULTS

The median age (interquartile range=IQR) is 22 (19-27.75) in the PCOS group and 25 (22-30) in the control group (p=0.130). Other baseline characteristics and descriptive statistics between both groups were summarized in table 1. The median (IQR) value of serum endocan level was 420.7 ng/L (355.2-570.3) in the PCOS group and 320.0 ng/L (219.9-455.9) in the control group (p=0.003) (figure 1).

Serum endocan levels were 311.42 ng/L in those with normal BMI (n= 46) in the control group and 376.64 ng/L in those overweight (n=13), and this difference was not significant (p= 0.149). Similarly, serum endocan levels were not different in subgroups formed according to BMI in PCOS group (p= 0.923) (table 2). In addition, when examining the difference between serum endocan levels compared to PCOS and control groups, it was evaluated whether BMI had an effect on this and it was found that it did not affect the endocan levels in the groups (p=0.837). No correlation was found between the serum endocan level and the total testosterone level (r= 0.022, p= 0.826), which is within the PCOS diagnostic criteria. While there was no significant correlation between serum endocan and some cardiovascular risk factors such as waist circumference (r= 0.172, p= 0.072), hip circumference (r= 0.169, p= 0.076), BMI (r= 0.154, p= 0.107), LDL (r= 0.008, p= 0.933), triglyceride (r=

0.053, p= 0.579), systolic (r= 0.077, p= 0.423) and diastolic arterial tension (r= 0.081, p= 0.397), a positive correlation was found between homeostatic model assessment insulin resistance (HOMA-IR) (r= 0.276, p= 0.003) (table 3).

Table 1. Baseline characteristics of PCOS and control group and differences between groups.

	Median (interquartile range) *		
	PCOS (n=52)	Control (n=59)	p value
Age** (min-max)	23.5±5.3 (18-37)	24.1±3.9 (18-38)	0.130
BMI (kg/m2)	26.44 (22.36-30.48)	22.03 (19.84-24.44)	<0.001
Waist circumference (cm)	88.50 (76.75-97.75)	73.00 (67.00-80.00)	<0.001
Hip circumference (cm)	102 (95-110)	95 (91-101)	0.002
Waist/hip circumference ratio	0.850 (0.819-0.895)	0.766 (0.714-0.822)	<0.001
Fasting blood glucose (mg/dL)	80. (75-88)	78 (72-83)	0.058
İnsülin (fasting) (mIU/L)	15.10 (11.92-20.60)	8.70 (6.40-10.50)	<0.001
HOMA-IR*	3.03 (2.17-4.10)	1.64 (1.28-2.10)	<0.001
TG (mg/dL)	93 (69-149.25)	76 (57-106)	0.031
HDL (mg/dL)	50 (45-58)	52 (50-60)	0.033
LDL (mg/dL)	96 (86-115.5)	89 (77-100)	0.007
Cholesterol (mg/dL)	161 (146-178)	155 (142-180)	0.434
FSH (IU/L)	5.50 (4.55-6.77)	5.00 (4.50-7.30)	0.614
LH (IU/L)	5.55 (3.90-12.07)	5.00 (3.80-7.00)	0.185
Serum estradiol (pg/mL)	48.50 (35.75-67.25)	96 (54.30-125)	<0.001
Total testosterone (ng/dL)	64.88 (47.28-85.33)	31.60 (23.00-35.00)	<0.001
Ferriman-Gallway score	14 (12-16.75)	7 (6-8)	<0.001
Systolic blood pressure (mmHg)	115 (100-130)	100 (95-120)	0.001
Diastolic blood pressure (mmHg)	75 (70-80)	70 (65-80)	0.052

*Since it does not show normal distribution, all data are expressed as median (interquartile range).
** mean
BMI; Body mass index, HOMA-IR; homeostasis model assessment of insulin resistance, FSH; follicle-stimulating hormone, LH; luteinizing hormone, HDL; high-density lipoprotein, LDL; low-density lipoprotein, TG; triglyceride

Table 2. Serum endocan levels were compared between groups according to body mass index.

	Endocan (ng/L)			
	Normal (BMI<25 kg/m2)	**Overweight (BMI=25-29.99kg/m2)**	**Obese (BMI≥30 kg/m2)**	**p value**
Control*	**311.42** (218.00-448.21) (n= 46)	**376.64** (284.51-510.60) (n= 13)	- - (n= 0)	0.149
PCOS*	**413.39** (313.20-599.41) (n= 21)	**454.75** (344.29-547.52) (n= 17)	**424.05** (356.43-580.72) (n= 14)	0.923

*Results for continuous variables were expressed as medians and interquartile ranges.
PCOS; Polycystic ovary syndrome, BMI; Body mass index

Table 3. Correlation analysis between serum endocan level and other cardiovascular risk factors.

	r value	p value
BMI	0.154	0.107
Waist circumference	0.172	0.072
Hip circumference	0.169	0.076
HOMA-IR	0.276	0.003
FGS	0.236	0.013
TG	0.053	0.579
HDL	-0.195	0.041
LDL	0.008	0.933
Total testosterone	0.022	0.826
Systolic blood pressure	0.077	0.423
Diastolic blood pressure	0.081	0.397

BMI; Body mass index, HOMA-IR; homeostasis model assessment of insulin resistance, FGS; Ferriman-Gallwey skoru, HDL; high-density lipoprotein, LDL; low-density lipoprotein, TG; triglyceride

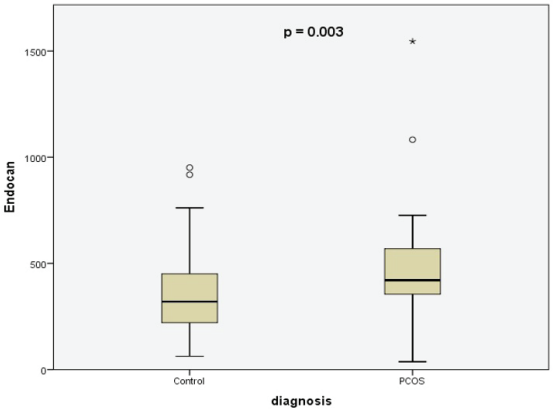


Figure 1. Serum endocan levels of PCOS and control groups are shown schematically.

DISCUSSION

In our study, as expected, serum endocan level was found higher in PCOS patients than healthy control group with similar age distribution. However, endocan level did not change with the increase of BMI in both the PCOS group and the control group. This result is inconsistent with some studies showing the relationship between PCOS and endocan. In a study, it was found that PCOS patients had higher endocan levels than healthy control group, and it was reported that the endocan level decreased with increasing BMI.[1] This is actually a contradictory result showing that Endocan and the severity of obesity act in the opposite direction rather than together. However, there are studies showing that endocan and BMI are positively correlated in PCOS patients.[2]

Obesity is a traditionally known increased cardiovascular mortality risk factor.[24] In our study, the median baseline BMI level of PCOS patients was higher than the control group. However, no correlation was found between endocan and BMI regardless of the group. These results indicate that the inflammation associated with endothelial dysfunction in PCOS patients is caused by reasons other than obesity.

Endocan is now accepted as a marker of inflammation that is associated with endothelial dysfunction.[15,25] At the same time, there are studies showing that there is endothelial dysfunction in PCOS.[26,27] Therefore, studies investigating the relationship between PCOS and cardiovascular disease and mortality have been conducted.[4] In these studies, no relationship was found between cardiovascular mortality and PCOS diagnostic criteria such as menstrual irregularity and anatomical ovarian changes, but a positive relationship was found with hyperandrogenism. However, some risk factors such as obesity, dyslipidemia, insulin resistance, waist circumference, hip circumference and arterial hypertension have been shown to be associated with cardiovascular disease, although they are not among the diagnostic criteria of PCOS.[4,28,29]

In our study, almost all of these cardiovascular risk factors show a negative change in the PCOS group compared to the control group, only HOMA-IR showed a positive correlation with endocan among these differences. In the current study, selected PCOS patients were young, and many of the risk factors mentioned above may not have contributed to endothelial dysfunction, which is an important part of the development of cardiovascular disease. Insulin resistance is a risk factor that prepares and contributes to the development of subclinical atherosclerosis, which is an early stage indicator of endothelial dysfunction.[30] A positive correlation between HOMA-IR and serum endocan level has also been shown.[2] Therefore, the correlation between serum endocan and only HOMA-IR among the risk factors may be related with the early stage of endothelial dysfunction.

This study has some limitations. The first of these is the small number of PCOS patients and the lack of information about the PCOS phenotype. Second, the case-control randomization according to BMI was not done correctly and BMI of groups did not match. As the last limitation, high-sensitivity C-reactive protein (hs-CRP) was not evaluated in our study.

In conclusion, serum endocan levels are higher in PCOS patients, in line with the literature. Endocan level shows a significant correlation with insulin resistance, one of the metabolic parameters. This may be a sign of early endothelial dysfunction in PCOS.

Conflict of Interest

There is no conflict of interest to be declared.

Authors' contributions

All authors contributed to this project and article equally. All authors readand approved the final manuscript.

Funding

This research received no grant from any funding agency

in the public, commercial or not-for-profit sectors.

This study was evaluated by the Clinical Research Ethics Committee of Health Sciences University Yıldırım Beyazıt Dışkapı Training and Research Hospital and was approved with the decision number 24/30, dated 30.06.2015.

References

1. *Delibas IB, Yapca OE, Laloglu E. Does endocan level increase in women with polycystic ovary syndrome? A case - control study. Ginekol Pol 2018; 89 (9):500-505.*
2. *Bicer M, Guler A, Unal Kocabas G, Imamoglu C, Baloglu A, Bilgir O, et al. Endocan is a predictor of increased cardiovascular risk in women with polycystic ovary syndrome. Endocr Res 2017; 42 (2):145-153.*
3. *Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab 2004; 89 (6):2745-2749.*
4. *Carmina E, Lobo RA. Is There Really Increased Cardiovascular Morbidity in Women with Polycystic Ovary Syndrome? J Womens Health (Larchmt) 2018; 27 (11):1385-1388.*
5. *Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, et al. Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood. New England Journal of Medicine 2016; 374 (25):2430-2440.*
6. *Ganie MA, Hassan S, Nisar S, Shamas N, Rashid A, Ahmed I, et al. High-sensitivity C-reactive protein (hs-CRP) levels and its relationship with components of polycystic ovary syndrome in Indian adolescent women with polycystic ovary syndrome (PCOS). Gynecological Endocrinology 2014; 30 (11):781-784.*
7. *Diamanti-Kandarakis E, Alexandraki K, Protogerou A, Piperi C, Papamichael C, Aessopos A, et al. Metformin administration improves endothelial function in women with polycystic ovary syndrome. Eur J Endocrinol 2005; 152 (5):749-756.*
8. *De Freitas Caires N, Legendre B, Parmentier E, Scherpereel A, Tsicopoulos A, Mathieu D, et al. Identification of a 14 kDa endocan fragment generated by cathepsin G, a novel circulating biomarker in patients with sepsis. J Pharm Biomed Anal 2013; 78-79:45-51.*
9. *Diamanti-Kandarakis E, Paterakis T, Alexandraki K, Piperi C, Aessopos A, Katsikis I, et al. Indices of low-grade chronic inflammation in polycystic ovary syndrome and the beneficial effect of metformin. Human Reproduction 2006; 21 (6):1426-1431.*
10. *Samy N, Hashim M, Sayed M, Said M. Clinical significance of inflammatory markers in polycystic ovary syndrome: Their relationship to insulin resistance and Body Mass Index. Disease Markers 2009; 26:163-170.*
11. *Diamanti-Kandarakis E, Spina G, Kouli C, Migdalis I. Increased endothelin-1 levels in women with polycystic ovary syndrome and the beneficial effect of metformin therapy. J Clin Endocrinol Metab 2001; 86 (10):4666-4673.*
12. *Kao YH, Chiu WC, Hsu MI, Chen YJ. Endothelial progenitor cell dysfunction in polycystic ovary syndrome: implications for the genesis of cardiovascular diseases. Int J Fertil Steril 2013; 6 (4):208-213.*
13. *Paradisi G, Steinberg HO, Hempfling A, Cronin J, Hook G, Shepard MK, et al. Polycystic ovary syndrome is associated with endothelial dysfunction. Circulation 2001; 103 (10):1410-1415.*
14. *Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab 1999; 84 (1):165-169.*
15. *Celik T, Balta S, Karaman M, Ahmet Ay S, Demirkol S, Ozturk C, et al. Endocan, a novel marker of endothelial dysfunction in patients with essential hypertension: comparative effects of amlodipine and valsartan. Blood Press 2015; 24 (1):55-60.*
16. *Mihajlovic DM, Lendak DF, Brkic SV, Draskovic BG, Mitic GP, Novakov Mikic AS, et al. Endocan is useful biomarker of survival and severity in sepsis. Microvascular Research 2014; 93:92-97.*
17. *Balta S, Mikhailidis DP, Demirkol S, Ozturk C, Celik T, Iyisoy A. Endocan: A novel inflammatory indicator in cardiovascular disease? Atherosclerosis 2015; 243 (1):339-343.*
18. *Lee W, Ku S-K, Kim S-W, Bae J-S. Endocan Elicits Severe Vascular Inflammatory Responses In Vitro and In Vivo. Journal of Cellular Physiology 2014; 229 (5):620-630.*
19. *Adekola H, Romero R, Chaemsaithong P, Korzeniewski SJ, Dong Z, Yeo L, et al. Endocan, a putative endothelial cell marker, is elevated in preeclampsia, decreased in acute pyelonephritis, and unchanged in other obstetrical syndromes. The Journal of Maternal-Fetal & Neonatal Medicine 2015; 28 (14):1621-1632.*
20. *Laloglu E, Kumtepe Y, Aksoy H, Topdagi Yilmaz EP. Serum endocan levels in endometrial and ovarian cancers. Journal of Clinical Laboratory Analysis 2017; 31 (5):e22079.*
21. *Hatch R, Rosenfield RL, Kim MH, Tredway D. Hirsutism: Implications, etiology, and management. American Journal of Obstetrics and Gynecology 1981; 140 (7):815-830.*
22. *Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2013;98(12):4565-92. (In eng). DOI: 10.1210/jc.2013-2350.*
23. *Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19 (1):41-47.*
24. *Chen Y, Copeland WK, Vedanthan R, Grant E, Lee JE, Gu D, et al. Association between body mass index and cardiovascular disease mortality in east Asians and south Asians: pooled analysis of prospective data from the Asia Cohort Consortium. BMJ : British Medical Journal 2013; 347:5446.*
25. *Aparci M, Isilak Z, Uz O, Yalcin M, Kucuk U. Endocan and Endothelial Dysfunction. Angiology 2015; 66 (5):488-489.*
26. *Rajendran S, Willoughby SR, Chan WPA, Liberts EA, Heresztyn T, Saha M, et al. Polycystic ovary syndrome is associated with severe platelet and endothelial dysfunction in both obese and lean subjects. Atherosclerosis 2009; 204 (2):509-514.*
27. *Rostamtabar M, Esmaeilzadeh S, Tourani M, Rahmani A, Baee M, Shirafkan F, et al. Pathophysiological roles of chronic low-grade inflammation mediators in polycystic ovary syndrome. Journal of Cellular Physiology 2021; 236 (2):824-838.*
28. *Glintborg D, Rubin KH, Nybo M, Abrahamsen B, Andersen M. Cardiovascular disease in a nationwide population of Danish women with polycystic ovary syndrome. Cardiovasc Diabetol 2018; 17 (1):37.*
29. *Studen KB, Pfeifer M. Cardiometabolic risk in polycystic ovary syndrome. Endocrine Connections 2018; 7 (7):R238.*
30. *Randrianarisoa E, Lehn-Stefan A, Hieronimus A, Rietig R, Fritsche A, Machann J, et al. Visceral Adiposity Index as an Independent Marker of Subclinical Atherosclerosis in Individuals Prone to Diabetes Mellitus. Journal of Atherosclerosis and Thrombosis 2019; 26 (9):821-834.*

RESEARCH ARTICLE / *Araştırma Makalesi*

The Effects of Undergraduate Nursing Education in Diagnosing the Symptoms of Child Abuse and Neglect

Hemşirelik Lisans Eğitiminin Çocuk İstismar ve İhmalinin Belirtilerinin Teşhisine Etkileri

Mert Kartal[1], Muhammet Bayraktar[2]

[1] Harran University, Faculty of Health Sciences, Public Health Nursing Department, Şanlıurfa
[2] Niğde Ömer Halisdemir University, Faculty of Medicine, Public Health Department, Niğde

Yazışma Adresi / *Correspondence:*
Muhammet Bayraktar

Niğde Ömer Halisdemir Üniversitesi Merkez Yerleşkesi, Tıp Fakültesi Bor Yolu Üzeri 51240 Merkez/NİĞDE
T: **+90 388 225 60 50** E-mail **: drmbayraktar@gmail.com**

Geliş Tarihi / Received : **27.09.2020** Kabul Tarihi / Accepted : **01.02.2021**

Orcid :

Mert Kartal https://orcid.org/0000-0001-7840-7554
Muhammet Bayraktar https://orcid.org/0000-0002-2242-8046

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):162-169) DOI: 10.31832/smj.800669**

Abstract

Objective	Health professionals are expected to properly identify all the four dimensions of child abuse that are discussed as physical, sexual, emotional abuse, and neglect. This study was conducted to measure the impact of education given in the nursing department on the knowledge level of students about child neglect and abuse and to identify areas that require intervention.
Materials and Methods	The population of this study is 425 students studying in all four grades of the nursing department.A sample was not determined, those who volunteered to participate and completed the questionnaire forms of the study were included (n=313, 74%). A questionnaire form for socio-demographic information and scale by Uysal were used to collect data. Statistical Package for the Social Sciences programme was used for data analysis.
Results	Of the participants 64.9% were female and 74.4% did not want to receive an education on the topic. The mean total scale score was 244.92 ± 22.96 and the mean response to the items in the scale was 3.65. Compared with male students (3.59 ± 0.34), the mean score of female students (3.68 ± 0.33) was significantly higher (p = 0.020). Compared with other grades, the mean score of fourth grade students was significantly higher (p < 0.001).
Conclusion	In the nursing education curriculum, topics related to child abuse and neglect should be included in each year. Higher participation of male students in these trainings should be ensured. Further studies on this topic should be conducted with students.
Keywords	Undergraduate Education; Nursing; Student; Child Abuse; Neglect

Öz

Amaç	*Sağlık çalışanlarının çocuk istismarının fiziksel, cinsel, duygusal istismar ve ihmal olarak tartışılan dört boyutunu da doğru bir şekilde tanımlamaları beklenir. Bu araştırma, hemşirelik bölümünde verilen eğitimin öğrencilerin çocuk ihmali ve istismarı konusundaki bilgi düzeylerine etkisini ölçmek ve müdahale gerektiren alanları belirlemek amacıyla yapılmıştır.*
Gereç ve Yöntemler	*Bu çalışmanın evreni, hemşirelik bölümünün dört sınıfında öğrenim gören 425 öğrencidir. Örneklem belirlenmemiş, çalışmaya katılmaya gönüllü olan ve anket formlarını dolduranlar dahil edilmiştir (n=313,%74). Veri toplamak için Uysal tarafından hazırlanan sosyo-demografik bilgiler için anket formu ve ölçek, verilerin analizinde Sosyal Bilimler için İstatistik Paketi programı kullanılmıştır.*
Bulgular	*Katılımcıların%64,9'u kadındıve%74,4'ü konuyla ilgili eğitim almak istemiyordu. Ortalama toplam ölçek puanı 244,92 ± 22,96 ve ölçekteki maddelere verilen yanıtların ortalama puanı 3,65'tir. Erkek öğrencilerle karşılaştırıldığında (3,59±0,34), kız öğrencilerin ortalama puanı (3,68±0,33) anlamlı olarak daha yüksektir (p=0,020). Diğer sınıflarla karşılaştırıldığında, dördüncü sınıf öğrencilerinin ortalama puanları anlamlı olarak daha yüksektir (p <0,001).*
Sonuç	*Hemşirelik eğitimi müfredatında her yıl çocuk istismarı ve ihmali ile ilgili konulara yer verilmelidir. Erkek öğrencilerin bu eğitimlere daha fazla katılımı sağlanmalıdır. Bu konuyla ilgili öğrencilere yönelik daha ileri çalışmalar yapılmalıdır.*
Anahtar Kelimeler	*Lisans Eğitimi; Hemşirelik; Öğrenci; Çocuk İstismarı; İhmal*

INTRODUCTION

Defined as the physical, psychological and social development and health of the child being negatively affected by the deliberate or unintentional behaviours of an adult, child abuse is discussed in four dimensions as physical, sexual, emotional abuse and neglect.[1,2]

In a review of various studies in Turkey, it has been reported that research on child abuse and neglect is being conducted for 20 years; the rate of physical abuse in society is between 15% and 75%, whereas the rate of sexual abuse is approximately 20%.[3] Similar studies carried out abroad have shown that abuse is more common in children of low-income families regardless of race, and children are exposed to both sexual and physical abuse at an age earlier than previously reported.[4] It takes time to realise that some practices and behaviours exhibited by the society and individuals can negatively affect the development of the child, which in other wordsis defined as neglect and abuse. This includes examples over a broad spectrum from the severe methods that try to change the behaviour of children using violence under the name of upbringing, to shocking behaviours such asparents leaving their children in cash or coin-operated lockers when they have errands to do in public places.[5] Such examples of the fact that such an unpleasant and unacceptable situation as child neglect and abuse (CNaA) is usually done by those closest to the child give us clues about how difficult it is to identify them and therefore eliminate the associated negative effects and traumas.[6]

Because of the fact that the applicable law requires notification when signs ofCNaA are detected, it has been reported that members of professional groups such as health workers, social workers, educators, etc,have begun to be more careful and attentive in this regard.[7] However, a recent literature review showed that due to the inability of health professionals to detect findings ofCNaA, there are still serious shortcomings in the notification and registration of such cases[8]. Studies conducted in different provinces at different times show that the ratio of thosereceiving pre-graduation and post-graduation training on this subjectvaries from 27% to 70% and from 6% to 83%, respectively, thereby indicating that the training received by health professionalson this topic should be furtherstandardised.[9-13]

For these reasons, this study was planned and conducted to measure the impact of standard education given in the nursing department, where the children are most open to learning and learning opportunities are the most plentiful, on the knowledge level of students about CNaA and to identify areas that require intervention.

MATERIALS and METHODS

Thisdescriptive study was conducted between January 2018 and April 2018 and the population of this study comprised 425 students studying in the first, second, third and fourth grades of the Nursing Department of Harran University Faculty of Health Sciences. In addition, a sample was not determined, all the 313 students (74%) those who volunteered to participate in the study and completed the questionnaire forms prepared within the scope of the study were included in the study.

An 11-itemsocio-demographic questionnaire form and 'Diagnosis of Symptoms and Risks of Child Abuse and Neglect (DSRCAN) Scale' was used to collect data.DSRCAN is a 67-item Likert-type scale. Its validity and reliability studies were conducted by Uysal.9The Cronbach's alpha value of the scale is 0.92. Out of 67 questions on the scale, 46 are scored as:'completely agree' five points, 'agree' four points, 'undecided' three points, 'disagree' two points and'completely disagree'one point. The remaining 21 items are scored in reverse. When calculating total scale and subscale scores, arithmetic average obtained by dividing the total score obtained by collecting the points from the questions of the related category by the number of questions in that category was used. The maximum score is 335. Arithmetic average approaching five means that the

questions have been answered correctly, and approaching one means that they have beenanswered incorrectly.[9]

Study data were analysed using IBM SPSS Statistics for Windows, version 16 (IBM Corp., Armonk, NY, USA) package program. Descriptive characteristics were evaluated by number, percentage and average.The distribution of the data was analyzed using the Kolmogorov Simirnov Z test and data conform to normal distribution.Independent samples T-test and analysis of variance tests were used to determine the relationship between descriptive characteristics and DSRCAN mean scores.Statistical significance level was takenat 0.05 in all tests.

The study was conducted with approval from the Harran University Faculty of Medicine Ethics Board dated 07.12.2017 and numbered 12/07 and the institution permit. An informed consent form was signed by all the participants before enrollment in the study.

RESULTS

Table 1 compares the socio-demographic characteristics of the students with the mean score they received from the scale. The meanscore of female students was 3.68 and it was higher than that of male students' 3.59.This difference was statistically significant (p=0.020). Scale scores were compared with respect to number of siblings, parents' education status, economic status and place of residence, and no significant relationship was found (p>0.05). When the willingnessof students to receive education related to CNaA was evaluated, it was found that the total score of those who wanted to receive education was higher than those who did not want to receive education. This difference was also statistically significant (p<0.001).

Table 2 shows the mean scores of students from the scale according to their grade. Fourth graders had the highest mean scores with 3.83 points and second graders had the lowest mean scores with3.56 points. The difference between the mean scores received by studentsin different grades was statistically significant (p<0.001).

Table 3 shows the subscale scores received by students in different grades. It was found that the scores obtained in recognition of physical signs of child abuse, knowing the behavioural symptoms related to child abuse, recognition of characteristics of parents prone to neglect and abuse, knowing the characteristics of children prone to neglect and abuse, and knowing family characteristics in CNaA sub-dimensions were significantly different with respect to the grade of the students, and fourth graders received the highest scores (p<0.05). The scores obtained in recognisingthe symptoms of neglect on the child sub-dimension were not significantlydifferent with respect to the grade of the students(p>0.05).

Table 4 shows the mean scoresof those obtained in DSRCAN sub-dimensions. Mean score of 'recognising the physical signs of abuse on the child' sub-dimension was 72.08. Mean score of'knowingthe behavioural symptoms related to child abuse'sub-dimension was 56.15. Mean score of 'recognising the signs of neglect on the child' sub-dimension was 27.21. Mean score of'recognition of characteristics of patients prone to neglect and abuse' sub-dimension was 41.23. Mean score of 'knowing the characteristics of children prone to neglect and abuse' sub-dimension was 18.39. Mean score of'knowing family characteristics in child neglect and abuse' sub-dimension was 29.34.

Table 5 shows the item response averages in DSRCAN sub-dimensions. The highest item response was obtained for the 'recognising the symptoms of neglect on the child'sub-dimensionwith an average of 3.88 points, while the lowest item responsewas obtained for the'recognising characteristics of parents prone to abuse and neglect' sub-dimensionwith an average of 3.17 points. The item response average for the entire scale was 3.65 points.

Table 1. Comparison of students' socio-demographic characteristics and mean DSRCAN scores

Characteristics	**n**	**%**	**Mean scale score (Mean ± SD)**	**Test**	**p**
Gender					
Male	110	35.1	3.59±0.34	t=-2.336	0.020
Female	203	64.9	3.68±0.33		
Total	313	100	3.65±0.34		
Number of siblings					
1-3	31	9.9	3.58±0.22	F=789	0.455
4-5	79	25.2	3.66±0.36		
6 and more	203	64.9	3.66±0.34		
Mother's education status					
Illiterate	176	56.2	3.64±0.32	F=2.297	0.078
Literate	33	10.5	3.71±0.42		
Primary school	66	21.1	3.71±0.32		
Secondary school and above	38	12.2	3.54±0.34		
Father's education status					
Illiterate	30	9.6	3.58±0.23	F=0.469	0.759
Literate	39	12.5	3.63±0.38		
Primary school	113	36.1	3.67±0.31		
Secondary school	62	19.8	3.66±0.37		
High school and above	69	22.0	3.65±0.37		
Economic status					
Bad	32	10.2	3.65±0.38	F=0.079	0.924
Middle	218	69.6	3.66±0.33		
Good	63	20.2	3.64±0.34		
Place of residence					
Rural	77	24.6	3.66±0.34	t=0.370	0.711
Urban	236	75.4	3.65±0.34		
Willingness to receive education related to CNaA					
Yes	80	25.6	3.81±0.32	t=5.064	**<0.001**
No	233	74.4	3.60±0.33		

DSRCAN=Diagnosis of Symptoms and Risks of Child Abuse and Neglect
CNaA=Child Neglect and Abuse
t=Independent sample t test
F=One Way Anova test

Table 2. Comparison of mean scale scores according to grade of the students

Year of study	**n**	**%**	**Mean scale score (Mean ± SD)**	**Test**	**p**
First grade	103	32.9	3.61±0.32	F=10.652	**<0.001***
Second grade	64	20.4	3.56±0.32		
Third grade	71	22.7	3.60±0.34		
Fourth grade	75	24.0	3.83±0.31		

Table 3. Subscalescores according to the grade of the students

Subscale groups	Year of study	n	%	Main subscale score (Mean ± SD)	Test	p
Recognition of physical signs of child abuse	1st grade	103	32.9	3.74±0.32	**F=8.439**	**<0.001**
	2nd grade	64	20.4	3.70±0.39		
	3rd grade	71	22.7	3.73±0.43		
	4th grade	75	24.0	3.98±0.40		
Knowing the behavioural symptoms related to child abuse	1st grade	103	32.9	3.74±0.38	**F=5.619**	**0.001**
	2nd grade	64	20.4	3.61±0.40		
	3rd grade	71	22.7	3.70±0.47		
	4th grade	75	24.0	3.88±0.31		
Recognising the symptoms of neglect on the child	1st grade	103	32.9	3.90±0.64	F=1.000	0.393
	2nd grade	64	20.4	3.81±0.63		
	3rd grade	71	22.7	3.84±0.68		
	4th grade	75	24.0	3.97±0.49		
Recognition of characteristics of parents prone to neglect and abuse	1st grade	103	32.9	3.12±0.42	**F=4.485**	**0.004**
	2nd grade	64	20.4	3.10±0.39		
	3rd grade	71	22.7	3.14±0.40		
	4th grade	75	24.0	3.31±0.37		
Knowing the characteristics of children prone to neglect and abuse	1st grade	103	32.9	3.60±0.65	**F=4.682**	**0.003**
	2nd grade	64	20.4	3.60±0.52		
	3rd grade	71	22.7	3.61±0.63		
	4th grade	75	24.0	3.91±0.62		
Knowing family characteristics in CNaA	1st grade	103	32.9	3.62±0.61	**F=10.681**	**<0.001**
	2nd grade	64	20.4	3.63±0.60		
	3rd grade	71	22.7	3.60±0.64		
	4th grade	75	24.0	4.07±0.54		

Table 4. DSRCAN sub-dimension total scores

Subscales (N=313)	Mean	SD
Recognition of physical signs of child abuse	72.08	7.57
Knowing the behavioural symptoms related to child abuse	56.15	6.07
Recognising the symptoms of neglect on the child	27.21	4.34
Recognition of characteristics of parents prone to neglect and abuse	41.23	5.29
Knowing the characteristics of children prone to neglect and abuse	18.39	3.16
Knowing family characteristics in CNaA	29.84	5.07

Table 5. Item response averages of DSRCAN sub-dimensions

Subscales (N=313)	Mean	SD
Recognition of physical signs of child abuse	3.79	0.39
Knowing the behavioural symptoms related to child abuse	3.74	0.40
Recognising the symptoms of neglect on the child	3.88	0.62
Recognition of characteristics of parents prone to neglect and abuse	3.17	0.40
Knowing the characteristics of children prone to neglect and abuse	3.67	0.63
Knowing family characteristics in CNaA	3.73	0.63
Scale's total	3.65	0.34

DISCUSSION

Child abuse and neglect is a violation of the fundamental human rights of a child and is one of the most critical issues that occupy the international human rights agenda.[14] This study was conducted to determine the effects of nursing undergraduate education on the level of knowledge in diagnosing the symptoms and risks of child abuse and neglect. The average total score of students from DSR-CANwas 244.92 and the average item response was 3.65. The highest item response average was obtained for the 'recognising the symptoms of neglect on the child' sub-dimension with 3.88 points, and the lowest item response average was obtained for the 'recognising characteristics of parents prone to abuse and neglect' sub-dimension with 3.17 points. Over a full score of 5.00, the students'over all knowledge level was intermediate with an average of 3.65 points. In the literature, limited studies on students have emphasised that they have insufficient knowledge of child abuse and neglect.[14-16]

In the present study, knowledge level of female students on CNaA was significantly higher than that of male students. Consistent with our results, literature data show that women have a higher level of knowledge about child abuse and neglect than men.[15-18] Burç stated that being a daughter was a risk factor for abuse and neglect, whereas Bozkurt et al. conducted a study onmidwifery students at a college-and reported that 40.6% of students had been exposed to domestic violence. Worldwide, girls are exposed to more abuse and neglect than boys.[19,20] They are therefore more sensitive about this issue, which may be the reason why female students' knowledge level of CNaA was higher than that of male students.

