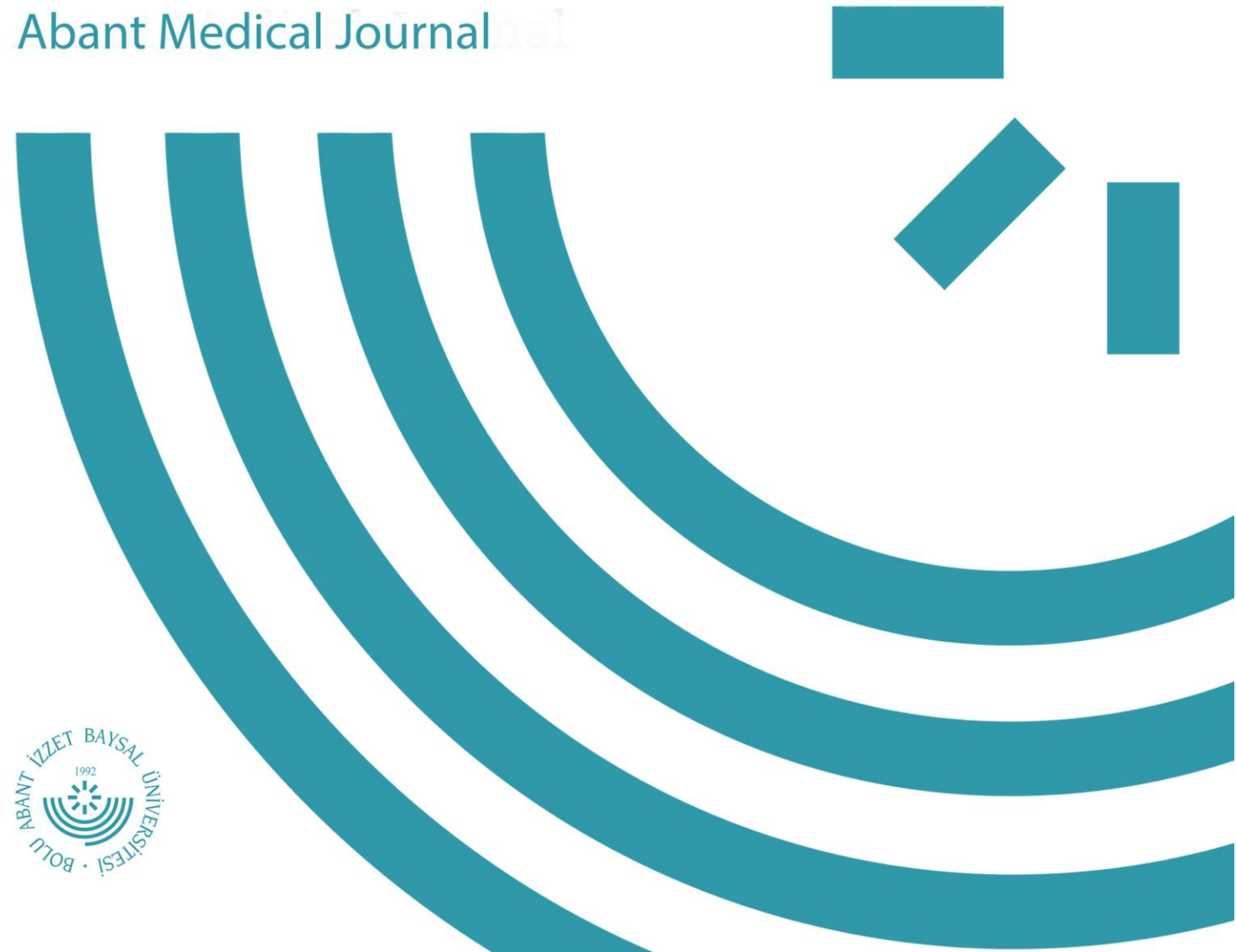
12. cilt volume | 2. sayı issue | 2023 ağustos august

ISSN: 1305-4392
e-ISSN: 2147-1800

Abant Tıp Dergisi

(abantmedj)

Abant Medical Journal



Abant Tıp Dergisi
Abant Medical Journal

Cilt/Volume:12 Sayı/ Issue: 2 - Nisan / April 2023
e-ISSN: 2147-1800

SAHİBİ / OWNER

Prof. Dr. Muhammet Güzel KURTOĞLU - abantmedj@ibu.edu.tr
Dean of Medical Faculty of Bolu Abant Izzet Baysal University, Bolu - Türkiye

BİLİMSEL YAYIN VE DERGİLER KOORDİNATORLÜĞÜ / SCIENTIFIC PUBLICATIONS AND JOURNALS COORDINATOR

Assoc. Prof. Dr. Mustafa YİĞİTOĞLU - mustafayigitoglu@ibu.edu.tr
Coordinator, Bolu Abant Izzet Baysal University, Bolu - Türkiye

Assist. Prof. Dr. Can DOĞAN – can.dogan@ibu.edu.tr
Coordinator Assistant, Bolu Abant Izzet Baysal University, Bolu - Türkiye

Assoc. Prof. Dr. Fatma DEMİRAY AKBULUT – demiray_f@ibu.edu.tr
Coordinator Assistant**,** Bolu Abant Izzet Baysal University, Bolu - Türkiye

BAŞ EDİTÖR/ EDITOR IN CHIEF

Assoc. Prof. Dr. Murat ALIŞIK - muratalisik@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Medical Biochemistry, Bolu - Türkiye

BAŞ EDİTÖR YARDIMCILARI/ DEPUTY EDITOR IN CHIEF

Assoc. Prof. Dr. Semih BOLU - semih.bolu@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Department of Child Health and Diseases, Bolu - Türkiye
Assist. Prof. Dr. Elif YAKŞİ - elifyaksi@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Physical Therapy and Rehabilitation, Bolu - Türkiye

ALAN EDİTÖRLERİ/ FIELD EDITORS

Prof. Dr. Akcan AKKAYA - akcanakkaya@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Bolu – Türkiye
Prof. Dr. Akif Hakan KURT- hakankurt@ibu.edu.tr
Bolu Abant Izzet Baysal University, Department of Medıcal Pharmacology, Bolu – Türkiye
Prof. Dr. Aslı ÇELEBİ TAYFUR- asli.celebitayfur@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Child Health and Diseases, Bolu - Türkiye
Prof. Dr. Fatih ULAŞ - fatihulas@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Ophthalmology, Bolu - Türkiye
Prof. Dr. Hikmet TEKÇE - hikmettekce@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Internal Medicine, Bolu - Türkiye
Prof. Dr. İbrahim EREN - ibrahimeren@sdu.edu.tr
Suleyman Demirel University, Faculty of Medicine, Department of Psychiatry, Isparta -Türkiye
Prof. Dr. İbrahim KÜRTÜL - ibrahimkurtul@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Anatomy, Bolu - Türkiye
Prof. Dr. Mahmoud MUSTAFA - m.Al-mustafa@ju.edu.jo
An-najah National University, Medical Faculty, Depertment of Urology, Nablus, Palestine
Prof. Dr. Şehmus ERTOP - drsertop@beun.ibu.edu.tr
Zonguldak Bulent Ecevit University, Department of Internal Medicine, Zonguldak -Türkiye
Assoc. Prof. Dr. Akif GÜNEŞ - akif.gunes@ibu.edu.tr
Bolu Abant Izzet Baysal University, Department of Otorhinolaryngology, Bolu – Türkiye
Assoc. Prof. Dr. Ayşegül DANIŞ- ayseguldanis7@gmail.com
BAIBU Izzet Baysal Training and Research Hospital, Pediatric Neurology, Bolu - Türkiye
Assoc. Prof. Dr. Elif KARALI - elifkarali@ibu.edu.tr
Bolu Abant Izzet Baysal University, Department of Otorhinolaryngology, Bolu – Türkiye
Assoc. Prof. Dr. Erkan KILINÇ - erkankilinc@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Physiology, Bolu - Türkiye
Assoc. Prof. Dr. Fatma AVCIOĞLU - fatmaavcioglu@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Medical Microbiology, Bolu - Türkiye
Assoc. Prof. Dr. Güray CAN - dr_guraycan@yahoo.com
Bursa Özel Doruk Yıldırım Hastanesi, Bursa - Türkiye
Assoc. Prof. Dr. Mehmet Özgür YİS - ozgurmehmetyis@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Medical Biochemistry, Bolu – Türkiye
Assoc. Prof. Dr. Mehmed Uğur IŞIK - mehmedugur@windowslive.com
Kastamonu University, Faculty of Medicine, Department of Ophthalmology, Kastamonu -Türkiye
Assoc. Prof. Dr. Murat YILMAZ - murat.yilmaz@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Neurology, Bolu – Türkiye
Assoc. Prof. Dr. Mustafa BEHÇET - mustafabehcet@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Medical Microbiology, Bolu - Türkiye
Assoc. Prof. Dr. Nadire KÜÇÜKÖZTAŞ - nadire.kucukoztas@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Internal Medicine, Bolu - Türkiye
Assoc. Prof. Dr. Sebahat GÜCÜK - sebahatgucuk@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Family Medicine, Bolu – Türkiye