Scale scores were compared according to the number of siblings, parents' education status, economic status and place of residence, and no statistically significant relationship was found ($p>0.05$). In their study on nursing students, Seferoğluet al. found that students whoseparents-were secondary school graduates and above, whose family had more economic income than expenses, who had a nuclear familyand had children had higher CNaA knowledge level, but the difference between groups was insignificant[15]. Unlike our study, it is reported in the literature that low level of education of parents and family income,in addition to an extended family structure increases the risk of CNaA.[21,22] It is believed that this is due to the differences in the regions where the studies are conducted, and therefore the differences in students'cultural perception of violence and knowledge and experience related to abuse.

When the willingness of students to receive education related to CNaA was evaluated, it was found that the mean score of those who wanted to receive education was higher than those who did not want to. This difference was also statistically significant ($p<0.001$). A study on the awareness levels of health care professionals about CNaA emphasises the necessity of organising trainings on this subject to increase their awareness.[23] In their study, Duman et al. stated that the awareness and sensitivity of the health care professionals could be increased with training on violence, and the education of the health care professionals on violence could improve their thoughts and attitudes.[24] We believe that students who wanted to receive education on CNaAwere more active in the trainings on related subjects that were provided previously and therefore the higher level of knowledge compared with those who did not want to receive education on CNaAwas an expected situation.

The mean scores of the students were compared according to their grade. Fourth graders had the highest mean scores, whereas second graders had the lowest meanl scores. The difference between the mean scores according to the grade of the studentswas statistically significant as seen from Table 2. It was found that the scores obtained in recognition of physical signs of child abuse, knowing the behavioural symptoms related to child abuse, recognition of characteristics of parents prone to neglect and abuse, knowing the characteristics of children prone to neglect and abuse, and knowing family characteristics in CNaA sub-dimensions

were significantly different with respect to the grade of the students, and fourth graders received the highest scores according to Table 3. In another study on health workers, it was reported that participants stating that they have received information about child abuse during their education received higher scores in the 'characteristics of parents prone to abuse and neglect'sub-dimension compared with those stating otherwise.[12]

In the study by Poreddiet al. on the knowledge level of nursing students about CNaA, it was found that fourth grade nursing students had higher knowledge levels[14]. Similar studies also found that students' experience and seniority increased their level of knowledge about child abuse.[25,26] Senior nursing students take paediatric nursing and public health nursing courses in third and fourth grades and take more applied courses by that time compared with other grades, which may be a factor for the higher knowledge level.

Conclusion

There are limited studies in the literature on the knowledge level of nursing students about child abuse and neglect. The results of the present study can be summarised as follows: The students who participated in the present study did not have enough knowledge about child abuse and neglect, knowledge level of those who wanted to obtain information about child abuse and neglect and of female studentswere higher than others and senior students received higher scores onboth the overall DSRCAN scale and its sub-dimensions.It was also found that undergraduatenursing education increases students' knowledge levels about child abuse and neglect.

In line with these results, topics related to child abuse and neglect should be included in the nursing education curriculum for each year, higher participation of male students in these trainings should be ensured, and necessary reinforcing repetitions should be conducted. Further, similar studies on this topic should be conducted with nursing students in different regions and cultures.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest Disclosures

The authors have no conflicts of interest

Ethical Issues

The study was conducted with approval from the Harran University Faculty of Medicine Ethics Board dated 07.12.2017 and numbered 12/07. An informed consent form was signed by all the participants before enrollment in the study.

References

1. *Dubowitz H. Preventing child neglect and physical abuse: a role for pediatricians. Pediatr Rev. 2002; 23:191-6.*
2. *Balci E, Gun I, Sarli SM, Akpinar F, Yagmur F, Ozturk A, et al. Still an unknown topic: child abuse and "shaken baby syndrome". Turkish Journal of Trauma and Emergency Surgery. 2011; 17:430–4. doi:10.5505/tjtes.2011.23427*
3. *HelvacıÇelik F, Hocaoğlu Ç. Childhood Traumas: A Review [Turkish]. Sakarya Med J. 2018; 8(4): 695-711.*
4. *Jones ED, Mccurdy R. The Link Between Types of Maltreatment and Demographic Characterictics of Children. Child Abuse and Neglect. 1992; 16(2): 201- 15.*
5. *Kouno A, Johnson CF. Child abuse and neglect in Japan: Coin-operated-locker babies. Child Abuse & Neglect. 1995; 19: 25–31. doi:10.1016/0145-2134(94)00108-7*
6. *Yılmaz G, İşiten N, Ertan Ü, Öner A. Child abuse: a case report [Turkish]. ÇocukSağlığıveHastalıklarıDergisi. 2003; 46: 295-8.*
7. *Showers J, Johnson CF. Child Development, Child Health and Child Rearing Knowledge among Urban Adolescents: Are They Adequately Prepared for the Challenges of Parenthood? Health Education. 1985; 16:37–41. doi:10.1080/00970050.1985.10615875*
8. *Bakır E, Kapucu S. Reflection of Child Neglect and Abuse to Researches In Turkey: A Literatüre Review [Turkish]. Journal of Hacettepe University Faculty of Nursing. 2017; 4(2): 13–24.*
9. *Uysal A. Determining the Knowledge Levels of Nurses and Midwives in Diagnosing the Symptoms and Risks of Child Abuse and Neglect [Turkish] (Master Thesis). Ege University, Turkey; 1998.*
10. *Kocaer Ü. Levels of awareness in doctors and nurses regarding child abuse and neglect [Turkish] (Master Thesis). Marmara University, Turkey; 2006.*
11. *Demir H. The knowledge, awareness and attitude of physicans working in family health centres in Edirne on child abuse and neglect [Turkish] (Speciality Thesis). Trakya University, Turkey; 2012.*
12. *Gölge ZB, Hamzaoğlu N, Türk B. Assesment of medical staff awareness about child abuse and neglect. Turkish Journal of Forensic Medicine. 2012; 26(2): 86–96.*
13. *Türker G. Levels of awareness in family doctors, nurses and midwifes regarding child abuse and neglect: sample of Burdur [Turkish] (Master Thesis). Selçuk University, Turkey; 2017.*
14. *Poreddi V, Pashapu DR, Kathyayani B, Gandhi S, El-ArousyW, Math SB. Nursing students' knowledge of child abuse and neglect in India. British Journal of Nursing. 2016; 25(5): 264-8. doi: 10.12968/bjon.2016.25.5.264*
15. *GüdekSeferoğluE, Sezici E, Yiğit D. Nursing Students' Level of the Diagnosing Symptoms and Risks of Child Abuse and Neglect [Turkish]. OPUS– International Journal of Society Researches. 2019; 10(17): 257-76. doi: 10.26466/opus.511405*
16. *AkgünKostak M,Vatansever C. Views and opinions of faculty of health sciences students about child abuse and neglect [Turkish]. Journal Of Health Science and Professions. 2015; 2(1): 1-11. doi: 10.17681/hsp.79915*
17. *Burç A,GüdücüTüfekçi F. Occurance of diagnosis by nurses of symptoms and risks of child abuse and neglect [Turkish]. AcıbademÜniversitesiSağlıkBilimleriDergisi. 2015; 6(3): 144-51.*
18. *Pakiş I, Demir F, Bektas G, Altun U,Yıldırım S. Investigation of the awareness and knowledge about child abuse and negligence among doctors and nurses working in the east part of Turkey. Romanian Journal of Legal Medicine. 2015; 23(2): 151-6. doi: 10.4323/rjlm.2015.151*
19. *Bozkurt ÖD, Daşıkan Z, Kavlak O, Şirin A. Determination of the knowledge, opinions and professional attitudes of midwifery students about violence during pregnancy. Balikesir Health Sciences Journal. 2013; 2(2): 99-107.*
20. *BurçA . The Level of Diagnosis of the Symptoms and Risks of the Child Abuse and Neglect of the Nurses (PhD thesis). Atatürk University, Turkey; 2014.*
21. *Kurt G, Dönmez S, Eren Ö, Balcı E, Günay O. The university last year students' perceptions of abuse, neglect and domestic violence; who are studying at three different sections. Journal of International Social Research. 2017; 10(50): 405-14.*
22. *Sinan Ö, Tosun B, Ünal N. Perspectives of nursing students on violence. TurkiyeClinics Psychiatric Nursing-Special Topics. 2017; 3(2): 108-14.*
23. *Uncu F, Oğuzöncül F. Health care workers' who work in the province of Elazig levels of awareness about child abuse and neglect, and the factors affecting. International Journal of Medical Investigation. 2013; 2(3): 129-42.*
24. *Duman ZÇ, Özdağ Ş, Özcan A. The opinions of nurse students on the subject of the effect of violence in the family on the child. Atatürk Üniv. HemşirelikYüksekokuluDergisi. 2003; 2: 50-6.*
25. *Adams B. Assessment of child abuse risk factors by advanced practice nurses. J PediatrNurs. 2005; 31(6): 498–502.*
26. *Elarousy W, Houaida H, Louise V. Child abuse and neglect: student nurses' knowledge and attitudes. J Am Sci. 2012; 8(7): 665–74.*

ARAŞTIRMA MAKALESİ / *Research Article*

Yara Kültürlerinden İzole Edilen Mikroorganizmalar ve Antibiyotik Duyarlılıkları

Microorganisms Isolated from Wound Cultures and their Antibiotic Susceptibilities

Hacer Yerlikaya[1], Özlem Kirişci[1], Merve Çilburunoğlu[1], Hacer Uğurlu[1], Murat Aral[1], Gürkan Muratdağı[2]

[1] Sütçü İmam Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Kahramanmaraş
[2] Sakarya Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Sakarya

Yazışma Adresi / *Correspondence:*
Gürkan Muratdağı

Sakarya Üniversitesi Tıp Fakültesi, Aile Hekimliği A.D, Sakarya
T: **+90 533 094 63 33** E-mail **: drgm54@gmail.com**

Geliş Tarihi / Received : **12.11.2020** Kabul Tarihi / Accepted : **01.02.2021**

Orcid :
Hacer Yerlikaya https://orcid.org/0000-0002-6347-5527
Özlem Kirişci https://orcid.org/0000-0003-4784-8183
Merve Çilburunoğlu https://orcid.org/0000-0001-8627-7366
Hacer Uğurlu https://orcid.org/0000-0001-6126-5502
Murat Aral https://orcid.org/0000-0002-3576-4380
Gürkan Muratdağı https://orcid.org/0000-0002-9629-3973

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):170-176) DOI: 10.31832/smj.824924**

Öz

Amaç Bu çalışmada, Ocak 2018-Ocak 2019 tarihleri arasında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Hastanesi Tıbbi Mikrobiyoloji Laboratuvarına gönderilen yara yeri örneklerinden izole edilen mikroorganizmaların retrospektif değerlendirilmesi ve antibiyotik direnç profillerinin saptanması amaçlanmıştır.

Gereç ve Yöntem Laboratuvarımıza farklı kliniklerden gönderilen yara yeri örnekleri konvansiyonel yöntemlerle ekilmiş ve izole edilen suşların tanımlanması ve antibiyotik dirençleri Becton Dickinson Phoenıx(USA) otomatize sistemle belirlenmiştir.

Bulgular Toplam 980 etkenin 606'sı (%61,80) Gram negatif bakteriler, 374'ü (%38,10) Gram pozitif bakteriler olarak tespit edilmiştir. İzole edilen mikroorganizmalar sırasıyla S. aureus (%22,30), E. coli (%22,20), P. aeruginosa (%16,60), A. Baumanii (%15,40), Enterococcus spp. (%8,06), S. epidermidis (%7,70), K. pneumoniae (%7,50) olarak belirlenmiştir. Gram negatif bakterilerin en duyarlı olduğu antibiyotik amikasin olarak belirlenmiştir. S. aureus suşlarında vankomisine direnç tespit edilmemiştir. Etkenlerin kliniklere göre dağılımı incelendiğinde yara yeri örneklerinin en sık yoğun bakım ünitelerinden geldiği belirlenmiştir.

Sonuç Belirli zaman aralıklarında enfeksiyon etkenleri ve bunların antibiyotik duyarlılıklarının belirlenmesi, hem direnç oranlarının azalmasına hem de tedavi maliyetlerinin düşmesine katkı sağlayacaktır.

Anahtar Kelimeler Yara yeri enfeksiyonu; tedavi; antibakteriyel ajanlar; bakteri

Abstract

Objective *In this retrospective study; between January 2018-January 2019 assessment of antibiotic susceptibility profile of micro-organism isolated from wound swaps which had been send to the Microbiology laboratory, faculty of medicine , Kahramanmaras sutcu Imam University were aimed.*

Materials and methods *Isolated wound swap samples which received from various clinics to our laboratory were evaluated by conventional methods. Identification and susceptibility patterns of the micro-organism were done by automated susceptibility testing (Becton Dickinson Phoenıx -USA).*

Results *Out of 980 (61,80%) samples, were Gram negative isolate; 374 (38,10%) were Gram positive isolates. Among them; Staphylococcus aureus were 22,30%, E. coli were 22,20%, P. aeruginosa were 16,60%, A. baumanii were 15,40%, Enterococcus spp. were 8.06%, S. epidermidis were %7,70, and K. pneumoniae were 7,50% respectively. Amikasin was found to be the most sensitive antibiotic against Gram negative bacteria. Also vancomycin resistant was not found among Staphylococcus aureus samples. When we analyzed wound sample rates according to different clinics; Intensive Care Department were the most source of infection samples.*

Conclusion *Periodically; monitoring susceptibility of antibiotic for pathogen organisms reduces resistant rate and cost of treatment.*

Keywords *wound infections; treatment; anti-bacterial agents; bacteria*

GİRİŞ

Enfeksiyon hastalıkları, gelişmekte olan ülkelerde halen önemli bir sağlık sorunudur.[1] Bunlar arasında yara yeri enfeksiyonları önemli bir yer tutmaktadır.[2] Yara bölgesinde, mikroorganizmaların virulans faktörlerinin bağışık yanıtı yenmesiyle mikroorganizmaların yara bölgesine yerleşmesi ve yayılması sonucu yara yeri enfeksiyonu oluşur.[3-5] Deri ve yumuşak dokuların enfeksiyonları gerek gösterdikleri klinik tablolar ve gerekse enfeksiyonu oluşturan mikroorganizmalar bakımından büyük çapta çeşitlilik gösterirler.[6]

Yara yeri enfeksiyonları, önemli bir morbidite ve mortalite nedenidir. Bu tür enfeksiyonlar geç iyileşmekte, hastada anksiyeteye ve hastanede kalış süresinin uzamasına neden olmakta, sağlık sistemine önemli ölçüde mali yük getirmektedir.[7] Ayrıca bakterilerde artan antimikrobiyal direnç bütün dünyada olduğu gibi ülkemizde de önemli bir sağlık sorunu olma özelliğini sürdürmektedir.[8] Bu nedenle belli zaman aralıklarında sık görülen enfeksiyon etkenleri ve bunların antibiyotik duyarlılık paternlerinin belirlenmesi ampirik tedaviye ışık tutması açısından önemlidir.[9] Yara yeri enfeksiyonlarının tedavisinde kültür ve antibiyogram değerlendirmeleri, klinisyenin yara tedavisindeki başarısına destek olacağı gibi antibiyotik kullanımının kontrolüyle dirençli bakterilerin yayılmasını da engelleyecektir.[10]

Bu çalışmada Ocak 2018-Ocak 2019 tarihleri arasında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Hastanesinde çeşitli kliniklerden Mikrobiyoloji Laboratuvarına gönderilen yara yeri örneklerinden izole edilen mikroorganizmaların dağılımları ve bunların çeşitli antibiyotiklere duyarlılıklarının değerlendirilmesi amaçlanmıştır.

GEREÇ ve YÖNTEMLER

Ocak 2018-Ocak 2019 tarihleri arasında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Hastanesi Mikrobiyoloji Laboratuvarında yara kültürlerinden izole edilen mikroorganizmalar ve antimikrobiyal duyarlılıkları retrospektif olarak incelenmiştir. Örnekler steril eküvyonla alınıp taşıyıcı besiyeri ortamında laboratuvara ulaştırılmış olan yüzeyel sürüntü örnekleridir. Laboratuvara kabul edilen tüm yara sürüntü örnekleri değerlendirilmiş olup sonuçlar hastane otomasyon sisteminden elde edilmiştir. Örneklerin mikrobiyolojik değerlendirilmesi aşamasında her numune %5 koyun kanlı, Eosin Metilen Blue (EMB) ve çikolata agara ekilmiş ve 37 0C'de 24-48 saat inkübe edilmiştir. Kültür değerlendirilmesi mikroskobik inceleme ile birlikte yapılmıştır. Örneklerden hazırlanan preperatlar Gram yöntemi ile boyanarak lökosit, epitel ve mikroorganizma yönünden incelenmiştir. Mikroskobik inceleme Q skorlama ölçütü kullanılarak değerlendirilmiş olup Q skor 1'de üreyen en fazla 1, Q skor 2'de üreyen en fazla 2, Q skor 3'te üreyen en fazla 3 bakteri tanımlanıp antimikrobiyal duyarlılık testi yapılmıştır. Kültürde üçten fazla farklı mikroorganizma üremesi varsa tanımlama ve duyarlılık testi yapılmayıp "Karışık flora elemanları üredi" şeklinde raporlanarak değerlendirilmeye alınmamıştır. Mikroorganizmalar konvansiyonel yöntemler ve Becton Dickenson Phoenix (USA) tam otomatize identifikasyon sistemi ile tanımlanmış ve antimikrobiyal duyarlılık testleri yapılmıştır. Sınır değerler ise EUCAST (European Committee On Antimicrobial Susceptibility Testing) önerileri doğrultusunda belirlenmiştir.

Çalışmamız kesitsel tipte tanımlayıcı bir çalışma olup Sakarya Üniversitesi Tıp Fakültesi Etik Kurulundan onam alınmıştır (Etik kurul onam sayı: 71522473/050.01.04/477, Tarih: 04.09.2020).

Veriler SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)) paket programıyla analiz edilmiştir. Kategorik değişkenlerin tanımlanmasında sayı (n) ve yüzde (%) kullanılmıştır.

BULGULAR

Toplam 1411 yara sürüntü örneği değerlendirildi. İzole edilen 980 etkenin 606'sı (%61,80) Gram negatif bakteriler, 374'ü (%38,10) Gram pozitif bakteriler olarak tespit edilmiştir. Tablo 1'de etkenlerin kliniklere göre dağılımları

Tablo 1. Yara yeri örneklerinden izole edilen etkenlerin (n=980) kliniklere göre dağılımı

Etken mikroorganizma	Klinikler							
	Genel Cerrahi n(%)	Çocuk Hasta.ı n(%)	Ortopedi n(%)	Yoğun Bakımlar n(%)	Dahiliye n(%)	Acil n(%)	Diğer n(%)	Toplam n(%)
S. aureus	18 (8,21)	10 (4,56)	64 (29,23)	14 (6,39)	7 (3,20)	5 (2,29)	10 (46,12)	219 (22,30)
S. epidermidis	6 (7,90)	-	9 (11,84)	8 (10,53)	1 (1,31)	-	52 (68,42)	76 (7,80)
Enterococcus spp.	13 (16,45)	-	12 (15,19)	22 (27,85)	2 (2,54)	1 (1,27)	29 (36,70)	79 (8,10)
E. coli	46 (21,10)	3 (1,38)	26 (11,93)	46 (21,10)	5 (2,30)	1 (0,45)	91 (41,74)	218 (22,20)
P. aeruginosa	21 (12,89)	2 (1,23)	15 (9,20)	49 (30,06)	1 (0,61)	-	75 (46,01)	163 (16,60)
A. baumanii	18 (11,93)	-	21 (13,91)	38 (25,16)	-	-	74 (49,00)	151 (15,40)
K. pneumoniae	9 (12,16)	2 (2,70)	9 (12,16)	26 (35,14)	-	1 (1,35)	27 (36,49)	74 (7,60)
Toplam	131 (13,37)	17 (1,73)	156 (15,92)	203 (20,71)	16 (1,63)	8 (0,82)	449 (45,82)	980 (100)

gösterilmiştir. Buna göre yara yeri enfeksiyonunun en sık yoğun bakım ünitelerinde görüldüğü (%20,70) bunu ortopedi kliniğinin (%15,90) izlediği tespit edilmiştir. Servislere göre mikroorganizmaların dağılımına bakıldığında, *S. aureus* ve *S. epidermidis* en sık ortopedi kliniğinden, *E. coli* en sık genel cerrahi kliniği ve yoğun bakım ünitelerinden, *P. aeruginosa, A. baumanii, K. pneumoniae* ve *Enterococcus spp*. yoğun bakım ünitelerinden izole edilmiştir. Yara yeri enfeksiyonuna neden olan etkenler arasında *S. aureus*'un birinci sırada yer aldığı ve bunu *E. coli*, *P. aeruginosa, A. Baumanii*'nin takip ettiği izlenmiştir.

İzole edilen *S. aureus* suşlarında vankomisine direnç tespit edilmemiştir. Stafilokok suşlarının diğer bazı antibiyotiklere direnç oranları Tablo 2'de gösterilmiştir.

Gram negatif bakterilerin antimikrobiyal duyarlılık oranları değerlendirildiğinde *E. coli* suşlarının %76,70'inin seftriaksona, %72,90'ının siprofloksasine, %65,80'inin sefepime, %2,30'unun amikasine dirençli olduğu belirlenmiştir. *P.aeruginosa* suşlarının piperasilin/tazobaktam, seftazidim ve gentamisine karşı olan direnç oranları sırasıyla %42,50, %1,40, %29,90 olarak belirlenmiştir. Gram negatif bakterilerin antimikrobiyal duyarlılık oranları Tablo 3'te gösterilmiştir.

Tablo 2. Yara örneklerinden izole edilen *S. aureus*'ta çeşitli antibiyotiklere direnç oranları

Antibiyotik	*S.aureus*	
	n	%
Siprofloksasin	212	8,90
Klindamisin	212	23,10
Penisilin	205	98,50
Eritromisin	214	23,30
Fusidik asit	218	18,80
Fosfomisin	213	1,80
Gentamisin	211	9
Vankomisin	218	0
Tetrasiklin	215	25,10

Tablo 3. Yara yeri örneklerinden izole edilen bazı Gram negatif bakterilerde antibiyotik direnç oranları

Antibiyotik	*E. coli*		*K. pneumoniae*		*P. aeruginosa*		*A. baumanii*	
	n	%	n	%	n	%	n	%
Amikasin	217	2,30	75	14,60	156	8,90	151	80,10
Ampicillin	208	93,75	74	100	1	100	1	100
Seftazidime	212	57,50	75	73,30	162	31,40	-	-
Ceftriaxone	215	76,70	75	74,60	4	50	-	-
Sefepime	211	65,80	75	73,30	154	40,90	-	-
Gentamisin	209	27,20	75	40	157	29,90	151	92
İmipenem	217	3,60	72	15,20	161	37,80	151	89,40
Meropenem	215	4,60	73	24,60	157	36,30	151	87,40
Piperasilin/tazobaktam	214	33,60	75	44	160	42,50	-	-
Siprofloksasin	207	72,90	74	56,70	155	40,60	-	-
Trimetoprim/sulfametoksazol	216	65,20	75	54,60	-	-	150	47,30

TARTIŞMA

Mikrobiyoloji laboratuvarının görevi yara yerinde üreyen mikroorganizmaları klinik semptomlarla birlikte değerlendirmek, klinik açıdan önemli olan izolatları belirlemek ve antibiyotik duyarlılık testlerini yaparak ilgili hekimlere yol göstermektir. Yara yeri enfeksiyonlarının tedavisinde kültür ve antibiyogramın tedavi başarısını arttırdığı gibi toplam maliyeti düşürmede de etkin olduğu düşünülmektedir. Bu uygulama hekimin yara tedavisindeki başarısını etkileyecek ve antibiyotik kullanımının kontrolü ile dirençli bakterilerin yayılması da engellenmiş olacaktır.[11] Sesli ve ark. 721 yara örneğini inceledikleri çalışmalarında en sık izole edilen bakterileri sırasıyla *S. aureus* 108 (%29,10), KNS 89 (%24), *E. coli* 42 (%11,30), *Enterococcus spp*. 25 (%6,70), *P. aeruginosa* 22 (%5,90) ve *A. baumannii* 21 (%,60) olarak belirlemişlerdir.[10] Zer ve ark. retrospektif olarak yaptıkları çalışmada 234 yara sürüntüsü örneklerinde üreme saptanan örneklerin 73'ünden (%31,20) S. aureus, 43'ünden (%18,40) KNS, 28'inden (%12) E. coli ve 19'undan (%8,10) *Enterococcus spp*. izole edildiğini bildirmişlerdir.[12] Yurtsever ve ark. yaptıkları çalışmada yara yerinden izole edilen bakterileri sırasıyla *E. coli* 302 (%26,80), *P. aeruginosa* 206 (%18,30), *S. aureus* 203 (%18), *A. baumannii* 131 (%11,60), *K. pneumoniae* 100 (%8,90), *Enterococcus spp*. 30 (%2,70), diğer *Enterobactericeae* suşları 139 (%12,30) ve KNS suşları 12 (%1,10) olarak belirlemişlerdir.[13] Sümer ve ark. yara yeri örneklerinde en sık izole edilen bakterileri KNS (%26,60), *S. aureus* (%24,90) ve *Pseudomonas spp*. (%13,60) olarak bildirmişlerdir.[9] Adalati ve ark. hastanede yatan hastaların toplam 1169 yara yeri örneğinin 775'inde (%66,30) üreme saptamış ve en çok üreyen mikroorganizmalar olarak sırasıyla *S. aureus*, *Pseudomonas spp*. ve *E. coli*'yi bildirmişlerdir.[14] Ankara Üniversitesinde 1994-1999 yılları arasında 1295 yara kültürü değerlendirilmiş, en sık rastlanan etkenler sırasıyla *S. aureus* (%28,20), *S. epidermidis* (%16), *P. aeruginosa* (%11,70) ve *E. coli* (%9) olarak saptanmıştır.[15] Meksika'da yapılmış bir çalışmada 313 yara yeri enfeksiyonunda sırasıyla %21,80 oranında *E. coli*, %13 oranında Koagülaz negatif stafilokok, %12,60 oranında Pseudomonas spp. %9,20 oranında *S. aureus* en sık izole edilen bakteriler olarak bildirilmiştir.[16] Yurtdışında yapılan bir başka çalışmada, cerrahi yara yeri enfeksiyonlarında izole edilme sıklığı açısından ilk üç sırayı, *S. aureus* (%39), koliform basil (%24) ve *P. aeruginosa* (%21) paylaşmaktadır.[17] Çalışmamızda ise en sık izole edilen bakteriler sırasıyla; *S. aureus* (%22,30), *E. coli* (%22,20), *P. aeruginosa* (%16,60), *A. baumanii* (%15,40), *Enterococcus spp.* (%8,06), *S.epidermidis* (%7,70), *K. pneumoniae* (%7,50) olarak belirlenmiştir.

Etkenlerin en sık görüldüğü klinikler incelendiğinde; Sesli ve ark. çalışmasında ortopedi kliniği, Yurtsever ve ark. ça-

lışmasında genel cerrahi kliniği, Sümer ve ark. çalışmasında cerrahi klinikler, Adalati ve ark.adaşlarının çalışmasında genel cerrahi kliniği olarak bulmuşlardır.[9,10,13,14] Yapılan çalışmalarda cerrahi kliniklerde en sık izole edilen mikroorganizma ise *E. coli* olarak tespit edilmiştir.[10,13] Çalışmamızda ise yoğun bakım ünitelerinde en sık *P.aeruginosa*, cerrahi kliniğinde ise *E. coli* izole edilmiştir. Ülkemizde yapılan bir çalışmada, kolorektal cerrahi uygulanan hastalarda gelişen cerrahi alan enfeksiyonlarındaki risk faktörleri belirlenmiş, yaş, cinsiyet, hastanede yatış süresi ve altta yatan hastalık varlığının enfeksiyon riskini artırdığı saptanmış, cerrahi alan enfeksiyonlarından izole edilen en sık etkenin ise *E. coli* olduğu gösterilmiştir.[18] Yapılan birçok çalışmada, çalışmamızda da olduğu gibi vankomisin direnci tespit edilmemiştir.[9,12,13] Bessa ve ark. *S.aureus* suşlarının %21,80'inin metisiline dirençli olduğunu belirtmişlerdir. Ayrıca penisilin direncini %71,20, klindamisin direncini %15,80, eritromisin direncini %41,60, gentamisin direncini %27,70, tetrasiklin direncini %7,90 olarak bildirmişlerdir.[19] Bizim çalışmamızda ise penisilin direnci %98,50, klindamisin direnci %23,10, eritromisin direnci %23,30, gentamisin direnci %9, tetrasiklin direnci %25,10 olarak bulunmuştur.

Gram negatif bakterilerin antimikrobiyal duyarlılıkları incelendiğinde Sümer ve ark.'nın çalışmalarında ampisilin duyarlılığının düşük olduğu (%8,80-%50) görülmektedir.[9] Amikasin duyarlılığı %69,60-%97,10 oranında iken gentamisin duyarlılığı %44,70-%91,30 oranında tespit edilmiştir. *Siprofloksasine Acinetobacter spp*. dışındaki gram negatifler oldukça duyarlı tespit edilmiştir (%81,80-%95,40). Aynı çalışmada mikroorganizmaların antibiyotik duyarlılığına bakıldığında *E.coli*'de meropenem (%98,70), amikasin (%97,10); *Klebsiella spp*.'de amikasin (%94,30), siprofloksasin (%91,20); *Pseudomonas spp*.'de meropenem (%92,20), siprofloksasin (%91,50); *Acinetobacter spp*.'de gentamisin (%91,30), meropenem (%90,50) en etkili antibiyotikler olarak bulunmuştur.[9] Yurtsever ve ark. yaptığı çalışmada gram negatif bakterilere en etkili antibiyotiklerin imipenem, sefaperazon ve aminoglikozitler olduğu saptanmıştır.[13] Yağcı ve ark. sefalosporin duyarlılığını *E. coli*'de yüksek, *Klebsiella spp*.'de düşük olarak bildirmişlerdir.[20] Usluer ve ark. üçüncü kuşak sefalosporinlere olan direnci *Pseudomonas* ve *Klebsiella* türlerinde oldukça yüksek saptamışlardır.[21] Tansel ve ark. yatan hastalardan izole ettikleri *Acinetobacter* türlerinde imipeneme karşı yüksek duyarlılık saptamışlardır.[22] Çalışmamızda ampisiline duyarlılığın düşük olduğu (%93,75-100) görülmektedir. Gram negatif bakterilere en etkili antibiyotik amikasin olarak saptanmıştır. Bessa ve ark. *E.coli* suşlarındaki ampisilin direncini %94,10, seftazidim direncini %5,90, sefepim direncini %11,80, siprofloksasin direncini %52,90 bulmuşlardır.[19] Ayrıca bütün suşların meropenem ve ertapeneme duyarlı olduğunu belirtmişlerdir. Türkiye'de yapılan bir araştırmada, yanık yaralarından izole edilen *E.coli* suşlarının %55'i seftazidime, %59'u sefepime, %32'si siprofloksasine dirençli bulunmuştur. İmipenem ve meropeneme karşı direnç rapor edilmemiştir.[23] Bizim çalışmamızda da *E.coli* suşlarına en etkili antibiyotikler amikasinden sonra imipenem ve meropenemdir. Bessa ve ark. *Pseudomonas spp*. suşlarındaki piperasilin/tazobaktam direncini %52,20, siprofloksasin direncini %45,60, meropenem direncini %30,40, seftazidim direncini %50 olarak bulmuşlardır.[19] Bayram ve ark.'nın yaptığı çalışmada ise piperasilin/tazobaktam direnci %31, imipenem direnci %46, siprofloksasin direnci %25, meropenem direnci %19 olarak raporlanmıştır.[23] Bizim çalışmamızda piperasilin/tazobaktam, siprofloksasin ve meropenem en dirençli antibiyotikler arasındadır ve bu çalışmalarla uyumludur. Bessa ve ark.'nın yaptığı çalışmaya göre ise seftazidim direnci daha düşüktür.

Sonuç olarak; enfeksiyon hastalıkları gelişmekte olan ülkelerde halen önemli bir sağlık sorunudur. Mikroorganizmaların artan oranda antibiyotiklere direnç geliştirmesi bunun önemli nedenlerinden biridir. Bunun önlenebilmesi için belirli zaman aralıklarında mikroorganizmaların tanımlanıp antibiyotik direnç profillerinin belirlenmesi gerekmektedir. Bu şekilde klinisyenlerin akılcı antibiyotik kullanımı konusunda bilinçlenmesi sağlanarak ampirik

tedavilere yön verilebilecek, direnç oranlarındaki artışın önüne geçilebilecek ve kurumlardaki toplam tedavi maliyetini düşürmeye katkı sağlanacaktır.

Çalışmanın etik kurul onayı, Sakarya Üniversitesi bünyesinde yer alan Girişimsel Olmayan Klinik Araştırmalar Etik Kurul'dan (04.09.2020 tarih ve 71522473/050.01.04/477 sayılı) alınmıştır.

Kaynaklar

1. *Gür D. Bakterilerde antibiyotiklere karşı direnç. Topçu AW, Söyletir G, Doğanay M, editör. İnfeksiyon Hastalıkları. 1. Baskı. İstanbul: Nobel Tıp Kitapevi; 1996. S:183-90.*
2. *Koneman EW, Stephan DA, Janda WM, Schreckenberger PC, Winn WC. Diagnostic Microbiology. 4 st ed. Philadelphia: Lippincott Co; 1992.*
3. *Barbul A. Wound healing. In: Brunicardi FC (ed.), Schwartz's Principles of Surgery. 8 st ed. New York: McGraw-Hill; 2005.p.223-49.*
4. *Peel ALG. Definition of infection. In: Taylor EW (ed.), Infection in Surgical Practice. Oxford: Oxford University Press; 1992.p.82-7.*
5. *Uzunköy A. Cerrahi alan infeksiyonları: Risk faktörleri ve önleme yöntemleri. Ulus Travma Derg 2005; 11: 269-81.*
6. *Bilgehan H. Klinik Mikrobiyolojik Tanı. 5.Baskı. İzmir: Barış Yayınları; 2009.*
7. *Zafar A, Anwar N, Ejaz H. Bacteriology of infected wounds - A study conducted at Children Hospital Lahore. Biomedica 2007; 23:1-4.*
8. *Özmen E, Geyik MF, Uluğ M, Çelen MK, Hoşoğlu S, Ayaz C. Yatan hastalardan izole edilen gram negatif bakteriler ve antibiyotik dirençlerinin değerlendirilmesi. Düzce Tıp Fak Derg 2010; 12:32-9.*
9. *Sümer Z, Bakıcı Z, Türkay C, Gökçe G, Gökgöz Ş. Yatırılarak izlenen hastaların yara yeri ve idrar örneklerinde izole edilen mikroorganizmaların değerlendirilmesi. Turk Mikrobiyol Cem Derg 2001; 31:48-52.*
10. *Sesli Çetin E, Kaya S, Taş T, Cicioğlu Arıdoğan B, Demirci M. Cerrahi alan infeksiyonlarında mikroorganizma profili ve antibiyotik duyarlılık durumu. ANKEM Derg 2006; 20:89-93.*
11. *Byrne DJ, Napier A, Cuschieri A. Rationalizing whole body disinfection. J Hosp Infect 1990; 15:183-7.*
12. *Zer Y, Korkmaz G, Çeliksöz C, Bayram A, Orhan G, Balcı İ. Yara örneklerlerinden izole edilen mikroorganizmalar ve antibiyotik duyarlılıkları. Anadolu Tıp Derg 2002; 4:76-80.*
13. *Gül Yurtsever S, Kurultay N, Çeken N, Yurtsever Ş, Afşar İ, Şener AG et al. Yara yeri örneklerinden izole edilen mikroorganizmalar ve antibiyotik duyarlılıklarının değerlendirilmesi. ANKEM Derg 2009; 23:34-8.*
14. *Adalati R, Yılboz DN, Akalın N. Hastanede yatan hastaların yara yeri örneklerinden izole edilen mikroorganizmaların değerlendirilmesi. Türk Mikrobiyoloji Cem Derg 2002; 32:35-9.*
15. *Güriz H, Çiftçi E, Gökdemir R, Aysev D. Ankara Üniversitesi Tıp Fakültesi Cebeci Hastanesindeki yara kültürlerinin değerlendirilmesi. Ankara Üniv Tıp Fak Mec 2001; 54:231-5.*
16. *Vilar-Compte D, Mohar A, Sandoval S, Rosa M, Gordillo P, Volkow P. Surgical site infections at the national cancer institute in Mexico. A case control study. Am J Infect Control 2000; 28:14.*
17. *Wong ES. The price of a surgical site infection:more than just excess length of study. Infect Control Hospital Epidemiol 1999; 20: 722-5.*
18. *Taşdelen Fışgın N, Tanyel E, Topgül K, Sarıkaya H, Doğancı L, Tülek T. Kolon cerrahisi uygulanan hastalarda gelişen cerrahi alan infeksiyonları ve risk faktörleri. İnfeks Derg 2008; 22:141-5.*
19. *Bessa LJ, Fazii P, DiGiulio M, Cellini L. Bacterial isolates from infected wounds and their antibiotic susceptibility pattern: some remarks about wound infection. Int Wound J. 2015;12(1):47-52.*
20. *Yağcı A, Çıragil P, Topkaya A, Söyletir G. Marmara Üniversitesi Tıp Fakültesi Hastanesinde yatırılarak izlenen hastalardan izole edilen mikroorganizmaların 1996 yılı analizi. İnfek Derg 1999; 13:39-43.*
21. *Usluer G, Başıbüyük N, Çolak H, Akşit F. Hastane ve hastane dışı infeksiyonlara neden olan bazı gram negatif bakterilerin çeşitli antibiyotiklere duyarlılıkları. Mikrobiyol Bül 1993; 27: 221-6.*
22. *Tansel Ö, Uzel WS, Özsüt H, Dilmener M, Çalangu S. Hastane kaynaklı Acinetobacter suşlarının dağılımı ve antibiyotiklere duyarlılıkları. V. Ulusal İnfeksiyon Hastalıkları Kongresi; 1995; İstanbul: Türkiye 1995. sayfa 47.*
23. *Bayram Y, Parlak M, Aypak C, Bayram İ. Threeyear review of bacteriological profile and antibiogram of burn wound isolates in Van, Turkey. Int J Med Sci 2013;10(1):19-23.*

ARAŞTIRMA MAKALESİ / *Research Article*

Alerjik Rinit Tanısı Alan Hastalarda Deri Prick Testi Yapılma Sıklığı Ve Etkileyen Faktörler

The Frequency of Skin Prick Test Application to the Patients Diagnosed with Allergic Rhinitis and Affecting Factors

Ali Güvey

Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, KBB Anabilim Dalı, Kütahya

Yazışma Adresi / *Correspondence:*
Ali Güvey

Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, KBB Anabilim Dalı, Kütahya
T: **+90 532 644 60 38** E-mail **: aliguvey76@gmail.com**

Geliş Tarihi / Received : **22.01.2021** Kabul Tarihi / Accepted : **02.01.2021**

Orcid :
Ali Güvey https://orcid.org/0000-0003-2972-4056

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):177-182) DOI:10.31832/smj.866441

Öz

Amaç Alerjik rinit toplumda sık görülen ve poliklinik muayenesi ile sık tanı konulan hastalıklardan biridir. Bu araştırmada hastaneye başvurup alerjik rinit tanısı alanlarda deri prick testi yapılma sıklığı ve buna etki eden faktörlerin incelenmesi amaçlanmıştır.

Gereç ve Yöntem Araştırma Sakarya Üniversitesi Eğitim Araştırma Hastanesine 2018 ve 2019 yıllarında başvurup J30 (Vazomotor ve Alerjik Rinit) ve alt tanı kodlarını (J30.0, J30.1, J30.2, J30.3, J30.4) alan kişilerin muayene kayıtlarının geçmişe yönelik taranmasıyla yapılmıştır. Toplam 8496 muayene kaydı incelenmiştir.

Bulgular Alerjik rinit tanısı alanların %55,5'i kadındır. İncelenenlerin %25,8'i 0-17 yaş arası, %67,8'i 18-64 yaş arası, %6,4'ü 65 yaş üstüdür. İncelenenlerin %77,6'sının alerjik rinit tanısıyla bu 2 yıl içerisinde tek başvurusu olmuştur. Başvuranların %11,5'ine deri prick testi yapılmıştır. Prick testi yapılanların %64,4'ünde en az bir alerjene karşı pozitif sonuç saptanmıştır. Yapılan Ki-kare analizlerine göre 18 yaş altında olanlara, kadın cinsiyete, başvuru sayısı birden fazla olanlara deri prick testi yapılma sıklığı artmaktadır.

Sonuç Alerjik rinit tanısı alanların çoğunda semptomatik tedavi uygulanmakta ve etiyolojiyi aydınlatmaya yönelik işlemler yapılmamaktadır. Daha çok çocuk yaş grubunda ebeveynlerin kaygılarıyla etiyolojinin aydınlatılmasına yönelik işlemlerin yapıldığı düşünülmektedir. Alerjik rinit tanısı alanlarda deri prick testi yapılmasının hekimlere rehber olacak şekilde geliştirilmesi klinikler arası farklılıkların ortadan kaldırılması yerinde olacaktır.

Anahtar Kelimeler alerjik rinit; deri testleri; alerjenler

Abstract

Objective *Allergic rhinitis is one of the diseases that is common in the community and diagnosed with outpatient examination. In this study, it was aimed to examine the frequency of skin prick testing in patients diagnosed with allergic rhinitis and the factors affecting it.*

Materials and methods *The research was conducted by examining the people who applied to Sakarya University Training and Research Hospital in 2018 and 2019 and received the J30 (Vasomotor and Allergic Rhinitis) and subdiagnosis codes (J30.0, J30.1, J30.2, J30.3, J30.4). A total of 8496 examination records were examined.*

Results *55.5% of those diagnosed with allergic rhinitis are women. 25.8% of those examined were under the age of 18, 67.8% were between 18-64 and 6.4% were over 65. 77.6% of those examined had a single application within these 2 years with the diagnosis of allergic rhinitis. Skin prick test was applied to 11.5% of the patients. A positive result with at least one allergen was found in 64.4% of those who had the prick test. According to the chi-square analysis, the frequency of skin prick test is increased for those under the age of 18, female gender, and those with more than one visit to the outpatient clinic.*

Conclusion *Symptomatic treatment is applied to most of those diagnosed with allergic rhinitis. There are no procedures to find the etiology. It is thought that procedures are carried out to enlighten the etiology with the concerns of parents mostly in the pediatric age group. Skin prick testing in those diagnosed with allergic rhinitis should be developed to guide physicians. It would be appropriate to eliminate the differences between clinics.*

Keywords *rhinitis;allergic; skin tests; allergens*

GİRİŞ

Alerjik rinit (AR), nazal mukozanın konjesyon, kaşınma ve seröz burun akıntısı ile seyreden inflamasyonudur.[1] Özellikle çocukluk çağında okul performansını ve hayat kalitesini etkilemektedir.[1] AR'nin kendisi yaşamı tehdit etmez ancak otit, sinüzit ve astım gibi hastalıklara zemin hazırlaması sebebiyle önemli bir sağlık sorunudur. Prevalansı değişmekle birlikte ortalaması %10 civarındadır.[1] Türkiye'de en yüksek prevalans %25,2 ile Sivas'ta yapılan bir çalışmada, en düşük prevalans %2,6 ile Bursa'da yapılan bir çalışmada bulunmuştur.[2,3] Türkiye'de 1993-2010 yılları arası Uluslararası Çocukluk Çağı Astım ve Alerjileri Çalışması yöntemiyle yapılan 18 çalışmanın ortalama prevalansı %10,7'dir.[2-19] AR sıklığının tüm dünyada giderek arttığı düşünülmektedir.[20]

AR gelişiminde risk faktörleri; aile öyküsü, gen polimorfizmleri, annenin gebelik döneminde yoğun alerjen maruziyeti, sezaryenle doğum, şehir yaşamı, yenidoğan sarılığı sayılabilir.[21-27]

Alerjik reaksiyonun önlenmesinde en temel adım, duyarlı olunan alerjenleri bilmek ve mümkün olabildiği ölçüde temastan kaçınmaktır.[28] Alerji deri testleri alerjene karşı duyarlılığı belirlemede gerek güvenilirliği, gerekse nispeten uygulama kolaylığı ve düşük maliyeti nedeniyle en önemli tanı aracı olup, yaygın olarak kullanılmaktadır.[29] Bu sebeple alerji ön tanısı olan kişiye etkenin belirlenmesi amacıyla ileri tanı testlerinin yapılması gereklidir. Kişiye özel alerjenin belirlendiği teste deri prick testi denilmektedir. Böylece kişinin özellikle önlem alması gereken alerjenler bilinmiş olur.

AR tanısı anamnez ve fizik muayene ile konabilmektedir. Ardından etken belirlenmeden doğrudan tedaviye geçilirse sadece semptomatik tedavi ile hastalık süreci geçiştirilmiş olur. Literatürde genellikle deri prick testi yapılan kişilerin hangi alerjenlere duyarlı olduğunun sonuçları ve yorumları yapılmıştır. Ancak polikliniklerde AR ön tanısı alan kişilerin ne kadarına deri prick testi uygulandığı genellikle belirlenmemiştir. Bu sebeple AR tanı kodunu almış kişilerden ne kadarına deri prick testi uygulandığının belirlenmesi gerekmektedir. Süreç içerisinde bir kez AR tanısı alanların bir daha başvurma ve tanı alma durumları da ortaya konulmalıdır.

Bu çalışmada bir hastaneye yapılan tüm muayene kayıtları içerisinden AR tanı kodu almış kişilere deri prick testi yapılma sıklığı ve yapılmasını etkileyen faktörlerin belirlenmesi amaçlanmıştır.

GEREÇ ve YÖNTEMLER

Araştırma Sakarya Üniversitesi Eğitim Araştırma Hastanesi'ne 2018 ve 2019 yıllarında başvurup ICD-10 tanı kodlarından J30 (Vazomotor ve AR) ve alt tanı kodlarını (J30.0, J30.1, J30.2, J30.3, J30.4) alan kişilerin muayene kayıtlarının geçmişe yönelik taranmasıyla yapılmıştır. Tanımlayıcı bir araştırmadır. Tanı kodları tüm poliklinik muayeneleri taranarak toplanmıştır. Toplam 8496 muayene kaydı retrospektif olarak incelenmiştir. Araştırmanın yapılması için Sakarya Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan 22.05.2020 tarihli 300 sayılı başvuru ile etik kurul onayı alınmıştır.

Hastaların yaş, cinsiyet, son 2 yıl içerisinde kaç kez tanı aldığı, deri prick testi yapılma durumu ve deri prick testinin sonucu (pozitif veya negatif) işlenmiştir.

Deri prick testi uygulanmadan önce, ön kol bölgesi alkol ile silindi. Allergopharma tekli prick test aplikatörleri epikutan olarak uygulandı. Değerlendirme için 20 dakika beklenildi. Pozitif kontrol olarak histamine hidroklorür, negatif kontrol olarak izotonik solüsyon kullanıldı. Testin geçerlilik kriteri; pozitif kontrolün 3 mm çapından büyük olması ve negatif kontrolün 0 mm çapında olması kabul edildi. Endürasyon çapının 3 mm ve üzerinde gözlendiği alerjene karşı cilt reaksiyonu pozitif yanıt olarak kabul edildi. İşlem yapılmadan önce hastaların aydınlatılmış yazılı onamı alınmıştır. Prick testinde sık görülen 18 alerjen ekstresi kullanıldı. Bunlar; ev tozu akarı, ağaç polenleri,

ot polenleri, yabani ot karışımı, hububat karışımı, duvar fesleğeni, ısırgan, hamamböceği, domates, bütün yumurta, çikolata, kümes hayvanları, köpek tüyü, kedi tüyü, mantar olarak listelendi.

Araştırmanın analizi için SPSS 15.0 paket programı kullanıldı. Tanımlayıcı istatistikler frekans, yüzde, ortalama±standart sapma olarak sunuldu. İstatistiksel analiz olarak Ki-Kare ve Student-T testi kullanıldı. İstatistiksel anlamlılık düzeyi için p<0,05 kabul edilmiştir.

BULGULAR

Toplam 8496 kişinin muayene kaydı incelenmiştir. Yaş ortalaması 32,1±18,7 olup yaş ortancası 29 (min:1 maks:96) dur.

AR tanısı alanların %55,5'i kadın, %44,5'i erkektir. İncelenenlerin %25,8'i 0-17 yaş arası, %67,8'i 18-64 yaş arası, %6,4'ü 65 yaş üstüdür. İncelenenlerin %77,6'sının AR tanısıyla bu 2 yıl içerisinde tek başvurusu olmuştur. En fazla başvurusu sayısı 4'tür. Başvuranların %11,5'ine deri prick testi yapılmıştır. (Tablo 1)

Tablo 1. İncelenenlerin Tanımlayıcı Özellikleri, Sakarya 2021

		Sayı	(%)*
Cinsiyet (n=8496)			
	Erkek	3779	44,5
	Kadın	4717	55,5
Yaş Grubu (n=8496)			
	0-17 yaş arası	2196	25,8
	18-64 yaş arası	5760	67,8
	65 yaş ve üstü	540	6,4
Başvuru Sayısı (n=8496)			
	Tek başvuru	6592	77,6
	Birden fazla başvuru	1904	22,4
Deri Prick Testi Yapılma Durumu (n=8496)			
	Yapılmış	7523	88,5
	Yapılmamış	973	11,5
*Kolon yüzdesi			

Yapılan Ki-kare analizlerine göre; kadınların %13,1'ine erkeklerin %9,4'üne deri prick testi yapılmıştır. Cinsiyete göre deri prick testi yapılma durumu arasında istatistiksel olarak anlamlı fark saptanmıştır. (p<0,001) Deri prick testi yapılma sıklığı en yüksek olan yaş grubu 0-17 yaş arasıdır. Yaş gruplarına göre deri prick testi yapılma durumu arasında istatistiksel olarak anlamlı fark bulunmuştur. (p<0,001) Yapılan ikili karşılaştırmalarda farkın 0-17 yaş arası gruptan kaynaklandığı görülmüştür. İncelenen 2 yıl içerisinde birden fazla kez hastaneye başvurup AR tanısı almış olanlar ile sadece 1 kez tanı almış olanlar arasındaki fark da karşılaştırılmıştır. Birden fazla kez başvuranların %16,1'ine sadece 1 kez başvuranların %10,1'ine deri prick testi yapılmıştır. Başvuru sayısına göre deri prick testi yapılma durumu arasında istatistiksel olarak anlamlı fark saptanmıştır. (p<0,001) Sonuç olarak 18 yaş altında olanlara, kadın cinsiyete, başvuru sayısı birden fazla olanlara deri prick testi yapılma sıklığı artmaktadır. (Tablo 2)

Tablo 2. Deri Prick Testi Yapılmasını Etkileyen Faktörler, Sakarya 2021

		Test Yapılma Durumu*	
		Yapılmayanlar n (%)	**Yapılanlar n (%)**
Cinsiyet	Erkek	3422 (%90,6)	357 (%9,4)
	Kadın	4101 (%86,9)	616 (%13,1)
X^2=26,996		**p<0.001**	
Yaş Grup	0-17 yaş arası	1806 (%82,2)	390 (%17,8)
	18-64 yaş arası	5200 (%90,3)	560 (%9,7)
	65 yaş ve üstü	517 (%95,7)	23 (%4,3)
X^2=130,699		**p<0.001**	
Başvuru Sayısı	Başvuru Sayısı Bir	5926 (%89,9)	666 (%10,1)
	Başvuru Sayısı Birden Fazla	1597 (%83,9)	307 (%16,1)
X^2=52,808		**p<0.001**	
*Satır yüzdesi verilmiştir Ki-Kare testi uygulanmıştır			

Birden fazla başvuru %23,4 ile en sık 18-64 yaş arası grupta gözlenmiştir. Yaş gruplarına göre başvuru sayısı arasında istatistiksel olarak anlamlı fark bulunmuştur. (p=0,005) Yapılan ikili karşılaştırmalarda farkın 18-64 yaş arası gruptan kaynaklandığı görülmüştür. Cinsiyete göre başvu-

ru sayısı durumuna bakıldığında kadınlarda birden fazla başvuru sıklığı daha fazla olsa da fark istatistiksel olarak anlamlı bulunmamıştır (p=0,405). (Tablo 3)

Tablo 3. Alerjik Rinit Bulgularıyla Birden Fazla Başvuru Yapılmasını Etkileyen Faktörler, Sakarya, 2021

		Başvuru Sayısı*	
		Bir Kez n (%)	**Birden Fazla Kez n (%)**
Cinsiyet	Erkek	2948 (%78,0)	831 (%22,0)
	Kadın	3644 (%77,3)	1073 (%22,7)
X^2=0,692		p=0,405	
Yaş Grup	0-17 yaş arası	1747 (%79,6)	449 (%20,4)
	18-64 yaş arası	4411 (%76,6)	1349 (%23,4)
	65 yaş ve üstü	434 (%80,4)	106 (%19,6)
X^2=10,651		**p=0.005**	

*Satır yüzdesi verilmiştir
Ki-Kare testi uygulanmıştır

Çalışmamızda deri prick testi yapılanların %64,4'ünde en az bir alerjene karşı pozitif sonuç saptanmıştır.

TARTIŞMA

AR ve diğer tüm alerjik hastalıklarda birincil önlem alerjene maruziyetin kesilmesidir.[28,30] İnsan vücudu için çok fazla sayıda alerjen sayılabilecek madde vardır. Bir kişinin neye veya nelere karşı alerjisi olduğu her zaman bulunamasa bile yaygın alerji nedenlerinin test edilmesiyle çoğunlukla etken saptanabilir.

Literatürde Türkiye'de pek çok farklı ilden deri prick testi pozitiflik oranları bildirilmiştir. Deri prick pozitifliğinin literatürde %29 ile %56 arasında değiştiğini bildiren yayınlar vardır.[30] İstanbul'da AR'li hastalar üzerinde yapılan bir çalışmada deri prick testi pozitifliği %36,3 bulunmuştur.[31] Kayseri ilinde AR'li hastalar üzerinde yapılan bir çalışmada ise deri prick testi pozitifliği %71,1 bulunmuştur.[32] Van ilinde AR'li hastalarda yapılan çalışmada deri prick testi pozitifliği %60, Ankara'da yapılan bir diğer çalışmada %56 bulunmuştur.[33,34]

Deri prick testi sadece AR tanısı alanlarda yapılmamaktadır. Astım, atopik dermatit, kronik ürtiker gibi hastalıklarda da yapılabilmektedir. Sadece astım hastalarının incelendiği iki çalışmada deri prick pozitifliği Kayseri'de %60, Sakarya'da %76 olarak bulunmuştur.[29,35]

Bingöl'de farklı polikliniklerden farklı ön tanılar alıp deri prick testi yaptıran hastalarda pozitiflik sıklığı %53 bulunmuştur.[36] Benzer metodla Elazığ'da yapılan çalışmada %30, Yozgat'ta yapılan çalışmada %64 deri prick testi pozitifliği bulunmuştur.[37,38] Görüldüğü üzere sadece AR'li hastalarda, sadece astımlı hastalarda veya tüm atopik özellik gösterebilecek durumlardaki hastalıklarda yapılan deri prick testlerinde pozitiflik sıklıkları benzerdir. Bazı çalışmalarda %70'lere varan sıklıklar görülmektedir ki bu istenen bir durumdur. Testin boşuna yapılmadığının bir göstergesi olabilir. Bizim çalışmamızda da AR tanısı alıp deri prick testi yapılanlarda pozitiflik sıklığı %64,4 bulunmuştur. Literatürdeki aralığın üst kısmına yakındır.

Çalışmanın ana inceleme konusu AR tanısı alanlardan kimlere daha sıklıkla deri prick testi yapıldığıdır. Yapılan analizlere göre 18 yaşın altında olanlarda, kadınlarda, başvuru sayısı birden fazla olanlarda deri prick testi yapılma sıklığı daha fazladır. Başvuru sayısı birden fazla olanlarda testin istenme sıklığının daha fazla olması çoğu hekimin ilk tanıda hastayı semptomatik tedavi ile geçiştirdiğini göstermektedir. Alerjiye sebep olabilecek durumun araştırılması hastanın birkaç kez aynı şikayetlerle başvurması sonrası yapılmaktadır. Özellikle 18 yaş altı hastalarda test isteme sıklığının yüksek olması bu yaş grubunun farklı bir disiplin olan Pediatri hekimlerince muayene edilmesi ve ebeveynlerin nedenin belirlenmesine yönelik ısrarları olabilir. Kadın cinsiyette neden daha sık istendiğine dair farklı analizlere ihtiyaç duyulmaktadır. Örneğin alerji semptomlarının şiddetinin kadınlarda daha fazla olması buna sebep olabilir.

Bir diğer önemli husus da AR'li hastaların tekrar aynı şikayetlerle başvurmasıdır. Çalışmamızda hastaların

%22,4'ünün birden fazla kez AR şikayetleriyle başvurduğu görülmüştür. Çalışan grubu temsil eden 18-64 yaş arası kişilerin daha sıklıkla birden fazla kez başvurmuş olması dikkat çekicidir. Ancak çalışmanın kısıtlılıklarından biri de semptomları devam eden hastaların tekrar aynı hastane yerine farklı bir sağlık kuruluşuna başvurmuş olabilme ihtimalidir.

Bir çalışmada AR tanısı alanların ICD-10 tanı kodları üzerinden tespit edilmesinin doğru olmadığı düşüncesi dile getirilmiştir.[39] Ancak AR tanı kodu herhangi bir sendromik sürveyansın parçası değildir. Bu sebeple çalışmamızda temel aldığımız AR tanı kodunun çoğunlukla doğru kullanılacağını düşünmekteyiz.

Sonuç olarak literatürde neredeyse hiç değerlendirmeye alınmayan deri prick testi yapılma sıklığı ve etkileyen faktörler hakkında daha fazla çalışma yapılması gerektiği kanaatindeyiz. Özellikle AR'li hastalarda deri prick testinin hekim tarafından istenmesinin daha belirli algoritmalar üzerinden yürütülmesi soruna çözüm olabilir. Hastaların testi reddetmesinin de ayrıca kayıt altına alınıp değerlendirilmesi gerekecektir.

Araştırmanın yapılması için Sakarya Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan 22.05.2020 tarihli 300 sayılı başvuru ile etik kurul onayı alınmıştır.