Assoc. Prof. Dr. Tacettin AYANOĞLU - tacettinayanoglu@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Orthopedics and Traumatology, Bolu – Türkiye
Assoc. Prof. Dr. Tuba TASLAMACIOĞLU DUMAN - tubaduman@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Internal Medicine, Bolu – Türkiye
Assist. Prof. Dr. Ali Can ÖNAL - acan.onal@beun.edu.tr
Zonguldak Bülent EcevitUniversity, Faculty of Medicine, Medical Pathology, Zonguldak - Türkiye
Assist. Prof. Dr. Emrullah SÖĞÜTDELEN - emrullahsogutdelen@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Urology, Bolu - Türkiye
Assist. Prof. Dr. Mustafa Enes DEMİREL - mustafaenesdemirel@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Emergency Medicine, Bolu - Türkiye
Assist. Prof. Dr. Samet ŞAHİN- sametsahin@mu.edu.tr
Muğla Sıtkı Koçman University, Department of General Surgery, Muğla -Türkiye
Assist. Prof. Dr. Tuğba ALIŞIK – dr.tugbaakkoyun@hotmail.com
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Bolu - Türkiye
Assist. Prof. Dr. Yunus YILMAZSOY- yunusyilmazsoy@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Radiology, Bolu - Türkiye

YAYIN KURULU / EDITORIAL BOARD

Prof. Dr. Akif Hakan KURT
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Medical Pharmacology, Bolu - Türkiye
Prof. Dr. Ali KILIÇGÜN
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Thoracic Surgery, Bolu – Türkiye
Prof. Dr. Fatma TÖRE
Biruni University, Faculty of Medicine, Department of Physiology, Istanbul - Türkiye
Prof. Dr. Fuat AKPINAR
Istanbul Medeniyet University, Faculty of Medicine, Department of Orthopedics and Traumatology, Istanbul - Türkiye
Prof. Dr. Hülya ÖZTÜRK
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Pediatric Surgery, Bolu - Türkiye
Prof. Dr. Mehmet ÖZDEMİR
Necmettin Erbakan University, Meram Faculty of Medicine, Department of Medical Microbiology, Ankara – Türkiye
Prof. Dr. Mustafa ŞİT
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of General Surgery, Bolu – Türkiye
Prof. Dr. Muzaffer KIRIŞ
Health Sciences University Gülhane Faculty of Medicine, Department of Otorhinolaryngology, Ankara - Türkiye
Prof. Dr. Ömer ANLAR
Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of Neurology, Ankara – Türkiye
Prof. Dr. Safiye GÜREL
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Radiology, Bolu - Türkiye
Prof. Dr. Seyit Ali KAYIŞ
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Biostatistics, Bolu - Türkiye
Prof. Dr. Yusuf Özgür BİÇER
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Otorhinolaryngology, Bolu - Türkiye
Assoc. Prof. Dr. Mehmet Özgür YİS
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Medical Microbiology, Bolu – Türkiye
Assist. Prof. Dr. Görker SEL
Zonguldak Bülent Ecevit Üniversitesi Tıp Fakültesi, Department of Obstetrics and Gynecology, Zonguldak - Türkiye
Assist. Prof. Dr. Hamdi AFŞİN
Bolu Abant Izzet Baysal University Faculty of Medicine, Department of Nuclear Medicine, Bolu – Türkiye
Dr. Khadijeh TAIYARI
Cardiff University, Centre for Trials Reserach, Cardiff- Galler
Dr. Muhammad AKHLAQ
Gomal University, Faculty of Pharmacy, Department of Pharmacognosy, Dera Ismail Khan – Pakistan

İNGİLİZCE DİL EDİTÖRLERİ / ENGLISH LANGUAGE EDITORS

Assist. Prof. Dr. Ömür Gülsüm DENİZ - omur.deniz @ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Histology and Embryology, Bolu – Türkiye

İSTATİSTİK EDİTÖRLERİ / STATISTICAL EDITORS

Assist. Prof. Dr. Oya KALAYCIOĞLU - oyakalaycioglu@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Biostatistics, Bolu - Türkiye