Kaynaklar

1. *Özdemir Ö, Elma B. Alerjik rinitin değişken prevalansı ve prevalansı etkileyen risk faktörleri. Kulak Burun Bogaz Ihtis Derg 2016;26(6):371-382.*
2. *Canitez Y, Sapan N. The prevalence of asthma, allergic rhinitis, and eczema in Bursa Turkey An ISAAC study. J Allergy Clin Immunol 2000;105:933*
3. *Arslan S, Uğurlu S, Demirel Y, Can G. Sivas yöresinde ilköğretim çocuklarında astım ve alerjik hastalıkların ilişkisi ve prevalansı. Nobel Med 2012;8:30-34.*
4. *Bayram I, Güneşer-Kendirli S, Yilmaz M, Altintaş DU, Alparslan N, Bingöl-Karakoç G. The prevalence of asthma and allergic diseases in children of school age in Adana in southern Turkey. Turk J Pediatr 2004;46:221-5.*
5. *Tamay Z, Akcay A, Ergin A, Guler N. Effects of dietary habits and risk factors on allergic rhinitis prevalence among Turkish adolescents. Int J Pediatr Otorhinolaryngol. 2013;77:1416-1423.*
6. *Akçay A, Tamay Z, İnan M, Gürses D, Zincir M, Öneş Ü. Denizli'deki 13-14 yaş okul çocuklarında alerjik hastalık belirtilerinin yaygınlığı. Turk Pediatr Ars 2006;41:81-86.*
7. *Tamay Z, Akcay A, Ones U, Guler N, Kilic G, Zencir M. Prevalence and risk factors for allergic rhinitis in primary school children. Int J Pediatr Otorhinolaryngol 2007;71:463-471*
8. *Karaman O, Turgut CS, Uzuner N, Olmez D, Babayigit A, Kose S, et al. The determination of asthma, rhinitis, eczema, and atopy prevalence in 9- to 11-year-old children in the city of Izmir. Allergy Asthma Proc 2006;27:319-324*
9. *Kuyucu S, Saraçlar Y, Tuncer A, Geyik PO, Adalioğlu G, Akpinarli A, et al. Epidemiologic characteristics of rhinitis in Turkish children: the International Study of Asthma and Allergies in Childhood (ISAAC) phase 2. Pediatr Allergy Immunol 2006;17:269-277.*
10. *Talay F, Kurt B, Tug T, Yilmaz F, Goksugur N. Prevalence and risk factors of asthma and allergic diseases among schoolchildren in Bolu Turkey. Acta Paediatr 2008;97:459-462.*
11. *Akçay A, Tamay Z, Dağdeviren E, Zencir M, Öneş Ü, Güler N. Denizli'deki 6-7 yaş okul çocuklarında alerjik hastalıklarının prevalansları. Ege Tıp Derg 2007;46:145-150.*
12. *Ece A, Ceylan A, Saraçlar Y, Saka G, Gürkan F, Haspolat K. Prevalence of asthma and other allergic disorders among schoolchildren in Diyarbakir, Turkey. Turk J Pediatr 2001;43:286-292*
13. *Selçuk ZT, Caglar T, Enünlü T, Topal T. The prevalence of allergic diseases in primary school children in Edirne, Turkey. Clin Exp Allergy 1997;27:262-269.*
14. *Karaman O, Türkmen M, Uzuner N. Allergic disease prevalence in Izmir. Allergy 1997;52:689-690.*
15. *Özkırış M. Kayseri'deki 14-17 yaş öğrencileri arasında allerjik rinit prevalansı Asthma Allergy Immunol 2010;8:163-169.*
16. *Çakır M, Çetinkaya F. Samsun'da ilköğretim okulu çocuklarında astım ve diğer allerjik hastalıkların sıklığı. Astım Allerji İmmünoloji 2004;2:139-142.*
17. *Anlar FY, Sancak R, Oztürk F. Childhood allergic disorders in Samsun, Turkey: discrepancy between reported and diagnosed. Pediatr Allergy Immunol 2006;17:635-638.*
18. *Yıldırım M, Ergür AT, Saraçlar Y, Tuncer A. Sivas il merkezindeki çocuklarda alerjik hastalıkların prevalansı. Çocuk Sağlığı ve Hastalıkları Dergisi 2002;45:226-232.*
19. *Zeyrek CD, Zeyrek F, Sevinc E, Demir E. Prevalence of asthma and allergic diseases in Sanliurfa, Turkey, and the relation to environmental and socioeconomic factors: is the hygiene hypothesis enough? J Investig Allergol Clin Immunol 2006;16:290-295.*
20. *Topal Ö, Erbek SS, Erbek S, Çakmak Ö. Konya yöresinde yaşayan perennial alerjik rinitli hastalarda epidemiyolojik özellikler, alerjen dağılımı ve semptom ciddiyeti. Kulak Burun Bogaz Ihtis Derg 2008;18(4):227-231.*
21. *Wei X, Zhang Y, Fu Z, Zhang L. The association between polymorphisms in the MRPL4 and TNF-a genes and susceptibility to allergic rhinitis. PLoS One 2013;8:579-581.*
22. *Li ZP, Yin LL, Wang H, Liu LS. Association between promoter polymorphisms of interleukin-4 gene and allergic rhinitis risk: a meta-analysis. J Huazhong Univ Sci Technolog Med Sci 2014;34:306-313.*
23. *Torres-Borrego J, Molina-Terán AB, Montes-Mendoza C. Prevalence and associated factors of allergic rhinitis and atopic dermatitis in children. Allergol Immunopathol (Madr) 2008;36:90-100.*
24. *Li Y, Jiang Y, Li S, Shen X, Liu J, Jiang F. Preand postnatal risk factors in relation to allergic rhinitis in school-aged children in China. PLoS One 2015;10(1):14-22.*
25. *Sun HL, Lue KH, Ku MS. Neonatal jaundice is a risk factor for childhood allergic rhinitis: a retrospective cohort study. Am J Rhinol Allergy 2013;27:192-196.*
26. *Tamay Z, Akcay A, Ergin A, Güler N. Dietary habits and prevalence of allergic rhinitis in 6 to 7-year-old schoolchildren in Turkey. Allergol Int 2014;63:553-562.*
27. *Tamay Z, Akcay A, Ones U, Guler N, Kilic G, Zencir M. Prevalence and risk factors for allergic rhinitis in primary school children. Int J Pediatr Otorhinolaryngol 2007;71:463-471.*
28. *Kündig TM, Klimek L, Schendzielorz P, Renner WA, Senti G, Bachmann MF. Is The Allergen Really Needed in Allergy Immunotherapy?. Curr Treat Options Allergy 2015;2(1):72-82.*
29. *Aydemir Y, Çoban H, Güngen AC, Düzenli H, Taşdemir C. Sakarya Bölgesinde deri prick testi sonuçlarının mevsimsel özelliklerle değerlendirilmesi. Kocaeli Tip Dergisi 2015;4(3):10-13.*
30. *Konuk S, Bilgin C, Çoban H, Nalbant A. Assessment of the Results of the Prick Tests Carried Out in Düzce Province. Aasrc 2017;9:232-236.*
31. *Yeğin Y, Şimşek B, Çelik M. İstanbul Bakırköy'de alerjik rinitli hastalara uygulanan deri prick test sonuçlarının mevsimsel dağılımı. KBB Uygulamaları 2016;4(3):97-104.*
32. *Kökoğlu K, Kutlu Ö. Kayseri ilinde alerjik rinit hastalarının ve deri prick testi sonuçlarının değerlendirilmesi. KBB Uygulamaları 2020;8(3):137-144*
33. *Gür MH, Uluyol S, Kılıçaslan S, Karakaya NE, Zeki M, Erdem FA. Van ilinde alerjik rinitli hastalarda prik test sonuçlarının değerlendirilmesi. Van Tip Dergisi 2017;24(4):279-282.*
34. *Karabulut H, Karadağ AS, Acar B, Demir M, Babademez MA, Karaşen RM. Ankara Keçiören bölgesinde deri prik testi sonuçlarının meteorolojik ve demografik özelliklere göre değerlendirilmesi. KBB-Forum Dergisi 2009;8(3):46-54.*
35. *Bayram A, Oymak S, Gülmez İ, Demir R, Büyükoğlan H. Astımda Atopi ve Alerjik Rinit Sıklığı. Erciyes Medical Journal 2010;32(1):27-34.*
36. *Torun E, Şeremet S. Allerjik Hastalığı Olan Hastalarımızda Deri Prick Testi Sonuçlarının Değerlendirilmesi. İzmir Göğüs Hastanesi Dergisi 2010;24(2):87-92.*
37. *Çiçek D, Kandi B, Bakar S, Ucak H. Elazığ yöresinde allerjik astma, allerjik rinit, allerjik konjunktivit, kronik ürtiker ve atopik dermatitli olgularda prick test sonuçlarının değerlendirilmesi. Fırat Üniversitesi Sağlık Bilimleri Tip Dergisi 2008;22(4):193-196.*
38. *Çölgeçen E, Özyurt K, İntepe YS, Gencer ZK, Özkırış M, Ede G et al. Yozgat yöresinde atopik semptomlu hastalarda deri prick testi sonuçları. Journal of Clinical&Experimental Investigations 2014;5(1):64-68*
39. *Biçer YÖ, Köybaşı S, Oral M. Üçüncü Basamak Sağlık Kuruluşunda Alerjik Rinit Reçetelerinin Değerlendirilmesi ve ICD-10 Kodlarıyla Uyumu. KBB-Forum 2015;14(2)*

ARAŞTIRMA MAKALESİ / *Research Article*

Akut Miyokardiyal İnfarktüs Sonrası Primer Anjiyoplasti Uygulanan Hastalarda Kontrastla İlişkili Nefropatinin Bir Prediktörü: Kontrast Madde Hacminin Glomerüler Filtrasyon Hızına Oranı

A Predictor of Contrast Induced Nephropathy in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction: The Ratio of Contrast Media Volume to Glomerular Filtration Rate

Sedat Taş[1], Eren Ozan Bakır[2], Ümmü Taş[3]

[1] Department of Cardiology, Manisa City Hospital, Manisa, Turkey
[2] Department of Cardiology, Manisa Celal Bayar University, Manisa, Turkey
[3] Department of Cardiology, Manisa Akhisar State Hospital, Manisa, Turkey

Yazışma Adresi / *Correspondence:*
Sedat Taş
Department of Cardiology, Manisa City Hospital Manisa, Turkey
T: **+90 505 291 94 58** E-mail **: sedattas2000@yahoo.com**

Geliş Tarihi / Received : **26.08.2020** Kabul Tarihi / Accepted : **04.02.2021**

Orcid :
Sedat Taş https://orcid.org/0000-0001-8086-1318,
Eren Ozan Bakır MD; https://orcid.org/0000-0001-7168-9157
Ümmü Taş, MD; http://orcid.org/0000-0002-3725-2944

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):183-192) DOI: 10.31832/smj.786134**

Öz

Amaç Akut miyokard infarktüsü nedeni ile perkütan koroner girişim yapılan hastalarda, kontrast madde hacminin glomerüler filtrasyon hızına oranının (KV/GFH) kontrast ilişkili nefropatiyi (KİN) öngördürmedeki etkisini belirlemek ve KİN gelişiminden sakınmak amacı ile güvenli bir KV/GFH eşik değeri tanımlanması amaçlanmaktadır.

Gereç ve Yöntem Akut myokard infarktüsü nedeni ile perkütan koroner girişim yapılan 108 hasta değerlendirildi. Hastalar perkütan koroner girişimden 48 saat sonra bakılan serum kreatinin değerlerindeki değişime göre, KİN gelişen ve KİN gelişmeyen olarak iki gruba ayrıldı. Ardından KİN ile ilişkili olan risk faktörlerinin analizi yapıldı. Receiver operating characteristic (ROC) eğrisi kullanılarak KİN gelişimini belirlemek amacıyla KV/GFH için optimal bir eşik değer belirlendi ve lojistik regresyon kullanılarak KİN'i öngördüren bağımsız değişkenler tanımlandı.

Bulgular Hastalar içinde KİN gelişim oranı %24 olarak saptandı. KV/GFH anlamlı olarak KIN gelişen grupta daha yüksek bulundu. ROC eğrisi analizi ile elde edilen KV/GFH>2,68 değeri, KİN gelişimini öngörmede %92 sensitivite ve %89 spesifisiteye sahipti. KV/GFH dışında, yaş ve HDL-K da KİN için bağımsız risk faktörleri olarak saptandı.

Sonuç Akut myokard infarktüsü nedeni ile perkütan koroner girişim yapılan hastalarda, KV/GFH>2.68 değeri KİN'i öngördürmede anlamlı bağımsız bir değişkendir. Bu değer PKG yapılacak hastalarda kontrast madde kullanımını yönetmek açısından kullanışlı olabilir.

Anahtar Kelimeler Kontrast ilişkili nefropati; kontrast madde hacmi; akut miyokardiyal infarktüs; perkütan koroner girişim; yüksek dansiteli lipoprotein

Abstract

Objective *To evaluate contrast media volume to glomerular filtration rate (CV/GFR) ratio for predicting contrast-induced nephropathy (CIN) and to determine a safe CV/GFR cut off value to avoid CIN in patients with acute myocardial infarction during percutaneous coronary intervention (PCI).*

Materials and methods *A total of 108 patients with acute myocardial infarction undergoing percutaneous coronary intervention were enrolled. They were divided into the CIN and non-CIN groups according to the changes in serum creatinine levels within 48 hours after coronary artery intervention. Then the relevant risk factors of CIN were analyzed.Receiver operating characteristic (ROC) curves were used to identify the optimal cut off value of CV/GFR for detecting CIN and logistic regression analyse was used to identify independent variables to predict CIN.*

Results *Among them, CIN occurred in patients with an incidence of % 24. CV/GFRwas significantly higher in CIN patients group. In ROC curve analysis, at cut-off value of 2.68, CV/GFR had a sensitivity of 92% and specificity of 89% for predicting CIN development. Age and HDL-C alsowere identified as independent risk factors for CIN.*

Conclusion *CV/GFR>2.68 was a significant independent predictor of CIN in patients undergoing coronary artery intervention for acute myocardial infarction.It is possible that this score can be used in patients whenmanaging the PCI and CV.*

Keywords *contrast induced nephropathy; contrast medium volume; acute myocardial infarction; percutaneous coronary intervention; high-density lipoprotein*

GİRİŞ

Kontrast-ilişkili nefropati (KİN), akut böbrek yetmezliğinin kontrast maruziyetine bağlı olan büyük çoğunlukla geri döndürülebilir bir sebebidir. KİN, işlemden 48 saat sonra değerlendirilen serum kreatinin seviyesinde bazal değerlere kıyasla≥%25 rölatif artış veya ≥0.5mg/dl artış olarak tanımlanmaktadır. Serum kreatinin değerleri genellikle 3-5 gün içerisinde zirve yapmakta ve 2 hafta içerisinde bazal değerlere dönmektedir.[1]

Temel olarak kontrast maruziyeti sonrası böbreklerde uzun süreli vazokonstrüksiyon meydana gelir, bunun sonucunda böbrek kan akımı bozulur ve iskemi meydana gelir.İskemi reaktif oksijen radikallerinin oluşmasına sebep olur ve tübüler nekroz bunu takip eder. Sonuç olarak afferent arteriollerde de vazokonstrüksiyon olur ve glomerüler filtrasyon hızı (GFH) azalır.[2,3] Bu da akut böbrek yetersizliği ile sonuçlanır. Kontrast maddenin neden olduğu yüksek ozmotik yük direkt tübüler toksisite ile tübüler nekroza ve enzimüriye neden olarak da nefropatiye yol açabilir.

Hastane içi mortalite KİN gelişen hastalarda, gelişmeyenlere göre belirgin olarak fazla bulunmuştur (%21,4 vs. %0,9; P < 0,001).[4] KİN, %10-15 arası bir oranla hastane kaynaklı akut böbrek yetmezliğinin sık görülen bir sebebi olup, renal hipoperfüzyon (%42) ve postoperatif renal hasar(%18)'dan sonra 3. en sık hastane içi akut böbrek yetmezliği sebebidir ve nadiren geri dönüşümsüz böbrek hasarına yol açabilmektedir.[5] Perkütan koroner girişimlere bağlı gelişen KİN oranı % 0-24 arasında değişmektedir. Bu değişkenliğin nedeni hasta ve işleme bağlı nedenlerin her hastada farklı olmasıdır. Ancak en yüksek KİN oranları acil perkütan koroner girişimler sonrasında ortaya çıkmaktadır.[6] Kontrast maruziyeti sonrasıKİN gelişmiş hastalarda bazen kısa süreli diyaliz ihtiyacı ve bazen de kalıcı diyaliz ihtiyacı olabilmektedir. KİN sadece böbrekleri etkileyen bir komplikasyon değildir. Uzun dönemde ölüm, inme ve miyokard infarktüsü oranlarının KİN geçiren hastalarda daha yüksek olduğunu gösteren verilerin sayısı giderek artmaktadır.[7] Sağlık hizmetinin maliyetini artırması ve klinik seyir üzerine olumsuz etkisi gibi nedenlerle klinisyenlerin bilmesi gereken önemli problemlerden biridir. KİN'ı ortaya çıkaran nedenler 2 grupta toplanabilir: i-) hasta ilişkili nedenler ve ii-) işlem ilişkili nedenler. Kronik böbrek yetmezliği ve diyabetes mellitus, hasta ilişkili nedenler içinde en önemlileridir. Bunun yanında; kontrolsüz hipertansiyon, >75 yaş, anemi, kalp yetmezliği ve siroz da bu grupta değerlendirilir. İşlem ilişkili nedenler; kontrast madde miktarı, 72 saat içinde tekrar kontrast maddeye maruz kalma, kullanılan ajanın viskozitesi ve hastanın eş zamanlı kullandığı diüretik ve non-steroid antiinflamatuvar ilaçlar(nsaii) gibi nefrotoksik ilaçlar olarak sıralanabilir.KİN gelişiminde yukarıda sayılan risk faktörleri içinde verilen kontrast madde miktarı önemli bir yer tutmaktadır.[8] Kontrast maddeler temel olarak böbreklerden atılır ve 24 saat sonunda %98 kadarı vücut dışına atılmış olur, ancak %1 kadarı böbrek dışı organlardan atılır. İyot bazlı kontrast maddeler, osmolaritelerine göre düşük, yüksek ve izoosmolar olarak 3 gruba ayrılırken, iyonik özelliğine göre de iyonik ve non-iyonik olarak iki kısımda değerlendirilir. Genel olarak intravasküler görüntüleme ve işlemlerde düşük veya izoosmolar non-iyonik kontrast ajanlar tercih edilir. Bunun en önemli nedeni bu gruptaki ajanların akut yan etkilerinin (% 0,2-0,7) ve ciddi yan etkilerinin (% 0,04) daha az olmasıdır.[9-10] Kontrast ajanların birbirine üstünlüğü ile ilgili yapılan çalışmalarda farklı sonuçlar mevcuttur. Düşük osmolar ve izoosmolar non-iyonik kontrast ajanlar ile ilgili yapılan çalışmalarda, KİN için risk faktörleri taşıyan ya da öncesinde böbrek yetmezliği olan hastalarda izoosmolar kontrast ajanların kullanımının daha düşük KİN oranlarına neden olduğunu savunan çalışmalar olduğu gibi,[11-12] aralarında hiçbir üstünlük olmadığını belirten çalışmalar da vardır.[13-14] Amerikan Kalp Cemiyeti perkütan koroner girişim kılavuzu, düşük osmolar ve izoosmolar non-iyonik kontrast ajanların her ikisinin de anjiyografi yapılacak hastalarda kullanılabileceğini ve diğer kontrast ajanlara üstün olduğunu belirtmiştir.[15]

KİN gelişimini önlemek için çeşitli farmakolojik ve non-farmakolojik yöntemler geliştirilmiştir. Ancak KİN

için tanımlanmış kesin bir tedavi yöntemi bulunmamaktadır, bu nedenle KİN gelişimini engellemeye yönelik önlemler almak daha fazla önem taşımaktadır. Bunlardan en önemlileri kontrast madde miktarını mümkün olan en az miktarda kullanmak, sıvı kaybını engellemek ve renal vazokonstrüksiyona neden olabilecek etkenlerden uzaklaşmaktır. Hastanın kullandığı nefrotoksik ajanların kesilmesi de yine önleyici yöntemlerden biridir.

Yukarıda belirttiğimiz gibi kontrast maddelerin böbrek üzerine etkileri verilen kontrast madde miktarına ve osmolaliteye bağlıdır. Kontrast madde miktarı ve KİN gelişimi arasındaki ilişkiyi araştıran çalışmalarda, kontrast madde volümü (KV)/ Glomerül Filtrasyon Hızı (GFH) oranı ve kontrast madde miktarı için çeşitli eşik değerler öne sürülmüştür.[16-18] Bu çalışmalarda kontrast madde miktarı için eşik değerler 70 cc ve 240 cc aralığında değişmektedir. Bu çalışmalarda genel olarak kontrast madde miktarının mümkün olduğunca az kullanılması ve tanımlanan eşik değerlere gelindiğinde komplikasyon gelişimi açısından dikkatli olunması önerilmektedir.

KİN, perkutan koroner girişimin morbiditeyi, hastanede yatış süresini ve hatta mortaliteyi arttıran ciddi bir komplikasyonudur.[19] Perkutan koroner girişim sırasında kullanılan kontrast madde miktarı tanısal anjiyografilere göre belirgin miktarda fazla olup, kontrast madde miktarının mümkün olduğunca minimalize edilmesi ve KV/ GFH oranının belirli bir oranın altında tutulması Avrupa Kardiyoloji Derneği 2018 miyokardiyal revaskülarizasyon klavuzunda da klas 1 endikasyon ile önerilmektedir. Çalışmamızın verilerinin bu bağlamda değerli olacağını düşünmekteyiz.

Araştırmamızın amacı, perkutan koroner girişim esnasında kullanılacak kontrast madde miktarının hastanın GFH'si ve klinik durumu dikkate alınarak hesaplanması ve miktarının sınırlandırılması ile önemli bir morbidite ve mortalite nedeni olan kontrast nefropatisinin azaltılmasına katkı sunmaktır.

GEREÇ ve YÖNTEMLER

Çalışmamız prospektif ve tanımlayıcı bir çalışmadır. Çalışmada 10 Ocak 2019 ve 1 Nisan 2019 tarihleri arasında hastanemiz acil servisine başvuran akut miyokard infarktüs tanılı hastalar incelenmiştir. Çalışmanın dışlama kriterleri: Kreatinin klirensi <60 ml/dak,<18 yaş, kalp yetmezliği, böbrek transplantasyonu öyküsü, malign tümör, hematolojik astalık, gebelik, immunsupresif ilaç kullanımı, karaciğer yetmezliği, kardiyojenik şok, nefrotoksik ilaç kullanım öyküsü, kontrast madde alerjisi, son 10 gün içinde kontrast madde maruziyeti olarak belirlendi. Çalışmaya 120 hasta dahil edildi. 6 hasta kendi isteği ile 24. saat sonunda taburcu olduğundan 48. Saat kreatinin değerlerine bakılamadığı için, 2 hasta işlem öncesi kreatinin değeri bakılmadığı için, 4 hasta ise ek romatolojik hastalıkları nedeni ile yoğun non-steroid antiinflamatuvar ilaç kullanımları olması nedeni ile çalışma dışı bırakıldılar. Bazal kreatinin değerleri normal olan, 18 yaş üstü akut myokard enfarktüsü tanısı ile acil servise başvuran hastalardan, koroner anjiyografi (KAG) yapılmadan önce başta böbrek fonksiyon testleri olmak üzere kan örnekleri alındı. Hastaların demografik verileri ve vital bulguları başvuru anında kayıt altına alındı. Her hastaya başvuru anında 12-derivasyonlu elektrokardiyografi çekildi. Hastaların başvuru tanısı, yaşı ve kontrast ilişkili nefropatiye zemin oluşturabilecek diğer risk faktörleri not edildi. Her hastanın hastane yatış süresince günlük olarak vital bulguları ölçüldü. Hastanın kreatinin değerleri işlem günü, işlem yapılmadan önce ölçüldü ve işlem sonrası 24. ve 48. saatlerde tekrar kreatinin ölçümü yapıldı. KİN açısından değerlendirilmek üzere 48. saatteki kreatinin ölçümü baz alındı.

GFH ölçümünde Cockroft-Gault formülü [Kreatinin klirensi (CrCI): 140(yaş)x kilo(kg)/ 72xSCr(mg/dl)] kullanıldı. İşlem günü hastanın GFH ölçümü mevcut formül ile hesaplandı ve kontrast miktari (ml cinsinden) ile GFH değeri oranlanarak KV/GFH elde edildi. Kateter laboratuvarına alınan hastanın KAG işlemi tecrübeli bir invaziv

kardiyolog tarafından yapıldı.İşlem sırasında non-iyonik izoosmolar kontrast madde kullanıldı. İşlemden önce standart olarak her hastaya 1cc/kg/saat hızında serum fizyolojik infüzyonu açıldı.

KİN tanısı bazal kreatinin değerinde (işlem günü, işlem öncesi alınan kreatinin) gelişecek ≥%25 rölatif artış veya ≥0.5mg/dl absolü artış olarak kabul edildi. Her hastadan yazılı ve sözlü olarak aydınlatılmış onam alındı.Aydınlatılmış onam formları hastalara imzalatıldı.Çalışmamız 10.01.2019 tarih ve 1921 protokol numarası ile Manisa Celal Bayar Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmıştır.

İstatistik

Çalışmanın istatiksel analizi SPSS 21 (Statistical Package for Social Sciences) istatistik programı kullanılarak yapıldı. Temel istatistikler ile hastaların özellikleri özetlendi, sayısal parametrelerin özetlenmesinde aritmetik ortalama ve standart sapma; kategorik değişkenlerde ise sayı ve yüzde değerleri kullanıldı. Karşılaştırmalarda tüm değişken gruplarının dağılımını tespit etmek için Kolmogorov-Smirnow testi uygulandı. Normal dağılım gösteren değişkenlerde parametrik; çarpık dağılım gösteren değişkenlerde non-parametrik istatistiksel yöntemler kullanıldı. Parametrik test olarak Student T Testi (Independent Sample T Testi) ve non-parametrik test olarak Mann-Whitney U Testi kullanıldı. Kategorik değişkenlerin karşılaştırılmasında ise çapraz tablo istatistikleri kullanıldı (Ki-kare).KİN üzerinde anlamlı etkisi olan uygun değişkenleri saptamak için lojistik regresyon analiziyapıldı. Bunlara ek olarak KV/GFH değeri için bir sınır değer belirlemek amacı ile receiver operator characteristic (ROC) eğrisi analizi yapıldı. Tüm analizlerde istatistiksel anlamlılık sınırı p 0,05 olarak kabul edildi.

BULGULAR

Çalışma grubumuz 108 hastadan oluşmakta ve hastaların çoğunluğunu erkekler oluşturmakta idi (77 [%71,2] erkek, 31 [%28,8] kadın) ve 108 hastanın yaşlarının ortalaması 63,9 ± 10,9 idi.Hastalar 48. saat sonunda alınan kreatinin değerlerine göre 2 gruba ayrıldı. Birinci gruba KİN gelişmeyen 82 hasta (%76) alındı (KİN-, 57 erkek/25 kadın; ortalama yaş: 62,2±10,0). İkinci gruba ise KİN gelişen 26 hasta (%24) alındı (KİN+, 20 erkek/6 kadın; ortalama yaş: 69,2±12,0). KİN+ hasta grubu diğer gruba göre anlamlı derecede daha yaşlı hastalardan oluşmakta idi (p=0,004). Sigara içme oranları KİN+ hasta grubunda anlamlı olarak daha yüksek bulunurken (p<0,001),serum HDL-kolesterol değerleri anlamlı olarak daha düşük bulundu (p=0,006). KİN+ hasta grubunda anlamlı olarak daha yüksek oranda acei/arb kullanıldığı görüldü (p=0,049) ancak diyabetes mellitus tanılı hasta oranında iki grup arasında anlamlı fark görülmedi. Bazal GFH değerleri KİN+ hastalarda normal sınırlarda olmasına ragmen KİN- hastalara göre anlamlı olarak daha düşük bulundu. Hastaların klinik, laboratuvar ve demografik özellikleri Tablo 1'de özetlenmiştir. Hastaların KAG işlemi sırasında kullanılan kontrast miktarı (p<0,001), 48. Saat sonunda bakılan kreatinin (p<0,001) ve KV/GFH (p<0,001) değerleri anlamlı olarak KİN+ hasta grubunda daha yüksek bulundu (Tablo 2).

KV/GFH oranı ile yaş (r=0,291, p=0,002), beden kitle indeksi (BKİ) (r=0,246, p=0,001), trombosit- lenfosit oranı (PLR) (r=0,250, p=0,008), ortalama trombosit volümülenfosit oranı (MPVLR) (r=0,238, p=0,013) ve nötrofillenfosit oranı (NLR) (r=0,270, p=0,005) arasında pozitif yönde korelasyon saptandı. Diğer parametrelerle KV/GFH arasında anlamlı korelasyon saptanmadı (Tablo 3). Yaş değişkenine göre düzeltilmiş korelasyon analizi sonucunda ise PLR ve MPVLR değişkenlerinin istatiksel anlamlılığa ulaşmadığı saptandı.Yüksek dansiteli lipoprotein–kolesterol (HDL-K) ile diğer değişkenler arasında yapılan korelasyon analizinde; HDL-K ile kadın cinsiyet (r=0,206, p=0,033), PLR (r=0,221, p=0,022), MPVLR(r=0,269, p=0,005) ve NLR (r=0,300, p=0,002) arasında pozitif yönde korelasyon, BKİ (r= -0,215, p=0,026) ve sigara kullanımı (r= -0,218, p=0,023) ile negatif yönde korelasyon saptandı (Tablo 4).

Tablo 1: AMI Sonrası KAG Yapılan Hastaların Bazal Klinik ve Demografik Özelliklerine Göre 2 Grup Arasında Karşılaştırılması

	Grup 1 (KİN-) (n=82) (%76.0)	Grup 2 (KİN+) (n=26) (% 24.0)	P değeri
Kadın cinsiyet, n (%)	25 (%30,4)	6 (%23)	0,467
Yaş (yıl) (Ort±SS)	62,2±10	69,2±12	**0,004**
BKİ (kg/m2) (Ort±SS)	25,6±3,5	28,6±3,9	< **0,001**
Sigara, n (%)	29 (%30,5)	18 (%69,2)	< **0,001**
Diyabetes mellitus, n (%)	27(%32,9)	7(%26,9)	0,566
ADEİ/ARB, n (%)	16 (%19,5)	10(%38,5)	**0,049**
AKS Tipi, n (%)			
STEMI	32 (%29,6)	8 (%7,4)	
NSTEMI	50 (%46,2)	18 (%16,6)	
Bazal kreatinin (mg/dl) (Ort±SS)	0,88±0,24	1,03±0,16	**0,003**
GFH (ml/min/1.73 m2 (Ort±SS)	92,1±23,4	74,6±20,6	**0,001**
Lenfosit (x109/L) (Ort±SS)	2,48±1,24	2,38±1,14	0,715
Nötrofil (x109/L) (Ort±SS)	7,24±3,25	7,43±3,26	0,797
Lökosit (x109/L) (Ort±SS)	10,6±3,6	10,7±3,3	0,822
KK (x109/L) (Ort±SS)	4,58±0,59	4,62±0,44	0,765
Trombosit (x109/L) (Ort±SS)	247,2±74,3	253,2±44,9	0,616
Hct (%)	39,8±4,6	41,0±5,0	0,232
Hb (g/dl) (Ort±SS)	13,0±1,8	13,2±1,7	0,483
RDW (%)	14,4±1,8	14,6±1,4	0,578
PCT (Ort±SS)	0,24±0,06	0,24±0,04	0,824
MPV (fl) (Ort±SS)	9,75±1,10	9,82±0,82	0,737
Bazal NLR (Ort±SS)	3,6±2,9	4,0±3,4	0,540
Bazal MHR (Ort±SS)	0,016±0,011	0,019±0,010	0,251
Bazal MVPLR (Ort±SS)	4,78±2,21	5,13±2,58	0,504
Bazal PLR (Ort±SS)	120,5±65,7	128,5±57,0	0,579
Üre (mg/dl) (Ort±SS)	42.7±22.9	41.2±16.0	0,758
Glukoz (mg/dl) (Ort±SS)	160,4±93,3	184,8±106,2	0,264
Potasyum (mmol/l) (Ort±SS)	4,2±0,4	4,5±0,6	0,109
AST (U/L) (Ort±SS)	66,9±97,6	56,2±79,5	0,613
ALT (U/L) (Ort±SS)	25,3±17,3	23,0±14,0	0,540
Kalsiyum (mg/dl) (Ort±SS)	8,9±0,4	9,1±0,4	0,092
Total kolesterol (mg/dl) (Ort±SS)	190,7±38,4	188,9±52,1	0,848
LDL- K (mg/dl) (Ort±SS)	113,1±35,1	112,9±45,4	0,980
HDL- K (mg/dl) (Ort±SS)	45,5±12,3	39,1±9,3	**0,006**
Trigliserid (mg/dl) (Ort±SS)	172,8±90,8	197,6±124,9	0,272

Ort±SS:Ortalama ve standart sapma; ADEİ: Anjiyotensin dönüştürücü enzim inhibitörü; AKS: Akut koroner sendrom; ARB: Anjiyotensin reseptör blokeri; BKİ: Beden kitle indeksi; GFH: Glomerüler filtrasyon hızı; Hb: Hemoglobin; Hct: Hemotokrit; HDL- K: Yüksek dansiteli lipoprotein-kolesterol; KK: Kırmızı küre;LDL- K: Düşük dansiteli lipoprotein-kolesterol; MHR: Monosit- HDL-K oranı; MPV: Ortalama trombosit volümü; MPVLR: MPV-lenfosit oranı; NLR: Nötrofil-lenfosit oranı; NSTEMİ: ST eleve olmayan myokard infarktüsü; PCT: Trombosit platekriti; PLR: Trombosit-lenfosit oranı; RDW: Eritrosit dağılım genişliği; STEMİ: ST eleve myokard infarktüsü; KİN-: Kontrast ilişkili nefropati gelişmeyenler; KİN+: Kontrast ilişkili nefropati gelişenler; AMI:Akut myokard infaktüsü; KAG: Koroner anjiyografi

Tablo 2: AMI Sonrası KAG Yapılan Hastaların KAG Prosedürü ile İlişkili Değişkenlerinin 2 Grup Arasında Karşılaştırılması

	Grup 1 (KIN-) (n=82) (%76) Ort±SS	Grup 2 (KIN+) (n=26) (% 24) Ort±SS	P değeri
Kreatinin (48. saat)	0,84±0,26	1,49±0,23	< **0,001**
Kontrast hacmi (ml)	177,2±76,2	248,4±67,5	< **0,001**
KV/GFH	1,95±0,75	3,35±0,58	< **0,001**

KAG: Koroner anjiyografi; KV/GFH: Kontrast volümü-Glomerüler filtrasyon hızı oranı; Ort±SS:Ortalama ve standart sapma; AMI:Akut myokard infaktüsü; KAG: Koroner anjiyografi

Tablo 3: AMI Sonrası KAG Yapılan Hastaların KV/GFH Değerleri ile Laboratuvar ve Demografik Parametreleri Arasında Spearman İki Değişkenli ve Parsiyel Korelasyon Analizi

	KV/GFH			
	Düzeltilmemiş		Düzeltilmiş*	
Bağımsız değişkenler	r coefficient	p value	r coefficient	p value
Yaş	0,291	**0,002**	-	-
Cinsiyet(Kadın)	-0,114	0,239	-0,123	0,238
BKİ	0,246	**0,010**	0,213	**0,039**
Bazal NLR	0,270	**0,005**	0,215	**0,037**
Bazal PLR	0,250	**0,008**	0,186	0,073
Bazal MPVLR	0,238	**0,013**	0,129	0,215
Bazal MHR	-0,026	0,798	-0,031	0,766
HDL-K	-0,022	0,821	-0,024	0,817
MPV	0,109	0,263	0,045	0,667
RDW	0,075	0,445	0,092	0,376
PCT	0,089	0,368	0,163	0,116

BKİ: Beden kitle indeksi; HDL- K: Yüksek dansiteli lipoprotein-kolesterol;KV/GFH: Kontrast volümü-Glomerüler filtrasyon hızı oranı; MHR: Monosit- HDL-K oranı; MPV: Ortalama trombosit volümü; MPVLR: MPV-lenfosit oranı; NLR: Nötrofil-lenfosit oranı; PCT: Trombosit platekriti; PLR: Trombosit-lenfosit oranı; RDW: Eritrosit dağılım genişliği; AMI:Akut myokard infaktüsü; KAG: Koroner anjiyografi

KİN gelişiminde bir öngördürücü olarak tanımladığımız KV/GFH için sınır değer saptamak amacı ile Receiver operating characteristic (ROC) analizi yapıldı (Şekil 1).KV/GFH için bu sınr değer 2,68 olarak hesaplandı. Bu değerin KİN gelişimini öngördürmede % 92 sensitivite ve % 89 spesifisiteye sahip olduğunu görüldü. Hastaların KV/GFH, yaş, sigara, MPVLR ve HDL-K değişkenleri kullanılarak lojistik regresyon analizi yapıldı.Modelin KİN

gelişimini tahminleme başarısı %90,7 olarak saptandı. Bu değişkenler içinde KV/GFH, yaş ve HDL-K,KİN gelişimini öngördürmede anlamlı ilişki gösterdi. Diğer değişkenler ile KİN arasında anlamlı ilişki saptanmadı. KV/GFH oranının bağımsız olarak KİN gelişme riskini arttırdığı gösterildi. Bir birim KV/GFH artışının KİN gelişim riskini 16,7 kat arttırdığı saptandı. Yaş değişkeni için bu risk artışı 1,09 kat olarak saptandı. KİN gelişimini öngördüren diğer değişken olan HDL-K'daki her bir birimlik artış ise KİN gelişim riskinde 1,1 kat azalma ile ilişkili bulundu. MPVLR ve sigara kullanımı değişkenleri ile KİN arasında anlamlı bir ilişki saptanmadı (Tablo 5).

Tablo 4: AMI Sonrası KAG Yapılan Hastaların HDL-Kolesterol Değerleri ile Laboratuvar ve Demografik Parametreleri Arasında Spearman İki Değişkenli Korelasyon Analizi

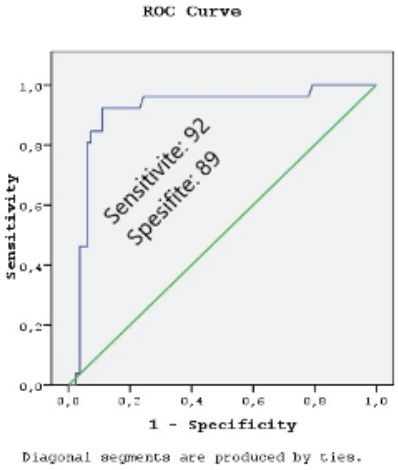
Bağımsız değişkenler	HDL-K	
	r coefficient	p value
Yaş	0,062	0,525
Cinsiyet (Kadın)	0,206	**0,033**
BKİ (kg/m2)	-0,215	**0,026**
Sigara	-0,218	**0,023**
Bazal NLR	0,300	**0,002**
Bazal PLR	0,221	**0,022**
Bazal MPVLR	0,269	**0,005**
RDW	0,059	0,552
PCT	-0,038	0,698

BKİ: Beden kitle indeksi; HDL- K: Yüksek dansiteli lipoprotein-kolesterol; MPV: Ortalama trombosit volümü; MPVLR: MPV-lenfosit oranı;NLR: Nötrofil-lenfosit oranı;PCT: Trombosit platekriti; PLR: Trombosit-lenfosit oranı; RDW: Eritrosit dağılım genişliği; AMI:Akut myokard infaktüsü; KAG: Koroner anjiyografi

Tablo 5: KİN ile KV/GFH, yaş, sigara, MPVLR ve HDL-K arasında lojistik regresyon analizi

Independent variables	Regression coefficient (B)	Wald (X2)	P value	Odds ratio	95% CI
CV/GFR	2,821	18,696	< 0,001	16,792	4,675-60,315
Yaş	0,088	4,734	0,030	1,092	1,009-1,181
Sigara	1,065	2,049	0,152	2,901	0,675-12,475
MPVLR	-0,118	0,527	0,468	0,889	0,646-1,223
HDL-K	-0,107	6,011	0,014	0,898	0,821-0,984
Constant	-10,156	11,097	< 0,001	0,000	

KV/GFH: Kontrast volümü-Glomerüler filtrasyon hızı; HDL- K: Yüksek dansiteli lipoprotein-kolesterol; MPVLR: Ortalama trombosit volümü-lenfosit oranı; KİN: Kontrast ilişkili nefropati



Şekil 1: Receiver operator characteristic (ROC) eğri analizi ile KIN gelişimini % 92 sensitivite ve % 89 spesifite ile tahminleyecek CV/GFR sınır değeri 2.68 olarak hesaplandı.

TARTIŞMA

Çalışmamızın temel sonuçları şunlardır: (a) Böbrek fonksiyonları normal olup akut myokard infarktüsü (AMI) ile başvuran hastalarda KİN gelişiminden sakınmak için güvenli kontrast madde sınırını belirlemeyi amaçladığımız çalışmamızda; KV/GFH oranının KİN ile anlamlı olarak ilişkili olduğunu gördük. Ayrıca KİN gelişiminde KV/GFH> 2,68 sınırının en iyi öngördürücü düzey olduğunu saptadık. (b) KV/GFH dışında, yaşlı hastalarda ve HDL-K değeri düşük olanlarda KİN gelişiminin daha fazla olduğunu gördük ve bu değişkenlerin KİN gelişimini öngördürmede anlamlı etkileri olduğunu saptadık.(c) HDL-K ile NLR, PLR, MVPLR, sigara,BKİ ve kadın cinsiyet değişkenleri arasında anlamlı korelasyon saptadık.

Girişimsel kardiyolojinin gelişip yaygınlaşması ile birlikte KİN koroner anjiyografi ve girişimsel işlemlerin başlıca komplikasyonu durumuna gelmiştir. Çalışmamızın giriş kısmında belirttiğimiz gibi perkütan koroner girişimlerden sonra %10-15 oranında KİN gelişimi görülmektedir ve önemli bir morbidite ve mortalite nedenidir. Bununla

birlikte biz çalışmamızda bu oranı %24 olarak saptadık. Genel ortalamadan yüksek olan bu oran hastalarımızın yaş ortalamasının yüksek olması ile açıklanabilir. Akut koroner sendrom nedeni ile perkütan koroner girişim yapılan hastalarda bu komplikasyon elektif olarak işlem yapılan hastalara göre daha yüksektir. Yang ve arkadaşlarının yaptığı bir metaanalizde akut koroner sendrom nedeni ile perkütan koroner girişim yapılan ve KİN gelişen hastalarda tüm nedenlere bağlı ölüm, major kardiyovasküler ve serebrovasküler olaylar ve stent restenozunun anlamlı olarak yüksek olduğu görülmüştür.[20]

Yüksek mortalite ve morbidite oranları nedeni ile, KİN gelişimini öngördürecek belirteçler ve önleyecek yaklaşımlar ile ilgili çalışmalara ilgi artmıştır. Human nötrofil lipocalin (NGAL), plazma sistatin-c (CysC), galectin-1, lipocalin-2, urinary interlökin-18 (IL-18), urinary kidney injury molekül-1 (KIM-1) başlıca üzerinde araştırma yapılan öngördürücü belirteçlerdir.[21-24] KİN'i önlemek amacıyla çeşitli yaklaşımlar öne sürülmüştür. Bu yöntemler içinde en etkili olanı sıvı tedavisi ile intravasküler hacmi arttırmaktır. Sıvı tedavisinin temel olarak 2 yol ile kontrast nefropatisini önlediği düşünülmektedir. Bunlardan biri, artmış damar içi hacmin kontrast maddenin seyrelmesine neden olması ve etkisini azaltmasıdır. Diğer olası mekanizma ise, intravasküler hacim artışınınrenin-anjiyotensin-aldosteron sistemini (RAAS) inhibe ederek vazokonstrüksiyonu azaltmasıdır.[25] Sıvı tedavisi dışında askorbik asit, sodium bikarbonat, N-asetil sistein, statinler, kalsiyum kanal blokerleri, allopurinol ve profilaktik hemodiyaliz/hemofiltrasyon gibi önleyici yöntemler denenmiş ama hiçbirinin faydalı olduğu kanıtlanamamıştır. Kesin önleyici bir yöntemin olmadığı ve tedavi stratejilerinin sınırlı olduğu bu komplikasyonu yönetmenin en akılcı ve pratik yolu kontrast madde miktarını azaltmak olarak görünmektedir. Bu nedenle KİN gelişimine neden olabilecek kontrast madde miktarı ve oranı ile ilgili eşik değerler tanımlamak için çok sayıda çalışma yapılmıştır. Çiçek ve arkadaşları tarafından yapılan, 645 ST eleve myokard infarktüsü (STEMİ) hastasını içeren bir çalışmada, KV/GFH oranının KİN gelişimi ve uzun dönem mortalite ile ilişkisi incelenmiş,KV/GFH oranı 3,3 ve üzerinde olanlarda mortalite anlamlı olarak yüksek bulunmuştur.[26] Benzer şekilde Mager ve arkadaşlarının yaptığı çalışmada, primer perkütan koroner girişim yapılan 871 STEMİ hastası incelenmiş ve KV/GFH oranı>3,7 olanlarda KİN riskinin belirgin olarak arttığı gözlenmiştir.[27] Zahler ve arkadaşlarının yaptığı benzer çalışmada ise KV/GFH oranı>2,13 olanlarda KİN gelişiminin anlamlı olarak daha fazla olduğu görülmüştür.[28] Biz de çalışmamızda KİN gelişimini öngördüren KV/GFH oranı için bir eşik değer tanımladık. Çalışmamızda bu eşik değeri 2,68 olarak saptadık. Bu eşik değerin üzerinde KİN gelişiminin belirgin olarak arttığını gördük.KV/GFH için tanımladığımız eşik değer literatürde tanımlanan eşik değerlere nispeten daha düşük bir değerdir. Bizim çalışmamızdaki hasta grubunun yaş ortalamasının yüksek olması bu durumun nedeni olabilir. Marenzi ve arkadaşları ise KİN gelişimini öngördürücü belirteç olarak kontrast madde miktarını kullanmışlardır. Çalışmalarında koroner girişim yapılan 561 STEMİ hastasını incelemişler, her hasta için işlemde kullanılan kontrast dozu, maximum kontrast dozuna bölünerek kontrast oranı elde edilmiş ve kontrast oran>1 olanlarda KİN gelişiminin 3 kat arttığı görülmüştür.[29] Bizim çalışmamızda da Marenzi ve arkadaşlarının çalışmalarına benzer olarak KİN gelişen grupta kullanılan kontrast miktarı anlamlı olarak daha fazla idi. Çalışmamızın aksine Yuan ve arkadaşları yaptıkları çalışmada yüksek GFH oranlarının KİN gelişim riskini arttırdığınıöne sürmüşlerdir.[30] Rodriguez ve arkadaşları yaptıkları çalışmada KAG sırasında kullanılan kontrast madde miktarını en aza indirmek için rotasyonel KAG yapmışlar ve konvensiyonel KAG yapılan hastalar ile karşılaştırmışlardır. Sonuçta rotasyonel KAG yapılan hasta grubunda daha az kontrast madde kullanımı ve daha az KİN gelişimi olduğunu tespit etmişlerdir.[31] Bunlar dışında akut koroner sendromlu hastalarda KİN gelişimini öngördürmede birçok değişken çalışılmıştır. Bunlardan literatürde sıkça karşımıza çıkanlar hemogram verilerinden formüle edilmiş değerlerdir. Gülcü'nün STEMİ olan hastalarda KİN gelişimini araştırdığı çalışmasında, NLR'nin KİN gelişimini öngörmede bağım-

sız bir değişken olarak kullanılabileceği öne sürülmüştür.[32] Zorlu ve arkadaşları'nın yaptığı benzer çalışmada NLR, MVPLR ve PLR değerleri KİN gelişen grupta anlamlı derecede yüksek bulunmuş ve bunlar içinde sadece MVPLR öngördürücü olarak anlamlı bulunmuştur.[33] Biz çalışmamızda NLR, MPVLR, Monosit-HDL-K oranı (MHR) ve PLR değişkenlerini KİN gelişen grupta daha yüksek bulduk ancak bu yükseklik istatistiksel olarak anlamlı değildi. Yaş ile birlikte KİN riskinin arttığını gösteren literatürde çok sayıda çalışma bulunmaktadır. Kaya ve arkadaşları KİN gelişim risk faktörleri içinde yaş etkeninin de önemli bir yere sahip olduğunu belirtmişler ve yaş değişkeninin KİN gelişimi için bağımsız bir öngördürücü olduğunu öne sürmüşlerdir.[34] Literatüre benzer şekilde bizim çalışmamızda da KİN gelişim oranları anlamlı derecede yaşlı hastalarda daha yüksek saptanmıştır. Ayrıca çalışmamızda yaş değişkeninin, KİN gelişimini öngördürmede anlamlı bir etkiye sahip olduğu saptanmış ve her bir yaş artışının-KİN gelişim riskini 1,1 kat arttırdığı görülmüştür. Sigara kullanımı ile KİN arasındaki ilişkiye yönelik literatürde birbirine zıt sonuçlar içeren çalışmalar vardır.[35-36] Biz çalışmamızda KİN gelişen olgularda sigara içme oranının anlamlı olarak daha yüksek olduğunu gördük ancak KİN gelişimini öngördürmede anlamlı bir etkisi olduğunu saptamadık. KİN riskini arttırdığı literatürdeki birçok çalışma ile desteklenmiş olan diyabetes mellitus (DM) hastalığının KİN ile ilişkisini incelediğimizde, literatürün aksine KİN riskini anlamlı derecede arttırdığına dair bir sonuç elde etmedik. Bu durum bizim çalışmamızdaki hasta sayısının az olmasına ve sadece oral antidiyabetik alan DM hastalarını almamıza bağlı olabilir. KİN gelişimi ile ilişkisini araştırdığımız bir diğer değişken olan HDL-K, anti-inflamatuvar, anti-oksidan ve anti-trombotik özellikleri olan bir moleküldür. Bu özelliklere dayanarak bir inflamatuvar süreç olan KİN gelişiminde HDL-K'nın rolü olabileceği üzerine çalışmalar yapılmıştır. Ulus ve arkadaşları STEMİ hastalarında yaptıkları çalışmada MHR'nin KİN gelişimini öngördürdüğünü öne sürmüşlerdir, Kirişci ise karotis arter hastalığını öngördürmede MHR'nin bir gösterge olarak kullanabileceğini öne sürmüştür. Turan ve arkadaşları ise yaptıkları çalışmada HDL-K düzeylerinin KİN grubunda daha yüksek olduğunu ve ayrıca düşük dansiteli lipoprotein- kolesterolün (LDL-K) KİN gelişimini öngördürdüğünü öne sürmüşlerdir.[37-39] Biz çalışmamızda HDL-K'nın KİN gelişen grupta anlamlı derecede daha düşük olduğunu gördük ve KİN gelişiminde öngördürücü bir prametre olarak saptadık. Her bir birimlik HDL-K artışının KİN gelişme riskinin 1,1 kat azalması ile ilişkili olduğu sonucunu elde ettik. Ayrıca beklendiği üzere BKİ ile HDL-K arasında anlamlı negatif yönde korelasyon saptadık. Benzer şekilde sigara kullanımı ve HDL-K arasında da anlamlı negatif korelasyon saptadık. Bu verimiz literatürdeki veriler ile uyumludur. Zaid ve arkadaşları HDL-K ile BKİ, sigara kullanımı ve alkol tüketimi arasındaki ilişkiyi inceledikleri çalışmalarında, HDL-K ileBKİ ve sigara kullanımı arasında negatif yönde güçlü korelasyon saptadılar.[40] MHR ve KİN arasında ise anlamlı bir ilişki saptamadık. Benzer şekilde trigliserid, LDL-Kolesterol ve total kolesterol için de böyle bir ilişki saptamadık.

Çalışmamızın bazı sınırlamaları mevcuttur. İlk olarak çalışma grubumuzun sayısının az olması, tek merkezli olması ve prospektif gözlemsel bir çalışma olması nedeni ile elde ettiğimiz sonuçlar randomize kontrüllü, çok merkezli çalışmalardan elde edilen sonuçlar ile desteklenmesi gerekir. İkincisi, çalışma grubumuzu STEMİ ve NSTEMİ tanılı hastalar oluşturmaktadır. Stabil olmayan anjina pectoris ve stabil anjina pektoris hastalarını içermemektedir. Üçüncüsü, çalışma grubumuzun yaş ortalaması yüksek olduğu için ölçtüğümüz GFH değerleri gerçek değerlerin altında hesaplanmış olabilir, ayrıca aynı nedenle KV/GFH için bulduğumuz eşik değeri tüm popülasyona uyarlamak uygun olmayabilir. Dördüncüsü, HDL-K ve diğer laboratuvar değerleri (kreatinin hariç) için tek seferlik ölçüm yaptık. Halbuki bu ölçümler zamanla değişiklik gösterebilir. Bu nedenle bu değişkenlerin dinamik değişiklikleri ile KİN ilişkisine dair bir verimiz bulunmamaktadır.

Sonuç olarak, önemli bir mortalite ve morbidite nedeni olan KİN gelişimini önlemek için kullanılacak kontrast

madde miktarı hakkındafarkındalığa sahip olmak en iyi strateji gibi görünmektedir. Perkütan koroner işlemler öncesinde hasta bazlı yapılacak basit bir hesaplama ile kullanabileceğimiz azami kontrast madde miktarını bilmenin bu komplikasyonu önlemeye büyük katkı sağlayacını düşünmekteyiz. Biz bu çalışmada KİN gelişimini öngördüren KV/GFH için optimal bir sınır değer tanımladık ve ayrıca yaş ve HDL-K'nın bu komplikasyonu öngörmede etkili bir yere sahip olduğunu gördük.

Çalışmamız 10.01.2019 tarih ve 1921 protokol numarası ile Manisa Celal Bayar Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmıştır.

Kaynaklar

1. *Toprak O. Risk markers for contrast-induced nephropathy. Am J Med Sci 2007; 334: 283-90*
2. *Romano G, Briguori C, Quintavalle C, Zanca C, Rivera NV, Colombo A, et al. Contrast agents and renal cell apoptosis. Eur Heart J. 2008;29:2569–76*
3. *Pucelikova T, Dangas G, Mehran R. Contrast-induced nephropathy. Catheter Cardiovasc Interv. 2008;71:62–72*
4. *Marenzi G, Assanelli E, Campodonico J, Lauri G, Marana I, De Metrio M et al. Contrast volume during primary percutaneous coronary intervention and subsequent contrast-induced nephropathy and mortality. - Ann Intern Med. 2009; 150:170-7.*
5. *Perrin T, Descombes E, Cook S. Contrast-induced nephropathy in invasive cardiology. Swiss Med Wkly. 2012;142:w13608*
6. *Bolognese L, Falsini G, Schwenke C, Grotti S, Limbruno U, Liistro F et al. Impact of iso-osmolar versus low-osmolar contrast agents on contrast-induced nephropathy and tissue reperfusion in unselected patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (from the Contrast Media and Nephrotoxicity Following Primary Angioplasty for Acute Myocardial Infarction [CONTRAST-AMI] Trial). Am J Cardiol 2012; 109:67-74.*
7. *Solomon RJ, Mehran R, Natarajan MK, Doucet S, Katholi RE, Staniloae CS et al. Contrast-Induced Nephropathy and Long-Term Adverse Events: Cause and Effect? CJASN. 2009; 4: 1162-1169.*
8. *Celik O, Ozturk D, Akin F, Ayca B, Yalçın AA, Ertürk M et al. Association Between Contrast Media Volume-Glomerular Filtration Rate Ratio and Contrast-Induced Acute Kidney Injury After Primary Percutaneous Coronary Intervention. Angiology. 2015; 66: 519-524*
9. *Cochran ST, Bomyea K, Sayre JW. Trends in adverse events after IV administration of contrast media. AJR Am J Roentgenol 2001; 176:1385–1388*
10. *Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K. Adverse reactions to ionic and nonionic contrast media: a report from the Japanese Committee on the Safety of Contrast Media. Radiology 1990; 175:621–628*
11. *Nie B, Cheng WJ, Li YF, Cao Z, Yang Q, Zhao YX, et al. A prospective, double-blind, randomized, controlled trial on the efficacy and cardiorenal safety of iodixanol vs. iopromide in patients with chronic kidney disease undergoing coronary angiography with or without percutaneous coronary intervention. Catheter Cardiovasc Interv. 2008;72:958–65*
12. *Jo SH, Youn TJ, Koo BK, Park JS, Kang HJ, Cho YS, et al. Renal toxicity evaluation and comparison between visipaque (iodixanol) and hexabrix (ioxaglate) in patients with renal insufficiency undergoing coronary angiography: The RECOVER study: A randomized controlled trial. J Am Coll Cardiol. 2006;48:924–30*
13. *Laskey W, Aspelin P, Davidson C, Rudnick M, Aubry P, Kumar S, et al. DXV405 Study Group. Nephrotoxicity of iodixanol versus iopamidol in patients with chronic kidney disease and diabetes mellitus undergoing coronary angiographic procedures. Am Heart J. 2009;158:822–8*
14. *Kuhn MJ, Chen N, Sahani DV, Reimer D, van Beek EJ, Heiken JP, et al. The PREDICT study: A randomized double-blind comparison of contrast-induced nephropathy after low- or iso-osmolar contrast agent exposure. AJR Am J Roentgenol. 2008;191:151–7*
15. *Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl SR, Cercek B et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions [published correction appears in Circulation. 2012 Feb 28;125(8):e412. Dosage error in article text]. Circulation. 2011; 124:e574-e651*
16. *Nyman U, Bjork J, Aspelin P, Marenzi G. Contrast medium dose-to- GFH ratio: A measure of systemic exposure to predict contrast-induced nephropathy after percutaneous coronary intervention. Acta Radiol. 2008;49:658–67*
17. *Manske CL, Sprafka JM, Strony JT, Wang Y. Contrast nephropathy in azotemic diabetic patients undergoing coronary angiography. Am J Med. 1990;89:615–20*
18. *Brown JR, Robb JF, Block CA, Schoolwerth AC, Kaplan AV, O'Connor GT, et al. Does safe dosing of iodinated contrast prevent contrast-induced acute kidney injury? Circ Cardiovasc Interv. 2010;3:346–50*
19. *Çiçek G, Bozbay M, Açıkgöz SK, Altay S, Uğur M, Köroğlu B et al. The ratio of contrast volume to glomerular filtration rate predicts in-hospital and six-month mortality in patients undergoing primary angioplasty for ST-elevation myocardial infarction. Cardiol J. 2015;22:101-107.*
20. *Yang Y, George KC, Luo R, Cheng Y, Shang W, Ge S et al. Contrast-induced acute kidney injury and adverse clinical outcomes risk in acute coronary syndrome patients undergoing percutaneous coronary intervention: a meta-analysis. BMC Nephrol. 2018; 19:374*
21. *Reyes LF, Severiche-Bueno DF, Bustamante CA, Murillo S, Soni NJ, Poveda M et al. Serum levels of neutrophil Gelatinase associated Lipocalin (NGAL) predicts hemodialysis after coronary angiography in high risk patients with acute coronary syndrome. BMC Nephrol. 2020; 21:143*
22. *He Y, Deng Y, Zhuang K, Li S, Xi J, Chen J. Predictive value of cystatin C and neutrophil gelatinase-associated lipocalin in contrast-induced nephropathy: A meta-analysis. PLoS One. 2020; 15:e0230934*
23. *Kuo CS, Chou RH, Lu YW, Tsai YL, Huang PH, Lin SJ. Increased circulating galectin-1 levels are associated with the progression of kidney function decline in patients undergoing coronary angiography. Sci Rep. 2020; 10:1435*
24. *Ling W, Zhaohui N, Ben H, Leyi G, Jianping L, Huili D et al. Urinary IL-18 and NGAL as early predictive biomarkers in contrast-induced nephropathy after coronary angiography. Nephron Clin Pract. 2008; 108:c176-c181*
25. *Mueller C. Prevention of contrast-induced nephropathy with volume supplementation. Kidney Int Suppl. 2006; 100:S16-S19*
26. *Çiçek G, Bozbay M, Açıkgöz SK, Altay S, Uğur M, Köroğlu B et al. The ratio of contrast volume to glomerular filtration rate predicts in-hospital and six-month mortality in patients undergoing primary angioplasty for ST-elevation myocardial infarction. Cardiol J. 2015; 22:101-107*
27. *Mager A, Vaknin Assa H, Lev EI, Bental T, Assali A, Kornowski R. The ratio of contrast volume to glomerular filtration rate predicts outcomes after percutaneous coronary intervention for ST-segment elevation acute myocardial infarction. Catheter Cardiovasc Interv. 2011; 78:198-201*
28. *Zahler D, Rozenfeld KL, Merdler I, Peri Y, Shacham Y. Contrast Volume to Glomerular Filtration Ratio and Acute Kidney Injury among ST-Segment Elevation Myocardial Infarction Patients Treated with Primary Percutaneous Coronary Intervention. Cardiorenal Med. 2020; 10:108-115*
29. *Marenzi G, Assanelli E, Campodonico J, Lauri G, Marana I, Metrio MD et al. Contrast volume during primary percutaneous coronary intervention and subsequent contrast-induced nephropathy and mortality. Ann Intern Med. 2009; 150:170-177*
30. *Yuan Y, Qiu H, Hu XY, Luo T, Gao XJ, Zhao XY et al. Relationship between High Level of Estimated Glomerular Filtration Rate and Contrast-Induced Acute Kidney Injury in Patients who Underwent an Emergency Percutaneous Coronary Intervention. Chin Med J (Engl). 2018; 131:2041-2048*
31. *Fernández-Rodríguez D, Grillo-Pérez JJ, Pérez-Hernández H, Rodriguez-Esteban M, Pimienta R, Acosta-Materan C et al. Prospective evaluation of the development of contrast-induced nephropathy in patients with acute coronary syndrome undergoing rotational coronary angiography vs. conventional coronary angiography: CINERAMA study. Nefrologia. 2018; 38:169-178*
32. *Gulcu O. The association between neutrophil to lymphocyte ratio and contrast induced nephropathy in patients with ST segment elevation myocardial infarction. Annals of Medical Research. 2019; 26:1184-8*
33. *Zorlu C, Koseoglu C. Comparison of the Relationship Between Inflammatory Markers and Contrast-Induced Nephropathy in Patients With Acute Coronary Syndrome After Coronary Angiography. Angiology. 2020; 71:249-255.*
34. *Kaya A, Karataş A, Kaya Y, Düğeroğlu H, Dereli S, Bayramoğlu A. A New and Simple Risk Predictor of Contrast-Induced Nephropathy in Patients Undergoing Primary Percutaneous Coronary Intervention: TIMI Risk Index. Cardiol Res Pract. 2018;2018:5908215*
35. *Cho JY, Jeong MH, Hwan Park S, Kim IS, Park KH, Sim DS et al. Effect of contrast-induced nephropathy on cardiac outcomes after use of nonionic isosmolar contrast media during coronary procedure. J Cardiol. 2010;56:300-306*
36. *Ni Z, Liang Y, Xie N, Liu J, Sun G, Chen S et al. Simple pre-procedure risk stratification tool for contrast-induced nephropathy. J Thorac Dis. 2019;11:1597-1610*
37. *Ulus T, Isgandarov K, Yilmaz AS, Uysal S, Vasi İ, Dural M et al. Monocyte to High-Density Lipoprotein Ratio Predicts Contrast-Induced Nephropathy in Patients With Acute Coronary Syndrome. Angiology. 2018; 69: 909-916*
38. *Kirişçi M. A Promising Marker for Carotid Artery Disease:Monocyte to High-density Lipoprotein Cholesterol Ratio. Sakarya Med J. 2020;10:93-98*
39. *Turan B, Erkol A, Gül M, Fındıkçıoğlu U, Erden İ. Effect of Contrast-Induced Nephropathy on the Long-Term Outcome of Patients with Non-ST Segment Elevation Myocardial Infarction. Cardiorenal Med. 2015; 5:116-124*
40. *Zaid M, Miura K, Okayama A, Nakagava H, Sakata K, Okuda Net al. Associations of High-Density Lipoprotein Particle and High-Density Lipoprotein Cholesterol With Alcohol Intake, Smoking, and Body Mass Index- The INTERLIPID Study. Circ J. 2018; 82:2557-2565*

RESEARCH ARTICLE / *Araştırma Makalesi*

Evaluation of Index of Cardiac-Electrophysiological Balance and Electrocardiographic Alternations in Patients with Sarcoidosis

Sarkoidozlu Hastalarda Kardiyak-Elektrofizyolojik Denge İndeksinin ve Elektrokardiyografik Değişimlerin Değerlendirilmesi

Yakup Alsancak[1], Celalettin Korkmaz[2]

[1] Necmettin Erbakan University, Meram School of Medicine, Department of Cardiology, Konya, Türkiye
[2] Necmettin Erbakan University, Meram School of Medicine, Department of Chest Diseases, Konya, Türkiye

Yazışma Adresi / *Correspondence:*
Yakup Alsancak

Necmettin Erbakan University, Meram Faculty of Medicine, Department of Cardiology, Meram, Konya, Türkiye
T: **+90 0332 223 65 00** E-mail **: yakupalsancak@yahoo.com**

Geliş Tarihi / Received : **14.10.2020** Kabul Tarihi / Accepted : **09.02.2021**

Orcid :

Yakup Alsancak https://orcid.org/0000-0001-5230-2180
Celalettin Korkmaz https://orcid.org/0000-0001-8602-0368

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):193-200) DOI: 10.31832/smj.810675**

Abstract

Objective	Cardiac sarcoidosis (CS) can manifest with different clinical signs and has a poor prognosis, but the heart is rarely affected alone. We aim to evaluate the arrhythmogenic effects of sarcoidosis by using electrocardiography (ECG) in patients with or without cardiac involvement.
Materials and Methods	A total of 61 patients under follow-up for pulmonary sarcoidosis were retrospectively reviewed and 50 healthy volunteers were enrolled in the study. Sarcoidosis patients were also grouped as with or without cardiac involvement (n=11/ n=35). QRS, QT, Tp-e (T peak to end) intervals, P wave morphology were measured manually on ECG. Then, Tp-e/QT, Tp-e/QTc, QT/QRS (index of cardiac electrophysiological balance, (iCEB)), and QTc/QRS (iCEBc) ratios were calculated and compared between groups.
Results	Heart rate on ECG, QT/QTc interval, Tp-e intervals and Tp-e/QT ratio and PWD were significantly higher (p values < 0.018) and iCEB or iCEBc values were lower in the sarcoidosis group than controls (p = 0.001). And we could not find a relationship between non-cardiac and CS and ECG parameters including QTc, Tp-e/QT ratio and iCEB (p= 0.501, p= 0.753 and p=0.490, respectively).
Conclusion	The present study demonstrated a lower iCEB value and higher repolarization findings in sarcoidosis patient. However, there are no differences between with or without cardiac involvement due to sarcoidosis.
Keywords	Arrhythmia; electrocardiography; iCEB; sarcoidosis

Öz

Amaç	*Kardiyak sarkoidoz (KS) farklı klinik bulgularla ortaya çıkabilir ve kötü bir prognoza sahiptir, ancak kalp nadiren tek başına etkilenir. Bu çalışmamızda, kalp tutulumu olan veya olmayan hastalarda elektrokardiyografi (EKG) kullanarak sarkoidozun aritmojenik etkilerini değerlendirmeyi amaçladık.*
Gereç ve Yöntemler	*Pulmoner sarkoidoz nedeniyle takip edilen toplam 61 hasta retrospektif olarak incelendi ve 50 sağlıklı gönüllü çalışmaya alındı. Sarkoidoz hastaları da kalp tutulumu olan veya olmayan olarak gruplandırıldı (n = 11 / n = 35). EKG üzerinde; QRS, QT, Tp-e (T peak to end) intervali, P dalga morfolojisi manuel olarak ölçüldü. Daha sonra Tp-e / QT, Tp-e / QTc, QT / QRS (kardiyak elektrofizyolojik denge indeksi, (iCEB)) ve QTc / QRS (iCEBc) oranları hesaplandı ve gruplar arası karşılaştırıldı.*
Bulgular	*Sarkoidoz grubunda, kontrol grubuna göre kalp hızı, QT / QTc aralığı, Tp-e aralıkları ve Tp-e / QT oranı ve PWD anlamlı olarak yüksek (p değerleri <0,018), iCEB ve iCEBc değerleri daha düşüktü (p = 0,001). Kardiyak sarkoidozu olan ve olmayan grupta ise QTc, Tp-e / QT oranı ve iCEB dahil EKG parametreleri arasında bir ilişki bulunmadı (sırasıyla p = 0,501, p = 0,753 ve p = 0,490).*
Sonuç	*Bu çalışma, sarkoidoz hastalarının repolarizasyon değerlerinin daha yüksek, iCEB değerinin ise daha düşük olduğunu göstermiştir. Bununla birlikte, sarkodioza bağlı kalp tutulumu olan hastalarla, olmayan hastalar arasında ECG parametrelerine göre anlamlı bir fark görülmemiştir.*
Anahtar Kelimeler	*Aritmi; elektrokardiyografi; iCEB; sarkoidoz*

INTRODUCTION

Sarcoidosis is known as a multisystemic granulomatous disease with unexplained etiology which affect many organs in the body. But also, current reports argue that sarcoidosis has occurred as a result of increased immunological response for any reason in individuals with genetic predisposition.[1] Asymptomatic pulmonary involvement is the most common form in daily practice, but the disease may also affect heart, liver, peripheral lymph nodes, spleen, skin, eyes, and parotid glands.[2] Unfortunately, cardiac exposure in sarcoidosis has a poor prognosis, and the heart is rarely affected alone.[3] Involvement of heart and the emergence of related cardiac symptoms constitute 2-5% of patients with sarcoidosis.[4] And, 20-25% patients with sarcoidosis have an asymptomatic cardiac involvement according to autopsy reports.[5]

Cardiac sarcoidosis (CS) can manifest itself with different clinical signs. The affected anatomically area of the heart, the active period and extent of the disease are decisive for this condition.[6] Mainly, the clinical implications of CS are primarily due to arrhythmias, conduction disorders and heart failure.[7] Pericardial disease, sudden cardiac death, coronary artery or cardiac valves involvement are less frequently demonstrated.[8,9] In this context, some studies have been conducted on surface electrocardiography to predict arrhythmia in patients with sarcoidosis. QT interval prolongation, which is the most known ECG finding that is a marker for electrical instability and sudden cardiac death, was shown in patients with sarcoidosis.[10] T peak to end (Tp-e) interval on ECG is considered as an index of transmural dispersion of left ventricular repolarization and Tp-e/QT ratio is also used as a novel electrocardiographic index of ventricular arrhythmogenesis. Previously published studies demonstrated that a prolonged Tp-e and higher Tp-e/QT ratio has been associated with an increased risk of ventricular arrhythmias.[11,12] It has been suggested that Tp-e and Tp-e/QT ratios were higher in sarcoidosis patients.[13] Index of cardiac electrophysiological balance (iCEB), estimated as QT interval divided by QRS duration, is a novel risk indicator for predicting malignant ventricular arrhythmias.[14] An elevated iCEB level is accepted as a predictor of torsades de pointes (TdP) ventricular arrhyhtmias wheares decreased iCEB level is linked with non-torsades de pointes ventricular arrhyhtmias.[15]

In this study, we aimed to investigate the iCEB and it's association between Tp-e and Tp-e/QT ratio in patients with or without cardiac involvement of sarcoidosis to evaluate proarrhythmogenic effect.