YAYIN EDİTÖRÜ, MİZANPAJ EDİTÖRÜ / BROADCAST EDİTOR, LAYOUT EDITOR

Lecturer Adnan ŞEN – adnan@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Information Technology, Bolu – Türkiye

TEKNİK EDİTÖR, WEB EDİTÖRÜ / TECHNICAL EDITOR, WEB EDITOR

Lecturer Adnan ŞEN – adnan@ibu.edu.tr
Bolu Abant Izzet Baysal University, Faculty of Medicine, Information Technology, Bolu – Türkiye

HAKEM KURULU / REFEREE BOARD

Abant Tıp Dergisi [Abantmedj], en az iki hakemin görev aldığı çift taraflı kör hakemlik sistemi kullanmaktadır. Hakem isimleri gizli tutulmakta ve yayımlanmamaktadır. / **Bu konuda genel bilgi için** https://dergipark.org.tr/tr/pub/abantmedj
Abant Medical Journal [Abantmedj] uses double-blind review fulfilled by at least two reviewers. Referee names are kept strictly confidential. **For detailed information, please click here:** https://dergipark.org.tr/tr/pub/abantmedj

ADRES/ADDRESS

Abant Tıp Dergisi Editörlüğü
Bolu Abant Izzet Baysal Üniversitesi Tıp Fakültesi Dekanlığı 14030 BOLU - TÜRKİYE
Tel: +90 374 253 46 56 Faks: +90 374 253 45 59
e-posta: abantmedj@ibu.edu.tr
Web: https://dergipark.org.tr/tr/pub/abantmedj

DİZİNLENME BİLGİLERİ / ABSTRACTING AND INDEXING SERVICES

Abant Tıp Dergisi, Türk Medline, Sobiad Atıf Dizini, Google Scholar, TR Dizin (2013 - 2015 yılları arası) tarafından taranmaktadır.

Abant Tıp Dergisi (Abantmedj), sağlık bilimlerindeki tüm etik yönergelere uygun olarak hazırlanmış klinik ve deneysel araştırma makaleleri, olgu bildirileri, derleme makaleleri, teknik notlar ve editöre mektupları yayınlamaktadır. Abant Tıp Dergisi Bolu Abant Izzet Baysal Üniversitesi Tıp Fakültesi'nin resmi yayın organı olan bir dergidir. Yılda 3 sayı halinde (Nisan, Ağustos, Aralık) elektronik ortamda yayınlanır. Derginin resmi yayın dili Türkçe ve İngilizce'dir. Dergimiz "Şeffaflık ve Akademik Yayıncılık En İyi Uygulamalar İlkelerine" (Principles of Transparency and Best Practice in Scholarly Publishing) (doaj.org/bestpractice) uygun olarak yayınlanmaktadır. Yayınlanan yazıların bütün yayın hakları **Abantmedj**'e ait olup, yayıncının izni olmadan kısmen veya tamamen basılamaz, çoğaltılamaz ve elektronik ortama taşınamaz. Yazıların yayınlanıp yayınlanmamasından yayın kurulu sorumludur."

Abant Medical Journal (Abantmedj), publishes all forms of clinical and research articles prepared in line with all ethical principles in the health sciences, case reports, review articles, technical notes, and letters to the editor. The Abant Medicine Journal is the official publishing organ of the Bolu Abant Izzet Baysal University Faculty of Medicine. It is published electronically three times a year (in April, August, and December). The journal's official languages are Turkish and English. It is published in accordance with the 'Principles of Transparency and Best Practice in Scholarly Publishing' (doaj.org/bestpractice). Published texts belong to abantmedj, and cannot be published partly or in full, reproduced, or transferred to an electronic environment without permission. The responsibility for whether or not texts should be published lies with the editorial board."

İçindekiler / Contents

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):91-97, doi:10.47493/abantmedj.1209807

Dialyzers as a Cause of Hemolysis

Hemoliz Nedeni Olarak Diyalizörler

Gürkan YURTERİ [1*], Sibel ADA [2]

[1] Rentek Hemodialysis Center, İstanbul, Türkiye

[2] Department of Nephrology, Prof.Dr.Cemil Tascıoglu City Hospital, İstanbul, Türkiye

Geliş Tarihi (*Received*): 25.11.2022 **Kabul Tarihi (*Accepted*):** 02.08.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Abstract

Objective: Hemolysis is a rare adverse effect of hemodialysis. ıt is induced by chemical pollution, heat, or mechanical harm to clogged hemodialysis lines. Lactate dehydrogenase transforms pyruvate to lactate in the absence of oxygen to make energy. LDH serum levels are raised due to tissue breakdown. A number of clinical illnesses, such as hemolytic disorders, are associated with high serum LDH.