MATERIAL and METHODS

2.1. Study population and patient selection

A total of 61 patients (30 males; mean age 43.4±10.6 years) under follow-up for pulmonary sarcoidosis and had cardiac magnetic resonance imaging for investigating for cardiac involvement were retrospectively reviewed and 50 healthy volunteers (32 males; mean age 42.4±8.6 years) were enrolled in the study. The study population was categorized as sarcoidosis group, control group and compared the parameters between groups. After that, we compared the parameters between in patients with cardiac (n= 11) and non-CS (n= 35). In sarcoidosis group, patients was diagnosed means of transbronchial ultrasound-guided lymph node or peripheric biopsy and biopsy-proven sarcoidosis was diagnosed in all patients. Patients with a history of myocardial infarction or coronary revascularization (via coronary artery bypass graft operation or percutaneous coronary intervention), those who documented atrial fibrillation, cardiac pacemaker implantation, sick sinus syndrome, any kind of bundle branch blocks, pre-excitation syndromes, atrioventricular block, left ventricular hypertrophy and valvular heart disease (moderate-to-severe), renal insuffiency (creatinin levels > 1.5 or glomeruler filtration rate below 50) electrolyte hemoastatis disorders, heart failure who need medical treatment, depressed left ventricular ejection fraction (EF < 55%) due to coronary artery disease were excluded from study. For this reason, a total of 14 patients (heart failure: 3, coronary artery disease: 3, documented atrial fibrillation: 3 insufficient

or inappropriate ECG data: 5, left bunddle block: 1) were excluded from this study, finally 46 patients data was analysed. A study flow chart has been illustrated in Figure 1.

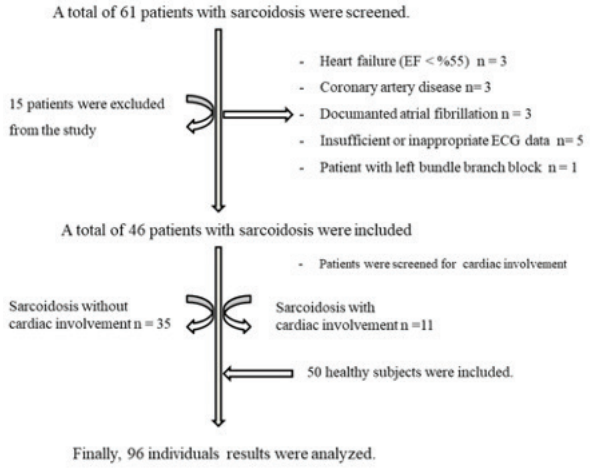


Figure 1. Flowcharts of the study

2.2. Definition of cardiac sarcoidosis

The electrocardiographic and echocardiographic features of the patients were evaluated. On electrocardiography, conduction abnormalities, branch blocks, atrial fibrillation, AV block presence were recorded. We could not investigate 24-hour Holter ECG monitoring records of patients because of retrospective design and lack of the records. In echocardiography, end-diastolic/end-systolic left ventricular diameter, interventricular septum and posterior wall end-diastolic thickness, regional or globally wall motion abnormalities, pressure of LV filling, mitral and tricuspid valves regurgitation, pericardial effusion, pulmonary artery pressure and ejection fraction were recorded. Myocardial wall motion abnormalities in patients with a history of obstructive coronary artery disease were excluded from study. The results of cardiac magnetic resonance (MR) imaging were evaluated of all patients with a diagnosis of sarcoidosis. Nevertheless, patients with late gadolinium enhacement (LGE) in cardiac MR imaging were examined with a definitive diagnosis of CS. Therefore, 11 patients were grouped as CS due to MR imaging findings.[16]

2.3. Electrocardiographical examinations

Heart rate, P-wave morphology, PR interval, QRS duration, QT distance and T-wave morphology were analyzed. All ECG samples were examined on a digital platform and measurements were then taken using special software (Adobe Photoshop) to provide the necessary magnification.

The beginning point of the P-wave was described as the first upward positive or downward negative deflection between the isoelectric line and the end of the P-wave was characterized as the point where the last deflection of the P-wave met the isoelectric line. Maximum (Pmax) and minimum P (Pmin) wave durations were recorded. P-wave dispersion (PWD) was defined as the difference between the maximum and minimum P-wave durations.[17] The QT interval was conventionally obtained by manually measuring from the onset of the QRS complex to the crossing point of the T wave and isoelectric line. The heart rate-corrected QT interval was calculated using Bazett's formula ($cQT = QT\sqrt{(R - R \text{ interval})}$). QT dispersion (QTd) was obtained by measuring the longest QT interval (QTmax) and the shortest QT interval (QTmin) in any lead.[18] QT interval measurements were taken by examining recordings from leads D2 and precordial V5, and the longer lead was recorded for statistical analysis. The distance from the peak of the T-wave (Tpeak) to the endpoint of the T-wave (T end) (Tpeak-end or Tp-e) was obtained from the chest leads. The Tp-e/QT ratio was obtained by dividing the Tp-e duration by the QT interval in the precordial V5 lead.[19] The index of cardiac electrophysiological balance (iCEB) was obtained by dividing the QT interval by the QRS duration in the same lead (D2 or V5).[14,15]

Statistical Analysis

SPSS® version 16.0 statistical package software (SPSS Inc., Chicago, IL, United States) was used for statistical analyses. We presented normally distributed quantitative variables as mean ± standard deviation or median value while we presented categorical variables in numbers and percentages. Normality of distribution was evaluated us-

ing the Kolmogorov–Smirnov test. Mean values of continuous variables were compared between independent groups using the Student's T-test, one-way ANOVA test, or Kruskal-Wallis test as appropriate. The chi-square test was performed to compare the study groups in terms of categorical variables. A p-value below 0.05 was considered statistically significant.

RESULTS

A total of 96 patients with a mean age of 59.46±11.12 years, 74 (77.1%) of whom were women, formed the study population. There was no statistically significant difference between the sarcoidosis group and control group in terms of gender, age and laboratory parameters except high density lipoprotein cholesterol, trigliseride and CRP (C-reactive protein). CRP levels were higher in sarcoidosis group as expected (p= 0.001). The study groups were comparable in terms of echocardiographic and electrocardiographical parameters. Accordingly, in patients with sarcoidosis, pulmonary artery pressure was higher and pericardial effusion rate was higher than control group (p= 0.002 and p= 0.045, respectively). Although QT maximum, QT minimum, P minimum were not different between groups, heart rate on ECG, QT/QTc interval, Tp-e intervals and Tp-e/QT ratio and PWD were significantly higher in sarcoidosis group (p values < 0.018). And also, iCEB or iCEBc values were lower in sarcoidosis group (p= 0.001). The demographic features, laboratory parameters, electrocardiographic and echocardiographic characteristics and comparison between groups are summarized in Table 1 and 2.

In the subgroup analysis, according to echocardiographic evaluation, we detected only that the left ventricular posterior wall thickness was increased in patients with CS (p = 0.001). And we found any relationship between non-cardiac and CS and ECG parameters including QTc, Tp-e/QT ratio and iCEB (p= 0.501, p= 0.753 and p= 0.490, respectively). Table 3 demonstrates the electrocardiographic parameters, echocardiographic characteristics and comparison between subgroups.

Table 1. Demographic and laboratory characteristics of patients and comparing parameters between Sarcoidosis group and Control group

Variables	Sarcoidosis group (n =46)	Control group (n= 50)	p value
Age (median, IQR)	57.54 (29-77)	61.24 (33-80)	0.528
Gender (female, n / %)	35 / 76,8	39 / 78	0.825
Smoking (n / %)	4 / 8.7	10 / 20	0.470
Hypertension (n / %)	19 / 41.34	25 / 50	0.395
Diabetes mellitus (n / %)	10 / 21.7	15 / 30	0.359
Hemoglobulin (mg/dl / mean±std)	13.24±1.33	13.65±1.57	0.186
Potasium (meq/L, mean±std)	4.34±0.32	4.27±0.71	0.121
Glomerular filtration rate (mL/min/ mean±std)	87.14±21.55	92.96±15.82	0.133
Total cholesterol (mg/ dl, mean±std)	203.11±52.99	203,64±44.41	0.961
LDL (mg/dl, mean±std)	122.59±39.73	123.13±37.11	0.949
HDL (mg/dl, mean±std)	42.5±12.45	48.30±12.48	**0.039**
Uric ascid (mg/dl, mean±std)	5.48±1.32	5.23±1.83	0.469
Glucose (mg/dl, median, IQR)	108.7 (89-112)	99.5 (89-129)	0.393
Creatinine (mg/dl, median, IQR)	0.78 (0.69-0.91)	0.71 (67-82)	0.063
Sedimantation (sn, median, IQR)	15 (13-20)	13.5 (6.7-24)	0.201
ALT (mg/dl, median, IQR)	19.25 (15.5-23.5)	20 (12.7-25)	0.638
AST (mg/dl, median, IQR)	19.5 (16.6-26)	20 (18-25)	0.336
Trigliseride (mg/dl, median, IQR)	162 (128-237)	135 (92-194)	**0.014**
CRP (mg/dl, median, IQR)	5.63 (3.6-9)	1.1 (0.1-3)	**0.001**

*ALT; alanine aminotransferase; AST; aspartate aminotransferase, CRP; C-reactive protein, HDL; high density lipoprotein cholesterol, IQR; interquartile range, LDL; low density lipoprotein cholesterol

Table 2. Comparing of echocardiographical and electrocardiographical parameters of groups

Variables		Sarcoidosis group (n =46)	Control group (n= 50)	p value
LVDD, (mm, mean±std)		44.16±4.6	47.02±4.9	**0.004**
LVSD, (mm, mean±std)		27.10±3.5	28.26±6.5	0.292
IVSD, (mm, mean±std)		10.55±1.4	9.84±0.97	0.006
PWT, (mm, mean±std)		10±1.67	9.48±1.7	0.084
LVEF (%, median, IQR)		61 (59-63)	60 (50-60)	0.122
Mitral inflow E velocity		71.32±16.3	71.32±19.7	0.919
Mitral inflow A velocity		79.34±20.8	76.3±18.5	0.453
Left atrial diameter, (mm, mean±std)		34.5 (31-39)	36.5 (33-38)	0.066
Mitral regurgitation (n/%)				
	- mild	45 (99)	47 (94)	0.268
	- moderate	1 (1)	3 (6)	
Tricuspid regurgitation (n/%)				
	-mild	44 (95.6)	47 (94)	
	-moderate	2 (4.4)	3 (6)	0.495
Pulmonary artery systolic pressure (mmHg, mean±std)		36.02±5.53	31.34±7.79	**0.002**
Pericardial effusion (n/%)		9 (19.5)	3 (6)	**0.045**
Electrocardiographical parameters				
Heart rate (pulse/min, mean±std)		80.19±16.97	72.74±12.38	**0.015**
P maximum (msn, mean±std)		91.5±17.78	78.4±26.6	**0.006**
P minimum (msn, mean±std)		47.39±12.6	49.20±19.7	0.597
PWD (mns, mean±std)		43.84±12.68	29.2±13.61	**0.001**
QT maximum (msn, mean±std)		389.13±38.35	380.24±32.82	0.224
QT minimum (msn, mean±std)		362±37.72	358.5±28.32	0.604
QT dispersion (msn, mean±std)		27.5±11.35	20.95±9.91	**0.004**
QRS (msn, mean±std)		91±17.33	71.64±24.68	**0.001**
Tpe interval (msn, mean±std)		79.13±18.83	67.20±20.77	**0.004**
QTc maximum (msn, mean±std)		412±27.33	413±32.77	0.763
QTc minimum (msn, mean±std)		385±28.8	392±31.1	0.244
QTc dispersion (msn, mean±std)		27±11.25	21.74±10.35	**0.018**
QT/QRS (iCEB) (mean±std)		4.37±0.65	5.92±1.97	**0.001**
cQT/QRS (iCEBc) (mean±std)		4.63±0.66	6.46±2.2	**0.001**
Tpe/QT ratio (mean±std)		0.20±0.04	0.17±0.05	**0.009**
Tpe/QTc (mean±std)		0.19±0.04	0.16±0.04	**0.002**

* IVSD; inter-ventricular septum, LVDD; left ventricular diastolic diameter, LVEF; left ventricular ejection fraction; LVSD ; left ventricular systolic diameter, PWD; P wave dispersion, PWT: posterior wall thickness, QTc; corrected QT interval, Tp-e; T peak to T end interval

Table 3. Comparing parameters of patients with and without cardiac sarcoidosis

Variables	Sarcoidosis without cardiac involvement (n =35)	Sarcoidosis with cardiac involvement (n = 11)	p value
CRP (mg/dl, mean±std)	7.7±6.6	7.8±7.2	0.960
Sedimantation (sn, mean±std)	19.55±11.2	16.45±9.09	0.411
Potasium (meq/L, mean±std)	4.6±0.28	4.35±0.36	0.052
IVSD, (mm, mean±std)	10.41±1.58	11±1.09	0.261
PWT, (mm, mean±std)	9.4±1.09	12.45±1.03	**0.001**
LVEF (%, median, IQR)	60.71±2.99	61.27±2.32	0.575
Pulmonary artery systolic pressure (mmHg, mean±std)	35.62±5.78	37.27±4.67	0.396
Pericardial effusion (n/%)	6 (17)	3 (27)	0.465
Electrocardiographical parameters			
Heart rate (pulse/min, mean±std)	79.97±18.13	80.9±13.30	0.875
P maximum (msn, mean±std)	93.71±18.68	84.72±12.98	0.146
P minimum (msn, mean±std)	51.57±11.61	34.09±2.02	**0.001**
PWD (mns, mean±std)	42±12.13	49.72±13.17	0.078
QT maximum (msn, mean±std)	388±34.72	392±50	0.726
QT minimum (msn, mean±std)	361.57±32.14	363.64±53.71	0.876
QT dispersion (msn, mean±std)	26.42±9.6	30.9±15.78	0.258
QRS (msn, mean±std)	91.82±18.18	88.36±14.77	0.569
Tp-e interval (msn, mean±std)	79.42±19.69	78.18±16.62	0.851
QTc maximum (msn, mean±std)	411.5±24.25	413.89±36.84	0.804
QTc minimum (msn, mean±std)	385±23	384.8±43.9	0.978
QTc dispersion (msn, mean±std)	26.42±9.62	29±15.78	0.501
QT/QRS (iCEB) (mean±std)	4.33±0.68	4.49±0.55	0.490
cQT/QRS (iCEBc) (mean±std)	4.6±0.7	4.74±0.54	0.535
Tp-e/QT ratio (mean±std)	0.20±0.05	0.20±0.04	0.753
Tp-e/QTc (mean±std)	0.19±0.04	0.18±0.03	0.802

* CRP; C reactive protein , IVSD; inter-ventricular septum, iCEB: index of cardioelectrophyslogical balance, LVEF; left ventricular ejection fraction, PWD; P wave dispersion, PWT: posterior wall thickness, QTc; corrected QT interval, Tp-e; T peak to T end

DISCUSSION

In the current study, our results indicate that Tp-e interval, Tp-e / QT ratio, PWD or index of cardiac electrophysiological balance value, knowns as predictors of the development of arrhythmia which can simply measured on standard 12-lead surface ECG, were higher in sarcoidosis patients than healthy subjects. However, the fact that these findings, were not supported in a small group of sarcoidosis with cardiac involvement, could not reveal that these markers were predictive of cardiac involvement.

The incidence of sarcoidosis in population is 10-20/100.000. Although CS is very rare, it has a poor prognosis and it is an indepented predictor for mortality and morbidity. And left ventricular systolic dysfunction is the most important marker for this situation.[20] CS is the main causes of 0.5% patients who who underwent to cardiac transplantation due to cardiomyopathy.[21] However, cardiac arrhythmias are still the first clinical presentation of symptomatic CS. A significant number of patients with CS (30%) can manifest themselves with complete AV block. Since the conduction system can be infiltrated with sarcoid granuloma, it is possible to see any degree of heart blocks.[22] Previously, it was speculated that atrial arrrhytmias may occur after atrial dilatation due to generalized cardiac involvement in sarcoidosis, instead of just atrial involvement.[23] However, supraventricular tachycardies has been detected 32% of patients with CS nearly in 6 years follow up period. It has been shown that atrial fibrillation is the most frequently supraventricular arrhythmia and left atrial enlargement is the main predictive factor.[24] In addition, sudden death due to malignant ventricular arrhythmias may be the first and only symptoms of cardiac involvement. Macroreentrany, re-entry, triggered activity and abnormal automaticity, due to granulomatous infiltration, inflammation and scaring of myocardium, are accepted as major reasons of ventricular arryhtmias.[25] The prevalence of CS in patients with unexplained ventricular tachycardia is 16-29% according to two studies with small sample size.[26,27] In this context, evaluation of cardiac involvement in patients with sarcoidosis is extremely important. Altough cardiac MR imaging, fluorodeoxyglucose positron emission tomography imaging or tissue biopsy are recommanded for diagnose cardiac involvement in patients with sarcoidosis, these advanced cardiac imaging tecniques is not recommended for patients without abnormalities on initial screening by symptoms/electrocardiogram/echocardiogram.[16] It has been demonstrated that the cardiac history (syncope, palpitation etc), ECG, 24 hours rhytm Holter monitoring and echocardiography have a specificity of 87% and a sensitivity of 100% for the diagnosis of CS.[28] From this point of view, ECG still maintains its place as the first diagnostic and screening test and, several parameters and intervals have been described on surface ECG to determine the arrhythmogenic risks.

The change of ECG parameters described above in sarcoidosis patients has been evaluated in several studies. Uyarel et al. demonstrated an increased QTd in patients with sarcoidosis and cardiac involvement. They also detected it was higher in sarcoidosis patients with cardiac involvement than those without.[10] Kasapkara and colleagues findings support increasing QT dispersion in patients with sarcoidosis and an elevated Tp-e and Tp-e/QT ratio were shown in the same study.[13] However, they did not grouped patients with cardiac or nonCS. In our study, we also found a higher QTd, Tp-e and Tp-e/QT ratio in sarcoidosis like these trials. But our study failed to demonstrate the significant difference between cardiac and non-cardiac sarcoidosis according to these parameters. Maybe the limited number of cardiac sarcoidos patient revealed of this result. The presence of patchy involvement away from the conduction system in MR imaging may also affect the results. In an another study which performed by Buyukoglan H. et al. have been shown a higher PWD in sarcoidosis patient that known as a predictor to the development of atrial fibrillation.[17,29] Herein, we also found a higher PWD value in patients with sarcoidosis than healthy subjects, but there was no statistically differences between cardiac and non-CS. The similarity of the left atrial diameter in both groups

may have caused such a result. And these results may have been seen due to early-stage CS of our study group. Finally, iCEB, which has been defined as a new risk predictor for malignant ventricular arrhythmias, was higher in patients with sarcoidosis. However, we also demonstrated that iCEB value was not different in patients with and without cardiac involvement.

In MR imaging, cardiac infiltration has a typically patchy and multifocal characteristics. The basal segments of the left ventricle are the most affected regions by granulomatosis involvement.[30] For this reason, small localized involvements away from the conduction system may not produce any signs on surface ECG. Perhaps, a large ventricular area should be involved to see surface ECG changes.

Study limitations

The most significant limitation in this trial was the insufficient number of patients with cardiac involvement and retrospective design of the study. In addition, the lack of patient history for previous arrhythmias is another limitation. Moreover, the lack of 24-hour electrocardiographic Holter monitoring to detect arrhythmic conditions in these patients may be considered as a limitation. Moreover, unknown using of drugs that affect the conduction system (beta-blockers, non-dihydropyridine calcium channel blockers or digital), and use of antibiotics with known efficacy on electrocardiography (erythromycin, azithromycin, etc.) may also be considered as a limitation.

CONCLUSION

To our knowledge, the present study is the first to use iCEB analysis in sarcoidosis patients to determine arrhythmogenic risk and we demonstrated a lower iCEB value in patients with sarcoidosis, but we failed to show statistically difference between cardiac and non-CS. Many of the patients with sarcoidosis may have a clinically silent cardiac involvement. Electrocardiography is still an easy-to-use and accessible diagnostic tool in daily practice. According to the literature, the predictors of arrhythmia in electrocardiography appear to be positive in patients with systemic sarcoidosis, but it is not possible to defend the same situation in patients with or without cardiac involvement. Further large scale, randomized, prospective, long-term follow-up studies are needed to clarify the role of iCEB and other electrocardiographical parameters in predicting ventricular arrhythmias and/or sudden cardiac death in patients with sarcoidosis.

Acknowledgment

None

Ethics Committee Approval

Before the beginning of the study, the necessary approval was received from Necmettin Erbakan University Meram School of Medicine's local ethics committee with 2020/2046 numbered decision in date 17.05.2020 and the study was conducted according to the Declaration of Helsinki.

Informed Consent

Patients included in the study were informed about the objective of the study and given written and verbal consents.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declared that this study received no financial support.

References

1. *Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Muller-Quernheim J. Sarcoidosis. Lancet 2013;385:1155–1167.*
2. *Oliver SJ. Nonpulmonary manifestations of sarcoidosis. Curr Rheumatol Rep 2002;4(2):170-178.*
3. *Kim JS, Judson MA, Donnino R, Gold M, Cooper LT, Prystowsky EN, et al. Cardiac sarcoidosis. Am Heart J 2009;157:9–21.*
4. *R.P. Baughman, A.S. Teirstein, M.A. Judson, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. American Journal of Respiratory and Critical Care Medicine 2001;15:1885–1889.*
5. *Iwai K, Tachibana T, Takemura T, Matsui Y, Kitaichi M, Kawabata Y. Pathological studies on sarcoidosis autopsy. I. Epidemiological features of 320 cases in Japan. Acta Pathol Jpn 1993;43:372-376.*
6. *Dubrey SW, Falk RH. Diagnosis and management of CS. Prog Cardiovasc Dis 2010;52:336-346.*
7. *Winters SL, Cohen M, Greenberg S, Stein B, Curwin J, Pe E, et al. Sustained ventricular tachycardia associated with sarcoidosis: assessment of the underlying cardiac anatomy and the prospective utility of programmed ventricular stimulation, drug therapy and an implantable antitachycardia device. J Am Coll Cardiol 1991;18:937–943.*
8. *Lam CS, Tolep KA, Metke MP, Glockner J, Cooper LT Jr. Coronary sarcoidosis presenting as acute coronary syndrome. Clin Cardiol 2009;32(6):68-71.*
9. *Garrett J, O'Neill H, Blake S. Constrictive pericarditis associated with sarcoidosis. Am Heart J 1984;107:394.*
10. *Uyarel H, Uslu N, Okmen E, Tartan Z, Kasikcioglu H, Dayi SU, et al. QT dispersion in sarcoidosis. Chest 2005;128(4):2619-2625.*
11. *Hetland M, Haugaa KH, Sarvari SI, Erikssen G, Kongsgaard E, Edvardsen T. A novel ECG-index for prediction of ventricular arrhythmias in patients after myocardial infarction. Ann. Noninvasive Electrocardiol 2014;19:330–337.*
12. *Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. J. Electrocardiol 2008;41:567–574.*
13. *Kasapkara HA, Sentürk A, Bilen E, Ayhan H, Karaduman BD, Turinay ZS, et al. Evaluation of QT dispersion and T-peak to T-end interval in patients with early-stage sarcoidosis. Rev Port Cardiol 2017;36(12):919-924.*
14. *Lu HR, Yan GX, Gallacher DJ. A new biomarker–index of cardiac electrophysiological balance (iCEB)–plays an important role in drug-induced cardiac arrhythmias: Beyond QT-prolongation and torsades de pointes (TdPs). J Pharmacol Toxicol Methods 2013;68:250–259.*
15. *Robyns T, Lu HR, Gallacher DJ, Garweg C, Ector J, Willems R, et al. Evaluation of Index of Cardio-Electrophysiological Balance (iCEB) as a New Biomarker for the Identification of Patients at Increased Arrhythmic Risk. Ann Noninvasive Electrocardiol 2016;21(3):294-304.*
16. *Birnie DH, Kandolin R, Nery PB, Kupari M. Cardiac manifestations of sarcoidosis: diagnosis and management. European Heart Journal 2017;38:2663–2670.*
17. *Dilaveris PE, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998;135:733–778.*
18. *Malik M and Batchvarov VN. Measurement, interpretation and clinical potential of QT dispersion. J Am Coll Cardiol 2000;36:1749–1766.*
19. *Castro Hevia J, Antzelevitch C, Tornés Bárzaga F, Dorantes Sánchez M, Dorticós Balea F, Zayas Molina R, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. J Am Coll Cardiol 2006; 47:1828-1834.*
20. *M.M. Sadek, D. Yung, D.H. Birnie, Beanlands RS, Nery PB et al. Corticosteroid therapy for Cardiac Sarcoidosis: a systematic review. Canadian Journal of Cardiology 2013;29:1034–1041.*
21. *Al-Kindi SG, Oliveira GH. Letter by Al-Kindi and Oliveira regarding article "Cardiac Sarcoidosis: epidemiology, characteristics, and outcome over 25 years in a nationwide study". Circulation 2015;132:211.*
22. *Nery PB, Beanlands RS, Nair GM, Green M, Yang J, McArdle BA, et al. Atrioventricular block as the initial manifestation of CS in middle-aged adults. J Cardiovasc Electrophysiol 2014;25:875–881.*
23. *Sharma S. Cardiac imaging in myocardial sarcoidosis and other cardiomyopathies. Curr Opin Pulm Med 2009;15:507-512.*
24. *Viles-Gonzalez JF, Pastori L, Fischer A, Wisnivesky JP, Goldman MG, Mehta D. Supraventricular arrhythmias in patients with Cardiac Sarcoidosis prevalence, predictors, and clinical implications. Chest 2013;143:1085–1090.*
25. *H. Furushima, M. Chinushi, H. Sugiura, Kasai H, Washizuka T, Aizawa Y. Ventricular tachyarrhythmia associated with Cardiac Sarcoidosis: its mechanisms and outcome. Clinical Cardiology 2004;27:217–222.*
26. *Nery PB, Mc Ardle BA, Redpath CJ, Leung E, Lemery R, Dekemp R, et al. Prevalence of CS in patients presenting with monomorphic ventricular tachycardia. Pacing Clin Electrophysiol 2014;37:364–374.*
27. *Tung R, Bauer B, Schelbert H, Lynch JP III, Auerbach M, Gupta P, et al. Incidence of abnormal positron emission tomography in patients with unexplained cardiomyopathy and ventricular arrhythmias: the potential role of occult inflammation in arrhythmogenesis. Heart Rhythm 2015;12:2488–498.*
28. *Mehta D, Lubitz SA, Frankel Z, Wisnivesky JP, Einstein AJ, Goldman M, et al. Cardiac involvement in patients with sarcoidosis: diagnostic and prognostic value of outpatient testing. Chest 2008;133:1426–1435.*
29. *Buyukoglan H, Kaya MG, Ardic I, Yarlioglues M, Dogdu O, Bol C, et al. Assessment of atrial conduction time in patients with sarcoidosis. J Investig Med 2011;59(1):15-21.*
30. *Patel AR, Klein MR, Chandra S, Spencer KT, Decara JM, Lang RM, et al. Myocardial damage in patients with sarcoidosis and preserved left ventricular systolic function: an observational study. Eur J Heart Fail 2011;13:1231–1237.*

Combined Percutaneous Aortic Valve Replacement and Unprotected Left Main Stenting in a Patients with Multiple Comorbidities;Stepwise Approach

Çoklu Komorbiditesi Olan Bir Hastada Perkütan Aortik Kapak Replasmanı ve Korumasız Sol Ana Koroner Stent İmplantasyonu;Basamaklı Yaklaşım

Cenk Sarı[1], Serdal Baştuğ[2], Mustafa Duran[2], Engin Bozkurt[2]

[1] Health Sciences University, Tepecik Education and Research Hospital, Department of Cardiology
[2] Yıldırım Beyazıt University, Faculty of Medicine, Department of Cardiology, Ankara

Yazışma Adresi / *Correspondence:*
Cenk Sarı

Health Sciences University, Tepecik Education and Research Hospital, Department of Cardiology, Yenişehir/Konak, Izmir/Turkey
T: **+90 232 444 35 60** E-mail: **drcenksari@gmail.com**

Geliş Tarihi / Received : **20.06.2020** Kabul Tarihi / Accepted : **07.01.2021**

Orcid:
Cenk Sarı https://orcid.org/0000-0003-1115-493X
Serdal Baştuğ https://orcid.org/0000-0002-1400-4614
Mustafa Duran https://orcid.org/0000-0001-5937-235X
Engin Bozkurt https://orcid.org/0000-0002-9783-7274

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):201-206) DOI: 10.31832 / smj.746025

Abstract

With increasing life expectancy, the prevalence of aortic stenosis (AS) also increases. Surgical aortic valve replacement (s-AVR) is performed with lower operative mortality in the absence of serious co-morbid conditions with both a recovery in symptoms and prolonged life expectancy. Nonetheless, 30% of patients cannot undergo AVR due to left ventricular dysfunction, advanced age and co-morbid conditions.

In addition, coronary artery disease has a high prevalence in these patients and shares many of the same causative factors. Herein, we report a patient who underwent both left main artery stenting and transcatheter aortic valve replacement in whom remarkable improvement observed after these procedures.

Keywords Transcatheter aortic valve replacement; Coronary Artery Stenoses: Aortic valve stenosis.

Öz

Yaşam beklentisi arttıkça, aort darlığı (AD) prevalansı da artar. Cerrahi aort kapak replasmanı (c-AVR), ciddi ko-morbid durumların yokluğunda düşük operatif mortalite ile gerçekleştirilir ve hem semptomlarda düzelme hem de survey katkısı sağlamaktadır. Bununla birlikte, hastaların % 30'unda sol ventrikül disfonksiyonu, ileri yaş ve eşlik eden hastalıklar nedeniyle AVR uygulanamaz. Ayrıca, bu hastalarda koroner arter hastalığı yüksek prevalansa sahiptir ve aynı nedensel faktörlerin çoğunu paylaşmaktadır. Bu vaka sunumumuzda basamaklı yaklaşımla sol ana arter stentleme ve transkateter aort kapak replasmanı yapılması sonrası dramatik iyileşme görülen bir hastayı sunuyoruz.

Anahtar kelimeler *Transkateter aort kapağının değiştirilmesi; Koroner Arter Darlıkları: Aort kapak stenozu.*

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has moved into the cardiology mainstream with rapid acceptance of this new technology since the first implant in 2002.[1] The two devices with the largest experiences are the self-expanding CoreValve Revalving™ system (Medtronic CoreValve, Luxembourg) and the balloon expandable Edwards Sapien XT valve (Edwards Lifesciences, Irvine, CA). Both are employed in patients whose peri-operative risk is deemed too high for surgical aortic valve replacement (sAVR). Coronary artery disease has a high prevalence in these patients and shares many of the same causative factors.[2,3]

The incidence of co-existing severe aortic stenosis (AS) and left main coronary artery (LMCA) disease is unknown, but is believed to be rising and presents a tremendous challenge to patients and clinicians.[3] If the patient is a poor surgical candidate due to multiple comorbidities, the remaining options are primarily palliative in nature.

In addition to these, renal functions are generally impaired in these patients due to advanced renal reserve and renovascular atherosclerosis, decreased renal perfusion depending on AS and the use of diuretics. Therefore, these patients are prone to cardio-renal syndrome (CRS). In this case, we report a patient who underwent LMCA stenting and transcatheter valve implantation. Although acute kidney injury occurred after coronary intervention on account of cardio-renal syndrome, noteworthy progression observed in terms of functional capacity and renal functions after procedure.

CASE REPORT

A 68 year old female patient with a history of coronary artery disease, atrial fibrillation, hypertension, ischemic stroke, severe aortic stenosis and congestive heart failure, was admitted to our hospital. She presented to the cardiology clinic with complaints of exercise induced angina and dsypnea. According to information from her family members, shortness of started a year ago, but has progressed rapidly in the last few months. Although, she had been hospitalized several times due to same symptoms, her medical condition was worsened by the day.

On admisssion, her cardiovascular system examination revealed 4/6 intensity systolic murmur at aortic focus and bilateral rales in two third lower bases of lungs accompanied by frothy and productive cough. Her neck veins were distended without carotid bruits. Abdominal examination revealed a palpable liver three centimeters below right costal margin, hepatojugular reflux was positive. There was a 3 positive pitting edema of lower extremities to the kness. Her nail beds minimaly cyanotic, and no clubbing was observed. Motor system examination revealed that muscle strength was 4/5 in left upper extremity and 3/5 in left lower extremity.

On physicial examination her blood pressure was 110/70 mmHg, heart rate 110 beats per minutes and oxygen saturation 92% on room air. Her laboratory tests revealed white blood cell 16.80 K/ul, hemoglobin 10.3 g/dL, hematocrit 30.4%, sodium 130 mMol/L, potassium 5.0 mMol/L, BUN 54 mg/dL, creatinine 1.78 mg/dL, Troponin T 7.6 pg/ml, CKMB 2.3 ng/ml, INR 1.96 IU. Medical tratment of patient consisted beta blocker, ace inhibitor, non-dihydropyridine calcium channel blocker, statin, and warfarin. Electrocardiogram (ECG) showed atrial fibrillation of 98 beats per minute. Echocardiography examination revealed segmental wall motion abnormalities with depressed ventricular function. Echocardiographic examination also showed severe aortic stenosis (mean aortic gradient:41 mm/hg, aortic valve area:0.41 cm2,) accompanied by mild mitral regurgitation and moderate tricuspit regurgitation. Systolic pulmonary artery pressure (sPAP) was 65 mm/hg and ejection fraction was calculated as %15-20 by Simpson' s rule. Where upon these results, we performed transesophageal echocardiography (TEE) and found a heavily calcified aortic valve with three leaflets, and severe aortic stenosis.

After administration of iv diuretics her symptoms improved and her vital signs came back to normal values. Soon after, we performed coronary angiography for further evaluation. Coronary angiography revealed crucial occlusions both in ostium of left anterior descending and circumflex arteries with distal left main coronary artery involvement (Figure1A).

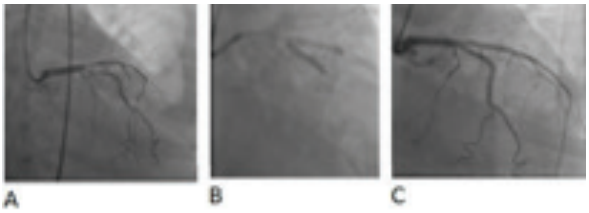


Figure 1A: *Coronary angiography from right anterior oblique projection: Severe stenosis both in ostium of left anterior descending and circumflex arteries.* ***Figure 1B:*** *Placement of stents in ostium of the left anterior descending and circumflex artery.* ***Figure 1C:*** *Final result*

Later, we discussed her condition with heart team which consisted of interventional cardiologist, anesthesiologist and cardiovascular surgeon. The STS score of the patients was 9.7, mean logistic EuroSCORE was 21.7%, and she was found to be in high risk group according to SURTAVI risk model. Due to her multiple comorbidities and prohibitive surgical risk percutaneous coronary intervention and transcatheter valve replacement was recommended.

After much deliberation between the patient and her family members, the patient elected to undergo percutaneous coronary intervention and transcatheter valve replacement. Afterwards, we deployed a 2.5*28 mm in size drug eluting stent to LAD mid segment. During same session 3.0*23 and 2.75*23 mm in size drug eluting stents extended to LAD ostial and circumflex artery ostial respectively (Figure 1B). V-stenting tecnique was choosen for left main coronary artery and than deployed succesfully (Figure 1C). After procedure she was monitored in coronary care unit. During her follow up her urine extraction decreased and contrast induced nephropathy occured. Due to impairment of renal function she was immediately transferred to coronary care unit and underwent temporary renal dialysis, Despite of all our attempts, we couldn't stabilize her vitals and urgent transcatheter valve replacement was considered to be needed. Four days after the first procedure 26 mm Edwards Sapien XT Transcatheter Heart Valve (Edwards Lifesciences Corporation; Irvine, Calif) valve deployed to aortic position without any complication (Figure 2). After the procedure she was monitored in coronary care unit and her urine extraction increased and vital signs returned to normal values. Two days after procedure she was transferred to cardiology clinic. Her temporary renal dialysis catheter was removed and control echocardiography performed. Her echocardiographic examination showed functional bioprosthesis in aortic position with mean pressure gradient 7 mm/hg. No paravalvuler leak observed and ejection fraction was calculated as %35 (2D) by Simpson's formula. She was discharged from the hospital eleven days after first admission.

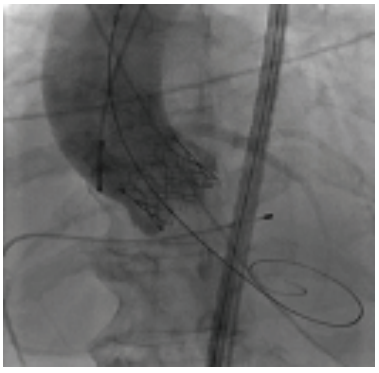


Figure 2: 26 mm Edwards Sapien XT valve deployed to aortic position.

DISCUSSION

Transcatheter aortic valve implantation (TAVI) has moved into the cardiology mainstream with rapid acceptance of this new technology since the first implant in 2002.[1] The two devices with the largest experiences are the self-expanding CoreValve Revalving™ system (Medtronic CoreValve, Luxembourg) and the balloon expandable Edwards Sapien XT valve. Both are employed in patients whose

peri-operative risk is deemed too high for surgical aortic valve replacement (sAVR). Coronary artery disease has a high prevalence in these patients and shares many of the same causative factors.[2,3]

The incidence of co-existing severe AS and LMCA disease is unknown, but is believed to be rising and presents a tremendous challenge to patients and clinicians.[4] If the patient is a poor surgical candidate due to multiple comorbidities, the remaining options are primarily palliative in nature.

LMCA stenting is a viable option in inoperable candidates and is associated with high rates of technical success, low procedural risk, and low rates of cardiac death (11.9%) at 3 year follow-up.[5]

Patients with symptomatic co-existing severe coronary artery disease, severe AS, and heart failure are frequently deemed to be poor surgical candidates, but these high-risk patients have percutaneous options. Ayhan et al showed that TAVI could be performed successfully in patient with AS and reduced ejection fraction(EF).[6] Also they reported that TAVI improves left ventricular function in the short and moderate periods. Similarly in our patient EF was improved from %25 to %35 but this effect could be attributed both TAVI and coronary revascularization.

Among the possible advantages of revascularization prior to TAVI may be a protective effect against the ischemic burden of the procedure, including as it does periods of hypotension. The absence of contractile reserve is associated with increased mortality after sAVR, and significant stenosis not intervened upon could contribute to this.[7] Surgical revascularization for multi-vessel coronary artery disease has been found to be an independent factor predictive of improvement of left ventricular ejection fraction (LVEF) after sAVR, and similar benefits for revascularization by percutaneous coronary intervention may exist. Improving coronary flow in symptomatic patients with significant flow-limiting stenoses may maximize this beyond the valvular intervention.[8]

In addition, renal functions are generally impaired in these patients due to advanced renal reserve and renovascular atherosclerosis, decreased renal perfusion depending on AS and the use of diuretics. Therefore, these patients are prone to cardio-renal syndrome (CRS). CRS occurs when acute or chronic heart, or kidney, disorder affects the other organ hemodynamically and neurohormonally. Type 2 CRS is characterized with the progressive renal dysfunction caused by cardiac dysfunction. Severe AS and low cardiac output and the decrease in renal perfusion activate the renin-angiotensin-aldosterone system and cause systemic inflammation, increased sympathetic activation, reduction of nitric oxide, endothelial dysfunction, tissue hypoperfusion and renal parenchymal fibrosis.[9]

In our case in whom we preferred step by step management because of co-existing severe coronary artery disease, severe aortic stenosis and heart failure. Although acute kidney injury occured on account of above-mentioned conditions,remarkable improvement observed after percutaneous valve implantation. Keles and his collegues reported that improving AS stops cardio-renal syndrome and provides progression in renal functions.[10]

In conclusion, combined transcatheter valve replacement and LMCA stenting is a viable option in patients who are deemed to be poor surgical candidates due to multiple comorbidites. While AVR and coronary artery bypass grafting remain the superior option, it is reasonable to offer these high-risk patients a combined percutaneous procedure for symptomatic relief.

Acknowledgements: This study is not funded by any organisations of individuals and there is not any reported conflict of interest between authors.

Conflict of Interest

There is no conflict of interest between the authors.

Informed Consent

Consent was obtained from the patient.

References

1. *Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F,et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002 Dec 10;106(24):3006-8.*
2. *Ortlepp JR, Schmitz F, Bozoglu T, Hanrath P, Hoffmann R. Cardiovascular risk factors in patients with aortic stenosis predict prevalence of coronary artery disease but not of aortic stenosis: an angiographic pair matched case-control study. Heart 2003 Sep;89(9):1019-22.*
3. *Dewey TM, Brown DL, Herbert MA, Culica D, Smith CR, Leon MB,et al. Effect of concomitant coronary artery disease on procedural and late outcomes of transcatheter aortic valve implantation. Ann Thorac Surg 2010 Mar;89(3):758-67;*
4. *Doshi SN, Sherman W. Balloon valvuloplasty and rotational atherectomy stenting in a 92-year-old patient with severe aortic stenosis and unprotected critical left main disease. Int J Cardiol 2005;99:477-8.*
5. *Takagi T, Stankovic G, Finci L, Toutouzas K, Chieffo A, Spanos V, et al. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. Circulation 2002 Aug 6;106(6):698-702.*
6. *Ayhan H, Kasapkara HA, Durmaz T, Keleş T, Aslan AN, Sarı C,et al. Impact of transcatheter aortic valve implantation in patients with reduced ejection fraction. Cardiol J 2015;22(1):108-14.*
7. *Monin JL, Quéré JP, Monchi M, Petit H, Baleynaud S, Chauvel C,et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. Circulation 2003 Jul 22;108(3):319-24.*
8. *Quere JP, Monin JL, Levy F, Petit H, Baleynaud S, Chauvel C,et al. Influence of preoperative left ventricular contractile reserve on postoperative ejection fraction in low-gradient aortic stenosis. Circulation 2006 Apr 11;113(14):1738-44.*
9. *Barbash IM, Ben-Dor I, Dvir D, Maluenda G, Xue Z, Torguson R, et al. Incidence and predictors of acute kidney injury after transcatheter aortic valve replacement. Am Heart J 2012 Jun;163(6):1031-6.*
10. *Keleş T, Ayhan H, Durmaz T, Sarı C, Aslan AN, Erdoğan KE, et al. Improvement in renal functions with transcatheter aortic valve implantation. J Geriatr Cardiol 2013 Dec;10(4):317-22.*

Is Blood Type Linked to COVID 19 Risk?

Kan Grubu Türü COVID 19 Riski İle Bağlantılı mı?

Hevi Ghafour, Mustafa Altındiş

Sakarya Üniversitesi Sağlık Bilimleri Enstitüsü Tibbi Mikrobiyoloji Anabilim Dalı, Sakarya

Yazışma Adresi / *Correspondence:*
Mustafa Altindiş

Tıp Fakultesi Tibbi Mikrobiyoloji Anabilim Dalı, Korucuk, Sakarya
T: **+90 533 661 52 63** E-mail: **maltindis@gmail.com**

Geliş Tarihi / Received : **15.01.2021** Kabul Tarihi / Accepted : **01.03.2021**

Orcid:
Hevi Seerwan Ghafour Ghafor https://orcid.org/0000-0002-5634-5257
Mustafa Altındiş https://orcid.org/0000-0003-0411-9669

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(1):207-217) DOI: 10.31832/smj.860739**

Abstract

New coronavirus SARS-CoV-2 had been stressed healthcare since their quick worldwide propagation which is a crucial quarrel. It has been estimated that blood group could impact the risk of serios COVID 19. we performed a review by going through number of article published regarding this subject, and found out that blood group has different impact on COVID 19 infection accordingly, findinig slightly increased infection prevalence among non-O types, risk of intubation was decreased among A and increased among AB and B types, compared with type O. Also estimate Rh-negative blood type to have a protective effect to the high COVID 19 infection epidemiology, while risk of death was increased for type AB and decreased for types A and B. Studies add to the growing body of evidence suggesting blood type may play a role in COVID 19 infection but further studies are needed to investigate more.

Keywords COVID 19 virus disease; ABO blood group system; Epidemiology

Öz

Yeni koronavirüs SARS-CoV-2'nin hızlı küresel yayılımı, sağlık hizmetlerini ve test kaynaklarını zorlayarak, en risk altındaki kişilerin tanımlanmasını kritik bir zorluk haline getirdi. Bu derleme çalışmasındaki yayınlara göre, kan grubu türünün COVID 19 enfeksiyon şiddeti riskini etkileyebileceğini göstermektedir. Kan grubu O'dan farklı olan kişiler arasında COVID 19 enfeksiyonu prevelansı biraz daha yüksek bildirilmektedir. Entübasyon riski, O kan grubu baz alındığında, A kan grubunda azalmış; AB ve B kan gruplarında artmış olarak saptanmıştır. Rh-negatif kan grubunun COVİD 19 enfeksiyon riskine karşı koruyucu etkisi olduğu; mortalite riskinin AB kan grubunda artmış A ve B kan gruplarında azalmış olduğu tahmin edilmektedir. Kan grubunun COVID 19'da rol oynayabileceğini öne süren kanıtlar artmakla birlikte bu konuda daha çok araştırmaya ihtiyaç vardır.

Anahtar Kelimeler *COVID 19; ABO kan grubu sistemi; Epidemiyoloji*

INTRIODUCTION

1. SARS CoV-2, COVID 19 and Pandemic

COVID 19 disease, caused by the SARS-COV-2 virus had rised at Wuhan province in China in Dec, 2019. and this disease affected the entire world in a short time.[1] The Virus Taxonomy International Committee formally decleared term to the novel coronavirus as "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2). Then, world Health Organization (WHO) has stated formal noun of the infection occured by SARS-CoV-2 as Corona Virus Disease 19 (COVID 19). On March 11, 2020 WHO changed the status of COVID 19 epidemic to be pandemic.[2,3] COVID 19 propagate quickly through world which had been resulted in more than 68.252.608 million certain cases also above 1.557.343 death universaly up to December 9, 2020.[3]

COVID 19 infection incubation period ranges from 2 to 14 days.[4] While incubation duration Individuals are contagious, might asymptomatic infection also act as the origin of the disease. Incubating patients, asymptomatic patients continue to spread the COVID 19 virus.[5,6] Such individuals can contribute to the spread of infection in society, the most widespred clinical features of COVID 19 disease are respiratory symptoms characterized by fever, fatigue and dry cough These clinical features show a broad spectrum of diseases ranging from mild to severe symptoms of influenza-like respiratory syndrome which complexes by pneumonia and acute respiratory distress syndrome (ARDS), high fever, headache.[7] In very severe cases, infected persons can be subjected to septic shock, acute respiratory distress syndrome, and might result mortality.[5,6] In data from China, about 80% of patients infected by COVID 19 had moderate to mild illness including pneumonia, nearly 14% had intense disease with blood oxygen saturation level (93%), and 6% reported crucial illness with septic shock, respiratory failure, and/or severe multi-organ inability or dysfunction.[8]

A global pandemic causing by COVID 19 disease has resulted in a quick rise in case and death rates. Mortality rate of this viral infection was almost about 2-3 percent and intensive respiratory diseases was associated with.[1] community had been impacted by raising COVID 19 disease. Elder individuals with cormorbid disease, such as cancer, cardiovascular disease, diabetes and immunosuppressive disease, have a higher risk of infection and complications and are more likely to get to the infection.[9]

Considering that COVID 19 disease has caused significant morbidity and mortality, there has been scientific concern in choosing information that specifying distinctives which might cause people most likley to get COVID 19 disease, also deciding which risk agents might contribute to the leading and seriosity of illness caused by a virus.[10] It has been reported that there are variety of risk agents regarding COVID 19 morbidity and mortality, containing age, smoking, chronic cardiovascular disease, sex, diabetes, hypertension and respiratory illnesses.[11]

Since the 1950s a correlation of human ABO blood group types with numerous illnesses had been recognized.[12] It has been pointed out that there is a relationship amongst ABO blood group, cancers, cardiovascular illnesses, also sensitivity to particular diseases, inclusive coronavirus – SARS For instance, non-O blood types people were very susceptible to promote coronary heart illness with venous thromboembolism in contrast to O blood group individual.[13] Lately, various researches regarding COVID 19 in China and America figuered relationship among ABO blood type with COVID 19 disease, severity along with decease Potential correlation among blood group A with a higher risk for COVID 19 infection together with mortality Has been found out in a study while in the same study O blood group had contributed to less risk of disease and mortality Zietz and Tatonetti stated as blood type A was related to a higher priority of checking positive for COVID 19 infection.[14]

In this review, the goal was to define s a relationship among

ABO blood type, risk of COVID 19 infection and if there is changeability in checking positive for COVID 19 infection among blood groups.

1.1. Viral Classification

The SARS-CoV-2 virus belongs to coronaviridae family due to their similarity in nucleic acid sequences to acute respiratory coronavirus syndrome (SARS-CoV) and Middle East respiratory coronavirus syndrome (MERS-CoV) viruses. SARS-CoV, MERS-CoV which recognized as coronaviridae family of viruses. In 2002 and 2013, those viruses (SARS-CoV in china and MERS-CoV in Saudi Arabia) resulted in serious human infections like severe pneumonia and bronchiolitis, meningitis even among most vulnerable societies, the virus family categorised into four genera: alpha, beta, gamma, and delta. While alpha coronaviruses are representative of four low-pathogenicity human coronaviruses HCoV-OC43, HCoV-HKU1, HCoV-NL63, and HCoV-229E. beta-coronaviruses are include the most well-known and more pathogenic zoonotic pathogens SARS-CoV and MERS-CoV, Coronaviruses are positive-sense, single-stranded RNA genome, which are enclosed into an envelope, Upper respiratory and digestive tract infections are primarily goes under the responsiblity of CoVs. Based on its sequence of genomes, 2019-nCoV shares almost 76% of the amino acid sequence similarity with SARS-CoV in the Spike (S)-protein sequence and 80 percent along with CoV ZXC21.[1,15,16]

SARS-CoV and SARS-CoV-2 utilize the similar receptor which is ACE2, for entrance into target cells.[17] Which had attracted the attention of the scientist to explore if the ABO blood group polymorphism is additionally related to host sensibility to SARS-CoV-2 infection. The hypotheses linked for this contribution include the prevalence and division of particular genetic loci.[18]

1.2. Pathogenesis

Attaching virus particle to the host superficies cellular receptors initiating the Viral infections. Therefore receptor realization is a crucial recognization of the cell and tissue tropism of the viral particle. Additionaly, obtaining function of a virus in order to attach to receptor takes place in other species which also is a precondition as inter-species transition.[19]

The S-protein coronavirus is the constitutionall protein which is accountable to tiara-like shape of viral CoV particles from which the initial noun "coronavirus" was stated. S-protein belongs to class I viral fusion proteins and linked to cell receptor attaching, tissue tropism, and pathogenesis. so for entrance and infecting cells, coronavirus must recognize (via its surface spike glycoprotein), bind to a membrane receptor (protein, lipid carbohydrate).[1,15]

Suprisingly, by exclusion of HCoV-OC43 and HKU1, which they had exhibit to utilize sugars for cell binding, in the other hand else human CoVs sense proteinaceous peptidases as receptors. HCoV-229E attaches to human aminopeptidase N , and MERS-CoV interacts with human dipeptidyl peptidase 4. SARS-CoV and hCoV-NL63 react together with angiotensin-converting enzyme 2 (ACE2) as the entrance into human cells In virtually all organs such as numerous extrapulmonary locations through the aerodigestive tract, containing the mucosa of the oral cavity of the heart, blood vessels, kidneys, and testes were found to be expressed ACE2 mRNAs.[15,20,21,22]

In a study in China, the ABO blood type was contributed to ACE activity which ACE inhibitor-induced cough between Chinese patients with hypertension an angiotensin-converting enzyme 2 (ACE2), an aminopeptidase that works like a putative receptor. Several in-vitro studies have found a positive association among ACE2 membrane expression and / or tissue activity and the risk of COVID 19 infection.[15,23]

1.3. Transmission

Bat has been considered to play role as a reservoir for the majority of human coronaviruses. Two of SARS-CoV and

SARS-CoV-2 are nearly linked and sourced in bats, coronaviruses are naturally hosted by bats, and they're evolutionary.[2] The reservoir of MERS-CoV is unequivocally dromedary camels.[24]

Palm civets, racoon and dogs had been defined as intermediate hosts for zoonotic transmission of SARS-CoV among bats and human beings, but the SARS-CoV-2 intermediate host remains unclear.[25] proposing that upcoming zoonotic transmission incident may be continue which is related to repeated spillovers of coronaviruses in humans side by side to discovery of various coronaviruses in bats, including many SARS-linked coronaviruses (SARSr-CoVs).[24]

In 2002, SARS-CoV rised in Guangdong city of China and propagate to five continents via air travel ways, affecting 8,098 individuals also resulting in 774 deaths MERS-CoV rised in the Arabian Peninsula in 2012, where this remained the main public health problem, and was transmitted to 27 countries, affecting overall almost 2,494 persons and risking 858 souls.[26]

The coronavirus (CoV) currently called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is responsible of coronavirus disease 2019 (COVID 19) and was revealed in Wuhan City in December 2019 in China. At first, COVID 19 disease was defined as a "pneumonia of unknown etiology" with high fever that was not reacting to drug medication and the early cases were engaged to the Huanan seafood market had been reported. Then, By January 2020 SARS-CoV-2 sequenced and isolated.27 The World Health Organization stated SARS-CoV-2 epidemic as a public health emergency of international concern On January 30, 2020.[28] As of March 3, 2020 COVID 19 pandemic has been affected over 90,000 people and killed more than 3,000 of those impacted in more than 60 countries.[29]

The way the SARS-CoV-2 is transported among humans is respiratory aerosols and close contact which were the main transmission ways.[30,6] Also, the transmission of SARS-CoV-2 by droplets is plausible under favorable conditions, particularly in relatively confined settings with poor ventilation and long duration exposure to high concentrations of aerosols.[31] Vertical transmission remains a subject of concern per researches including mothers delivering in both cesarian and normal delivery none of the neonates were tested positive for COVID 19. There are no published cases of clinical evidence of virus shedding in breast milk, vertical transmission are still to be discussed.[13,30,32] In a research it has been detected that 3 out of 33 neonates born from mothers positive to COVID 19 who were nasopharyngeal and rectal swabs COVID 19 positive. also fecal-oral transmission may be another transmission route due to positive stool sample has been detected even after COVID 19 was negative.[11,30]

Transmition by blood transfusion for the novel coronavirus disease 2019 (COVID 19) is not known yet, as long as there might be more people which are asymptomatic carriers or might donate blood, due to this it is crucial to realize whether the SARS-CoV-2 virus can be transmitted by blood transfusion or not. Although SARS-CoV-2 RNA had been detected in serum or plasma from infected patients, but there are no information and datas proposing the risk of transmission of SARS-CoV-2 by blood transfusion.[33] In a case study reported that in November 2019, a 21-year-old Korean male was diagnosed with serious aplastic anaemia, and gained transfusion of blood products from infected person who was not yet progressed signs and symptoms of COVID 19 and didn't lead to the disease. While the platelet of recipient was figured out with severe aplastic anaemia and was taking immunosuppressive medications.[4]

Transmissibility is determined using R0 which is the fundamental reproduction number, and is described as the number of additional persons one case infects over the course of their infection. If R0 is > 1, there's the possibility for sustained transmission. For two of SARS and MERS, R0 is < 1,4,5 whereas for COVID 19 the present rating is

much higher among 2.2 and 3.4 Therefore, it's potential that there's a greater risk from preoperative aerosols than with other diseases.[34,35]

1.4. Diagnosis

1.4.1. Laboratory Diagnosis

In order to determine disease also monitering transmission quick and early laboratory diagnosis is crucial. RT-PCR is routine assuring examination doing by WHO as the gold standard analysis for SARS-CoV-2 diagnosis. SARS-CoV-2 positivity should be confirmed by molecular methods.[35] RT-PCR is suggested as a screening assay having positive PCR results, sequence analyses of positive amplicons can aid to assure the result and to differentiate between 2019-nCoV and other genetically closed coronaviruses (e.g., SARS coronavirus).[36] in plasma or lymphocytes coronaviruses RNA could be detected. For this reason, staff in blood centers and laboratories should progress biosafety protection during the epidemic.[37]

Crucial point in the laboratory examination of COVID 19 is through Suitable sample collection. Upper respiratory tract specimens, lower respiratory tract specimens, stool specimens, whole blood specimens, and serum specimens, and the respiratory secretions is the most frequently agreeable specimens for diagnosis. presently, SARS-CoV-2 has been figuerd out in nasopharyngeal swabs, oropharyngeal swabs, throat swabs, sputum, bronchoalveolar lavage fluid (BALF), whole blood, serum, stool, urine, saliva, rectal swabs and conjunctival swabs.[38]

Depending only on odd negative PCR outcome is hard to eliminate SARS-CoV-2 infection, particularly when diagnosis was used for upper respiratory tract samples. Also suspicious to positive chest computed tomography scans might offer negative outcomes for SARS-CoV-2 by reverse-transcriptase polymerase chain reaction (RT-PCR). For this reason, the reporting of nucleic acid analysis outcome have to be accurate also negative outcomes should not eliminate SARS-CoV-2.[39]

1.4.2 Radiology

Utilizing of CT radiological outcomes to determine / scan COVID 19 is controversial and It was reported that CT results are not side of the testing standard to COVID 19 according to an American-Singaporean panel.[30]

Viral testing remains the only specific method of diagnosis as Centers for Disease Control (CDC) does not currently recommend CXR or CT to diagnose COVID 19. Assuring the viral test is required, even if radiologic findings are suggestive of COVID 19 on CXR or CT. For the initial diagnostic testing for suspected COVID 19 infection, the CDC suggests collecting and testing specimens from the upper respiratory tract (nasopharyngeal AND oropharyngeal swabs) or from the lower respiratory tract when available for viral testing.[40]

So as to study further the relation among ABO blood type and COVID 19 infection several review and studies was done about COVID 19 and ABO blood groups. The goal of this review is to investigate the division, correlation between the blood types and COVID 19 infection.

2. COVID 19 and BLOOD GROUP RELATION

In the meta-analysis study conducted by Golinelli et al., researchers tested odds of having every blood type between SARS-CoV-2 positive patients contrasted to controls. In their study, they did a scientific study on MEDLINE and LitCovid databases for studies published through July 15, 2020. There have been 7 researches match containment standards for meta-analysis, with a complete of 13 subgroups of populations (7503 SARS-CoV-2 positive cases and 2962160 controls) outcomes of their meta-analysis found that SARS-CoV-2 positive people were more likely to have blood group A (pooled OR 1.23, 95%CI: 1.09–1.40) and less likely to have blood group O (pooled OR = 0.77, 95%CI: 0.67–0.88).[18]

For analysing correlation among blood type and COVID 19, in a review researchers association from Europe and Australia stated outcomes of the research contrasting genome information from 1610 patients with intenise COVID 19 and 2205 healthy blood donors. In their study, whole participants were from Italy, Spain. Scientists figured out that gene variants in two sites of the human genome were related to severe COVID 19 and a higher risk of passing away from it. One amongst those sequences of DNA happens to hold the gene that deciedes blood group, and also the research discovered that, in contrast to individuals with other blood groups, those with group A had a 45% higher risk of promoting serious COVID 19 if infection, when individuals with group O had a 35% less risk.[42]

In an observational retrospective cohort study, scientists forwarded that ABO and Rh (D) blood groups don't seem to be accompanied with increasing or decreasing possibility of infection by SARS-CoV-2. Researchers were investigated 1,769 persons of airplane transporters staff, after which they undergo a physical testing and reverse transcriptase-polymerase chain reaction testing (RT-PCR). Results of observation illustrated that through the full staff, the ABO blood group exhibit a division of 39.9%, 10.8%, 4.1% and 44.0% for A, B, AB and O types, separately. The responding ratio for staff members infected with SARS-CoV-2 were 40.7%, 10.6%, 4.2%, and 43.2% for A, B, AB, and O types. In univariate diagnosis, no significant link was discovered among SARS-CoV-2 infection and ABO or Rh (D) groups.[43]

In a swedish study it was showed that blood group A or AB is contributed to higher risk of demanding crucial care or dying of COVID 19 within Swedish commuinty. In this study it was indicated that blood type A may be a risk agent for infection seriousness and passing away in COVID 19 regardless of the genetic context.[44]

In article published in April and updated in July, researchers used data from 7770 persons tested for SARS-CoV-2, 2206 of whom were checked positive for the virus the authors pooled their findings with data from China. In this study researchers found that through those with blood type, group B individual were more likely to check positive for SARS-CoV-2, and other people with group O were less likely to result positive. Yet, the data of study failed to provide solid evidence of a association among blood group and intubation or death through patients with COVID 19.[45]

In Latz et al. project which they are defininig whether if there is a relationship among ABO blood group and severity of COVID 19 determined by intubation or death as well as assuring if there is changinility in checking positive for COVID 19 through blood groups, tested 1289 patients who checked positive. Distribution of patients according to their blood groups type was 440 (34.2%) were A blood group, 201 (15.6%) were B blood group, 61 (4.7%) were AB blood group, and 587 (45.5%) were O blood group. According to their study results, blood group was not distinctly contributed with risk of intubation or passing away. A blood group had no association with positive diagnosis, B blood group was contributed with rised odds of checking positive for infection, AB blood type was also contributed with higher odds of checking positive, and O blood type was related with a lower risk of checking positive. Rh positive case was linked with higher odds of checking positive. Blood group was not correlated with risk of intubation or death in patients with COVID 19. Patients with B and AB blood groups who obtained an examination were more likely to check positive and O blood group was less likely to result positive. Rh positive patients were more likely to result positive.[10]

In study at the University of Cincinnati researchers tested the linkage of blood group and rhesus related hospitalization also infection seriousness between 428 COVID 19 patients examinied. In samples, 50.2% of participants had the O blood group, 38.7% had the A blood group, 17.5% had the B blood group, and 3.5% had the AB blood group.

In analyzation setted for sociodemographic cretiria and comorbidities, the blood groups A, B, AB, and O were not correlated with hospitalization for COVID 19. Identically, the A, B, AB, and O blood groups weren't correlated with admitting to intensive care unit or passing away in COVID 19. To conclude researchers stated that blood group is not correlated with hospitalization or disease seriousness in COVID 19.[45]

In a research at the Presbyterian hospital in New York 14,112 COVID 19 tested patients with known blood type were examined. It was discovered lightly raised infection propagation through non-O blood groups. risk of intubation was falln through blood type A and raised through AB and B blood groups, in contrast with blood type O, whereas risk of passing away was raised for AB blood type and reduced for A and B blood groups. Researchers assessed that Rh (-) blood group to have a defensive impact to whole 3 results. The results of the study adding evidence claiming that blood group may take part in COVID 19.[46]

In a study done to examine the relation among ABO histo-blood type phenotypes and COVID 19, researchers found ABO histo-blood phenotypes are associated with patients' sensitivity to the disease. A higher ratio of disease was noted through patients with the AB histo-blood type, while patients with the O histo-blood type have clarify lower ratio of infection. Also the Rh blood type phenotype wasn't statistically significant in defining patient's vulnerability.[47]

In the study performed in Sudan were concluded higher rate of women were infected compared to men, and people among 25 and 35 years old were the most influenced age group. Blood type O Rhesus-positive (O+) was the less influenced by the infection while A Rhesus positive (A+) blood type individuals were the most vulnerable. The researchers thought that the potentially low incidence of COVID 19 in the country may be due to the Sudanese population being largely composed of O Rhesus-positive residents (about 50%).[48]

In a study at Hacettepe University School of Medicine Hospitals, The most recurrent detected blood type was A blood type (57%) and type O (24.8%) through the COVID 19 patients. The A blood type was statistically significantly more recurrent through those infected with COVID 19 in contrast to controls (57% vs. 38%, P < 0.001; OR: 2.1). On the other side, the recurrence of O blood type was significantly lower in the COVID 19 patients, in contrast to the control group (24.8% vs. 37.2%, P: 0.001; OR: 1.8). When clinical outcomes are determined according to blood groups, the blood group types was not affected the clinical resultes.[49]

3.CONCLUSION

Relationship between COVID 19 and blood types with features such as clinical outcomes, length of stay in the hospital / intensive care unit, intubation status and survival / death of COVID 19 patients had examined in many studies (Table 1).

According to the researches took apart in this review, it can be argued that group A blood type might be on the higher risk in comparison to other blood groups where is blood type O took the lowest risk of the infection.

Many studys claimed that ABO blood types are relatively just contributed with risk varieties of COVID 19. One possible mechanism which will be taking part with raising risk connected to blood type antigen A is that it contains a galactose as end group saccharide. two blood groups B and O have a galactose amine in this site, and this could clarify the difference amongst blood types. The spike protein of SARS-COV-2 has been shown to bind carbohydrates, and a strong affinity among the A antigen and also the virus could aid in uptaking of the virus into the cells, Also other previous research estimated that although ABO blood group and/or cardiovascular diseases are sign of the seriosity of COVID 19 in patients, they're not agents predispo-

sing to the risk of gaining SARS-CoV-2 infection, there's a pathophysiological mechanism to support this estimation: subjects that A blood type are at risk of the expantion of cardiovascular diseases and severe COVID 19 due to positive correlation of this blood type with angiotensin-converting enzyme action, and therefore the binding of adhesion molecules on the vascular wall, which rise and reduce the inflammation.[42,43]

Suprisingly, while observing a reduced vulnerability to the infection between patients with an O histo-blood type, discordant results have been obtained reffering the raised possibility through people with an AB histo-blood type, unlike A histo-blood type in the past research.[47] study results show epidemiological proofs that women with blood group A were sensibile to COVID 19.[48]

In research evaluating clinical outcomes (i.e intubation or death/survival) in blood group and COVID 19 disease, it was found that the blood type was not contributed to the risk developing to serious infection demanding intubation or resulting in passing, nor was it correlated to increased status of inflammatory sign.[44] Yet, In a study investigating the Genome-Wide Relationship of Severe COVID 19 with Respiratory Failure, researchers descovered a 3p21.[31] Gene clump as a genetic sensibility site in patients with COVID 19 with respiratory failure and stated a potential involvement of the ABO blood-type system.[53] In another research, risk intubation was reduced amongst A and raised amongst types AB and B, in contrast to O group, wheareas risk of passing away was raised for type AB and reduced for types A and B. Also, reserchers guessed that Rh (-) blood group to have defensive impact for whole 3 results, the high COVID 19 infection epidemiology, severe infection and the need for intubation.[10]

In a research studying the connection among sociodemographic characteristics, comorbid factors and blood groups and COVID 19, sociodemographic cretiria and comorbidities, the blood groups A, B, AB, and O weren't correlated with hospitalization for COVID 19. Likewise, the blood groups A, B, AB, and O weren't correlated with submission to intensive care unit or passing away in COVID 19.[45]

However, there are several studies and researches showing that there is no significant difference among blood group and COVID 19 risk.[42]

Under the light of these researches and review, we can say that it is yet to be investigated whether if there is a correlation or significant difference among the ABO blood type and COVID 19 becauseconcept that blood type may have importance impact on COVID 19 is interesting. Wrapping it up, our present information propose that A blood type might be a risk factor for COVID 19 linked crucial disease between white patients, and that O blood type might be defensive. Future investigations are needed to determine the mechanisms for these outcomes.

Table 1: Explaing all the research article related to Blood group system and COVID 19.

Study	Study type	Study features	A	B	AB	O	Rh +	Rh -
Abdollahi et al.[48]	Original Article, cross-sectional survey	N=397	160 (40.3%)	89 (22.4%)	37 (9.3%)	111 (28%)	357 (89.9%)	40 (10.1%)
		ICU (n=127)	51 (40.2%)	28 (22%)	10 (7.9%)	38 (29.9%)	117 (92.1%)	10 (7.9%)
		General wards (n=270)	109 (40.4%)	61 (22.6%)	27 (10%)	73 (27%)	240 (88.9%)	30 (11.1%)
Zietz et al.[14]	Article, Descriptive cohort	N=14.112	4298 (32.9)	2033 (15.6)	559 (4.3)	6161 (47.2)	11,856 (90.8)	1195 (9.2)
		Descriptive cohort study	58 (37–72)	57 (37–72)	57 (37–71)	55 (36–71)	56 (37–71)	56 (37–70)
		Male (%)	1676 (39.0)	778 (38.3)	231 (41.3)	2339 (38.0)	4594 (38.7)	430 (36.0)
		COV+ Intubated (%)	111 (2.6)	78 (3.8)	17 (3.0)	193 (3.1)	375 (3.2)	24 (2.0)
		COV+Died (%)	104 (2.4)	46 (2.3)	15 (2.7)	166 (2.7)	320 (2.7)	11 (0.9)
Taha et al.[49]	Original Article, case–control study	N=557, Susceptibility towards infection with COVID 19	180 (32.3)	102(18.3)	34 (6.1)	241 (43.2)	511 (91.7)	46 (8.2)
Mendy et al.[46]	Original Article cross-sectional research	N=428	123	75	15	215	400	28
		cross-sectional research	37.4	42.7	33.3	35.8	-	-
		Age, years, median (SE)	50.5 (2.8)	49.5 (3.3)	44.0 (8.7)	38.9 (1.3)	-	-
		Hospitalization n: 192	56	34	5	97	178	14
		Severe COVID 19 n: 115	28	18	15	54	94	7
		Admission ICU %	20.3	20.0	6.7	23.3	-	-
		Death, %	10.6	6.7	0.0	6.5	-	-
Latz et al.[10]	Original Article, Retrospective study	N=1289	440	201	61	587	-	-
		Retrospective study	56.9 (18.6)	57.6 (18.1)	57.1 (19.9)	54.8 (18.1)	-	-
		Female sex	299 (68.0%)	136 (67.7%)	33 (54.1%)	404 (68.8%)	-	-
		Admitted	158 (35.9%)	85 (42.3%)	28 (45.9%)	213 (36.3%)	-	-
		ICU admission	41 (9.3%)	18 (9.0%)	7 (11.5%)	57 (9.7%)	-	-
		Dead	36 (8.2%)	14 (7.0%)	5 (8.2%)	34 (5.8%)	-	-
Göker et al.[50]	Research Article, Cross-sectional case–control study	Cases N=186	106 (57)	20 (10.8)	14 (7.5)	46 (24.8)	160 (86)	26 (14)
		Male sex, %	58	9	8	25	85	15
		Age (median)	43 (19–84)	48 (26–92)	33.5 (20–64)	41 (23–84)	41.5 (19–92)	47 (20–73)
		ICU (n/%)	17 (16)	3 (15.8)	4 (28.6)	7 (15.2)	25 (15.7)	6 (23.1)
		Intubation (n/%)	7 (6.6)	0	1 (7.1)	3 (6.5)	9 (5.7)	2 (7.7)
		Dead (n/%)	6 (5.7)	2(10)	0	1 (2.2)	8 (5)	1 (3.8)
Fan et al.[6]	Original Article, Case–control study	Case N=105	45 (42.8%)	28 (26.7%)	9 (8.57%)	23 (21.9%)	-	-
		Case–control study	21	17	6	11	-	-
Boudin et al.[43]	Letters to editor	Confirmed/suspected SARS-CoV-2 N=1279 (76.0)	521 (40.7)	135(10.6)	54(4.2)	553(43.2)	1092	171

Golinelli et al.[18]	Systematically research, Multicenter study	Wuhan Jinyintan Hospital N=1775	670 (37.75%)	469 (26.42%)	178 (10.03%)	458 (25.80%)	-	-
		Death= 206	85 (41.26%)	50 (24.27%)	19 (9.22%)	52 (25.24%)	-	-
		Renmin Hospital of Wuhan University N=113	45 (39.82%)	25 (22.12%)	15 (13.3%)	28 (24.78%)	-	-
Li et al.[55]	Case-control Controls study and Multicenter study	Central Hospital of Wuhan N= 265	104 (39.3)	67 (25.3)	26 (9.8)	68 (25.7)	-	-
		Male sex, % (n = 113)	48 (42.5)	30 (26.6)	9 (8.0)	26 (23.0)	-	-
		Less than 40 years (n = 69)	24 (34.8)	17 (24.6)	8 (11.6)	20 (29.0)	-	-
		Between 41–59 years (n = 79)	29 (36.7)	20 (25.3)	8 (10.1)	22 (27.9)	-	-
		Over 60 years (n = 117)	51 (43.6)	30 (25.6)	10 (8.6)	26 (22.2)	-	-
		Deaths (n = 57), %	20 (35.1)	15 (26.3)	8 (14.0)	14 (24.6)	-	-
		Three Wuhan Hospitals N=2153	819 (38.0)	561 (26.1)	219 (10.2)	554 (25.7)	-	-
		Less than 40 years (n = 342)	124 (36.3)	95 (27.8)	29 (8.5)	94 (27.5)	-	-
		Between 41–59 years (n = 784)	304 (38.8)	196 (25.0)	79 (10.1)	205 (26.2)	-	-
		Over 60 years (n = 1027)	391 (38.1)	270 (26.3)	111 (10.8)	255 (24.8)	-	-
		Male (n = 1143)	451 (39.5)	305 (26.7)	110 (9.6)	277 (24.2)	-	-
Wu et al.[51]	Retrospective study, Case-control	Cases N=187	69(36.90)	63(33.69)	14(7.49)	41(21.92)	-	-
		Age <40	22(31.88)	25(39.68)	14(34.15)	8(57.14)	-	-
		Age ≥40	47(68.12)	38(60.32)	27(65.85)	6(42.86)	-	-
		Male sex	35(50.72)	33(52.38)	22(53.66)	7(50.00)	-	-
Ellinghaus et al.[54]	N: 1980 Cases:835 Controls:1255	Italian Hospitals Cases N = 835	46.5%	10.9%	5.1%	37.5%	-	-
		Spanish Hospitals: Cases N= 775	48.6%	9.2%	4.6%	37.5%	-	-
Leaf et al.[53]	Cohort study, Multicentre	N = 2033 (100%)	666 (32.7%)	328 (16.1%)	89 (4.4%)	950 (46.7%)	-	-
		Male sex, n (%)	417 (62.6)	189 (57.6)	58 (65.2)	633 (66.6)	-	-
		Age, years, median (IQR)	64 (53–72)	63 (54–71)	66 (56–72)	61 (50–70)	-	-
		Invasive mechanical ventilation, n (%)	466 (70.0)	238 (72.6)	71 (79.8)	663 (69.8)	-	-
			268 (40.2)	129 (39.3)	41 (46.1)	361 (38.0)	-	-

References

1. *Coutard B, Valle C, de Lamballerie X, Canard B, Seidah NG, Decroly E. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. Antiviral research. 2020; 176:104742.*
2. *Xiaolu T, Changcheng W, Xiang L, Yuhe S, Xinmin Y, Xinkai W, Yuange D, Hong Z, Yirong W, Zhaohui Q, Jie C. On the origin and continuing evolution of SARS-CoV-2. National Science Review. 2020; 1012–1023:7.*
3. *Wu BB, Gu DZ, Yu JN, Yang J, Shen WQ. Association between ABO blood groups and COVID 19 infection, severity and demise: A systematic review and meta-analysis. Infection, Genetics and Evolution. 2020;84:104485.*
4. *Cho HJ, Koo JW, Roh SK, Kim YK, Suh JS, Moon JH, Sohn SK, Baek DW. COVID 19 transmission and blood transfusion: A case report. Journal of Infection and Public Health. 2020;13(11):1678-1679.*
5. *Sun T, Guan J. Novel coronavirus and the central nervous system. European Journal of Neurology. 2020;27(9):e52.*
6. *Fan Q, Zhang W, Li B, Li DJ, Zhang J, Zhao F. Association between ABO blood group system and COVID 19 susceptibility in Wuhan. Frontiers in cellular and infection microbiology. 2020;10:404.*
7. *Xu T, Qiao J, Zhao L, Wang G, He G, Li K, Tian Y, Gao M, Wang J, Wang H, Dong C. Acute respiratory distress syndrome induced by avian influenza A (H5N1) virus in mice. American journal of respiratory and critical care medicine. 2006;174(9):1011-7.*
8. *Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID 19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama. 2020;323(13):1239-42.*
9. *Kowalski LP, Sanabria A, Ridge JA, Ng WT, de Bree R, Rinaldo A et al. COVID-19 pandemic: effects and evidence-based recommendations for otolaryngology and head and neck surgery practice. Head & Neck. 2020 Jun;42(6):1259-1267. https://doi.org/10.1002/hed.26164*
10. *Latz CA, DeCarlo C, Boitano L, Png CM, Patell R, Conrad MF, Eagleton M, Dua A. Blood type and outcomes in patients with COVID 19. Annals of hematology. 2020;99(9):2113-8.*
11. *Schwartz DA. An analysis of 38 pregnant women with COVID 19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal coronavirus infections and pregnancy outcomes. Archives of pathology & laboratory medicine. 2020;144(7):799-805.*
12. *Garratty G. Blood groups and disease: a historical perspective. Transfusion medicine reviews. 2000;14(4):291-301.*
13. *Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records [published correction appears in Lancet. 2020 Mar 28;395(10229):1038] [published correction appears in Lancet. 2020 Mar 28;395(10229):1038]. Lancet. 2020;395(10226):809-815. doi:10.1016/S0140-6736(20)30360-3*
14. *Zietz M, Zucker J, Tatonetti NP. Associations between blood type and COVID 19 infection, intubation, and death. Nature communications. 2020;11(1):1-6.*
15. *Dashraath P, Jeslyn WJ, Karen LM, Min LL, Sarah L, Biswas A, Choolani MA, Mattar C, Lin SL. Coronavirus disease 2019 (COVID 19) pandemic and pregnancy. American journal of obstetrics and gynecology 2020; 222(6):521-531.*
16. *Chen Y, Guo Y, Pan Y, Zhao ZJ. Structure analysis of the receptor binding of 2019-nCoV. Biochemical and biophysical research communications. 2020;525(1):135-140.*
17. *Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. Bmj. 2003;327(7414):557-60.*
18. *Golinelli D, Boetto E, Maietti E, Fantini MP. The association between ABO blood group and SARS-CoV-2 infection: A meta-analysis. PloS one. 2020;15(9):e0239508.*
19. *Schneider-Schaulies J. Cellular receptors for viruses: links to tropism and pathogenesis. Journal of General Virology. 2000;81(6):1413-29.*
20. *Post A, Dullaart RP, Bakker SJ. Sodium status and kidney involvement during COVID 19 infection. Virus Res. 2020;286:198034.*
21. *Devaux CA, Rolain JM, Raoult D. ACE2 receptor polymorphism: Susceptibility to SARS-CoV-2, hypertension, multi-organ failure, and COVID 19 disease outcome. Journal of Microbiology, Immunology and Infection. 2020;53(3):425-435.*
22. *Dai X. ABO blood group predisposes to COVID 19 severity and cardiovascular diseases. European Journal of Preventive Cardiology. 2020;27(13):1436-1437.*
23. *Alexandre J, Cracowski JL, Richard V, Bouhanick B. Renin-angiotensin-aldosterone system and COVID 19 infection. InAnnales d'Endocrinologie Elsevier Masson 2020; 81(2-3):63-67.*
24. *Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell. 2020;281-292:181.*
25. *Yuan S, Jiang SC, Li ZL. Analysis of possible intermediate hosts of the new coronavirus SARS-CoV-2. Frontiers in Veterinary Science. 2020;7:379.*
26. *Meirson T, Bomze D, Markel G. Structural basis of SARS-CoV-2 spike protein induced by ACE2. bioRxiv. 2020;btaa744.*
27. *Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, Li H, Chen L, Xu H, Li X, Guo Y. Perinatal depressive and anxiety symptoms of pregnant women along with COVID 19 outbreak in China. American Journal of Obstetrics and Gynecology. 2020; 223(2):240.e1-240.e9.*
28. *Song P, Karako T. COVID 19: Real-time dissemination of scientific information to fight a public health emergency of international concern. Bioscience trends. 2020;14(1):1-2.*
29. *Shatzmiller S. Acceleration in COVID 19 Spreading. Genetics and Molecular Biology: Current Research. 2020:1: 002. GMBCR-002.000002*
30. *Mustafa NM, Selim LA. Characterisation of COVID 19 Pandemic in Paediatric Age Group: A Systematic Review. Journal of Clinical Virology. 2020;128:104395.*
31. *Tang S, Mao Y, Jones RM, Tan Q, Ji JS, Li N, Shen J, Lv Y, Pan L, Ding P, Wang X. Aerosol transmission of SARS-CoV-2? Evidence, prevention and control. Environment international. 2020;144:106039.*
32. *Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2020;2(2):100107. doi:10.1016/j.ajogmf.2020.100107*
33. *Katz LM. Is SARS-CoV-2 transfusion transmitted?. Transfusion. 2020;60(6):1111.*
34. *Chen W, Lan Y, Yuan X, Deng X, Li Y, Cai X, Li L, He R, Tan Y, Deng X, Gao M. Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity. Emerging microbes & infections. 2020; 9(1):469-73.*
35. *Yuan S, Jiang SC, Li ZL. Analysis of possible intermediate hosts of the new coronavirus SARS-CoV-2. Frontiers in Veterinary Science. 2020;7:379.*
36. *Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020;20(5):453-454. doi:10.1080/14737159.2020.1757437*
37. *Chu DK, Pan Y, Cheng SM, Hui KP, Krishnan P, Liu Y, Ng DY, Wan CK, Yang P, Wang Q, Peiris M. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. Clinical chemistry. 2020;66(4):549-55.*
38. *Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfusion medicine reviews. 2020;34(2):75-80.*
39. *Gouveia CC, Campos L. Coronavirus Disease 2019: Clinical Review. Acta Médica Portuguesa. 2020;33(7-8):505-511.*
40. *Waller JV, Allen IE, Lin KK, Diaz MJ, Henry TS, Hope MD. The Limited Sensitivity of Chest Computed Tomography Relative to Reverse Transcription Polymerase Chain Reaction for Severe Acute Respiratory Syndrome Coronavirus-2 Infection: A Systematic Review on COVID-19 Diagnostics. Invest Radiol. 2020;55(12):754-761. doi:10.1097/RLI.0000000000000700*
41. *Rubin, Geoffrey D., et al. "The role of chest imaging in patient management during the COVID 19 pandemic: a multinational consensus statement from the Fleischner Society." Chest 2020;296(1):172-180.*
42. *Rubin, R. Investigating Whether Blood Type Is Linked to COVID 19 Risk. Jama. 2020;324(13):1273.*
43. *Boudin L, Janvier F, Bylicki O, Dutasta F. ABO blood groups are not associated with the risk of acquiring SARS-CoV-2 infection in young adults. Haematologica. 2020;105(12):2841-2843.*
44. *Hultström M, Persson B, Eriksson O, Lipcsey M, Frithiof R, Nilsson B. Blood type A associates with critical COVID 19 and death in a Swedish cohort. Critical Care. 2020;24(1):1-2.*
45. *Zhao J, Yang Y, Huang HP, Li D, Gu DF, Lu XF, Zhang Z, Liu L, Liu T, Liu YK, He YJ. Relationship between the ABO Blood Group and the COVID 19 Susceptibility. medRxiv. 2020; 509:220-223.*
46. *Mendy, Angelico, et al. "Factors associated with hospitalization and disease severity in a racially and ethnically diverse population of COVID 19 patients." MedRxiv 2020 ;2020.06.25.20137323.*
47. *Zietz, Michael, and Nicholas P. Tatonetti. "Testing the association between blood type and COVID 19 infection, intubation, and death." MedRxiv 2020;11(1):5761.*
48. *Abdollahi, Alireza, et al. "The Novel Coronavirus SARS-CoV-2 Vulnerability Association with ABO/Rh Blood Types." Iranian Journal of Pathology 2020;15(3):156-160.*
49. *Taha SAH, Osman MEM, Abdoelkarim EAA, et al. Individuals with a Rh-positive but not Rh-negative blood group are more vulnerable to SARS-CoV-2 infection: demographics and trend study on COVID-19 cases in Sudan. New Microbes New Infect. 2020;38:100763. doi:10.1016/j.nmni.2020.100763*
50. *Göker, H , Karakulak, E , Demi roğlu, H , Ceylan, Ç , Büyükaşık, Y , İnkaya, A , Aksu, S , Sayınalp, N , Haznedaroğlu, İ , Uzun, Ö , Akova, M , Özcebe, O , Ünal, S . (2020). The effects of blood group types on the risk of COVID-19 infection and its clinical outcome . Turkish Journal of Medical Sciences , 50 (4) , 679-683 . DOI: 10.3906/sag-2005-395*
51. *Wu Y, Feng Z, Li P, Yu Q. Relationship between ABO blood group distribution and clinical characteristics in patients with COVID 19. Clinica Chimica Acta. 2020;509:220-3.*
52. *David, Ellinghaus, Degenhardt Frauke, Bujanda Luis, Buti Maria, Albillos Agustín, Invernizzi Pietro, Fernández Javier et al. "Genomewide Association Study of Severe COVID 19 With Respiratory Failure." The New England journal of medicine. 2020;383(16):1.*
53. *Leaf RK, Al-Samkari H, Brenner SK, Gupta S, Leaf DE. ABO phenotype and death in critically ill patients with COVID-19. British Journal of Haematology. 2020;190(4):e204-8.*
54. *Ellinghaus D, Degenhardt F, Bujanda L, Buti M, Albillos A, Invernizzi P, Fernandez J, Prati D, Baselli G, Asselta R, Grimsrud MM. The ABO blood group locus and a chromosome 3 gene cluster associate with SARS-CoV-2 respiratory failure in an Italian-Spanish genome-wide association analysis. MedRxiv. 2020 Jan 1. 20114991; doi: https://doi.org/10.1101/2020.05.31.20114991*
55. *Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, Kong Y, Ren L, Wei Q, Mei H, Hu C. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. Jama. 2020 Aug 4;324(5):460-70.*

Dermatological Manifestations in COVID-19 Disease

Covid-19 Hastalığında Dermatolojik Lezyonlar

Özdemir Öner[1], Pala Aşır Ayşegül[2], Şeker Elif[2]

[1] Sakarya University, Training and Research Hospital, Department of Pediatrics, Division of Allergy and Immunology, Sakarya, Turkey
[2] Sakarya University, Training and Research Hospital, Department of Pediatrics, Sakarya, Turkey

Yazışma Adresi / *Correspondence:*
Öner Özdemir

Sakarya University, Training and Research Hospital, Department of Pediatrics, Division of Allergy and Immunology, 54100, Sakarya, Turkey
T: **+90 (264) 444 5400** E-mail: **ozdemir_oner@hotmail.com**

Geliş Tarihi / Received : **04.10.2020** Kabul Tarihi / Accepted : **15.02.2021**

Orcid:
Öner Özdemir https://orcid.org/0000-0002-5338-9561
Ayşegül Pala https://orcid.org/0000-0001-9056-144X
Elif Şeker https://orcid.org/0000-0002-2975-6616

(Sakarya Tıp Dergisi / *Sakarya Med J* 2021, 11(1):218-220) DOI: 10.31832/smj.805026

Dear Editor

Although the etio-pathogenesis of skin lesions in COVID-19 is yet not clear, several theories have been proposed. One of them is cytokine storm causing thrombophilic arteritis in COVID-19 patients due to activation of endothelial cells and macrophages. Furthermore, involvement of activated keratinocytes and/or Langerhans cells of the skin may cause various clinical spectrum According to another theory, livedo reticularis-like lesions may be result of decreased blood flow to cutaneous micro-vascular system by accumulation of micro-thromboses derived from other organs.

From SARS-CoV-2 infected 148 patients, hospital records of 18 patients clinically showed skin involvement. 8 out of 18 patients showed the symptoms at the onset of COVID-19 and remained after hospitalization. Erythematous rash was observed in 14 patients, widespread urticaria in 3 patients, and chickenpox-like vesicles in 1 patient. Generally, affected area was trunk with low itching, but skin lesions healed in a few days. The authors emphasized skin manifestations are similar to cutaneous involvement occurring during common viral infections.[1]

Castelnovo et al reported skin involvement of two young COVID-19 patients. First patient presented widespread urticaria in the thigh and peri-malleolar area spontaneously improving in a few days.[2] Second patient had vasculitic purpura, then evolving to erythematous rash. The patient was recovered after a short time with corticosteroid.
In another study, a woman with COVID-19 was admitted with odynophagia. She later developed arthralgia and pruritic disseminated erythematous plaques involving face and acral areas. The authors suggested skin symptoms as an indicator for SARS-CoV-2 infection.[2-3]

The skin manifestations in 130 COVID-19 patients of two hospitals from Rome and Barcelona were examined. Vesicles surrounded by erythematous halos with mild pruritus were observed in only 2 patients of Rome. In Barcelona, only 1 patient had numerous isolated vesicular lesions in the back. The authors stated that skin lesions seen in COVID-19 are similar to dermatological manifestations seen in typical viral infection of Herpesviridae family.[4]

Fernandez-Nieto et al conducted a retrospective analysis of 132 patients with SARS-CoV-2 infection. The mean duration of skin lesions was 8.7 days.[5] In 95 patients, there were acute acro-ischemic (chilblain-like pattern) lesions in the form of red to violet macules, plaques, and nodules, usually at the distal aspects of toes and fingers. Rounded erythematous macules and vesicles in erythema multiforme-like pattern tending to coalesce were observed in 37 patients.

In conclusion; as of today, there are limited studies and reports available on dermatological manifestations in COVID-19 patients. Dermatological symptoms can start before or after SARS-CoV-2 infection. The region of involvement and healing time of symptoms varies. Some symptoms are the same as occurring during classical viral infections.

References

1. *Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol. 2020; 34(5):e212-e213.*
2. *Castelnovo L, Capelli F, Tamburello A, Faggioli PM, Mazzone A. Symmetric cutaneous vasculitis in COVID-19 pneumonia. J Eur Acad Dermatol Venereol. 2020;34(8):e362-e363.*
3. *Henry D, Ackerman M, Sancelme E, Finon A, Esteve E. Urticarial eruption in COVID-19 infection. J Eur Acad Dermatol Venereol. 2020; 34(6):e244-e245.*
4. *Tammaro A, Adebanjo GAR, Parisella FR, Pezzuto A, Rello J. Cutaneous manifestations in COVID-19: the experiences of Barcelona and Rome. J Eur Acad Dermatol Venereol. 2020; 34(7):e306-e307.*
5. *Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A, Moreno-Arrones OM, Saceda-Corralo D, Arana-Raja A, Ortega-Quijano D. Characterization of acute acral skin lesions in nonhospitalized patients: A case series of 132 patients during the COVID-19 outbreak. J Am Acad Dermatol. 2020; 83(1):e61-e63.*