Both the Rexeed and Leoceed dialyzers are made by AsahiKASEI. They had the same membrane architecture and permeability, but blood entry angle, chamber length, and hole count varied. The aim of this study is to examine if dialyzer design affects hemolysis.

Materials and Methods: A total of 142 patients who were chronically undergoing hemodialysis therapy at the Rentek Hemodialysis Center for a total of 12 hours per week were included. A retrospective examination of the patients was performed. The pre-HD and post-HD LDH levels of individuals who had undergone hemodialysis with both dialyzers during separate sessions of hemodialysis were compared.

Results: A hundred forty-two patients (63% female) on hemodialysis (HD) treatment were enrolled in the study. Twenty-eight patients (20%) had diabetes, 45 had hypertension (32%) and 16 had ischemic heart disease (11%) as a comorbid condition.

When LDH difference is compared between groups Leoceed dialyzer group) had statistically significantly higher LDH difference when compared with Rexeed dialyzer group (49.1 ± 20 U/l vs 229.8 ± 24.45 U/l; p=0.008).

Conclusion: It is possible that the design of the dialyzer contributes in some way to the cell damage that is caused by the larger serum LDH increase in the Leoceed dialyzer. In order to carry out corrective studies on dialyzer design, it would be helpful to analyze the impact of dialyzer design on cell damage using a larger series of patients.

Keywords: Hemodialysis, Dialyzer, Hemolysis

&

Öz

Amaç: Hemoliz, hemodiyalizin nadir görülen bir komplikasyonudur. Kimyasal kirlilik, ısı veya tıkanan hemodiyaliz hatlarına mekanik zarar verilmesi sonucu oluşur. Laktat dehidrogenaz, piruvatı laktata dönüştüren ve serum seviyeleri, doku parçalanması nedeniyle yüksen bir enzimdir. Hemolitik bozukluklar gibi bir dizi klinik hastalık, yüksek serum LDH'si ile ilişkilidir. Hem Rexeed hem de Leoceed diyalizörler AsahiKASEI tarafından üretilen aynı zar yapısına ve geçirgenliğine sahip diyalizörlerdir ancak kan giriş açısı, hazne uzunluğu ve por sayısı farklıdır. Bu çalışmanın amacı, diyalizör tasarımının hemoliz üzerine etkisini incelemektir.

Gereç ve Yöntemler: Rentek Hemodiyaliz Merkezi'nde, haftada toplam 12 saat hemodiyaliz tedavisi gören 142 hasta retrospektif olarak değerlendirildi. Ayrı hemodiyaliz seanslarında her iki diyalizör ile hemodiyalize giren bireylerin HD öncesi ve HD sonrası LDH seviyeleri karşılaştırıldı.

Bulgular: Çalışmaya hemodiyaliz (HD) tedavisi gören 142 hasta (%63 kadın) dahil edildi. Komorbid durum olarak 28 (%20) hastada diyabet, 45 hastada (%32) hipertansiyon ve 16 hastada (%11) iskemik kalp hastalığı vardı.

LDH düzeyi, Leoceed diyalizer grubunda Rexeed diyalizer grubuna göre istatistiksel olarak anlamlı düzeyde yüksekti (49,1 ± 20 U/l vs 229,8 ± 24,45 U/l; p=0,008).

Sonuç: Diyalizörün tasarımı, hücre hasarını arttırarak Leoceed diyalizördeki LDH yüksekiğine neden oluyor olabilir. Diyalizör tasarımı konusunda düzeltici çalışmalar yapabilmek için daha geniş hasta serileri kullanılarak diyalizör tasarımının hücre hasarı üzerindeki etkisinin analiz edilmesi faydalı olacaktır.

Anahtar Kelimeler: Hemodiyaliz, Hemoliz, Diyalizör

Atıf/Cite as: Yurteri G. , Ada S. Dialyzers as a cause of Hemolysis. Abant Med J. 2023; 12(2): 1-2. doi: 10.47493/abantmedj.1209807

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Gürkan Yurteri, **e-mail**: gyurteri@hotmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

Hemolysis is a well-known yet uncommon complication of hemodialysis. Hemodialysis hemolysis is often triggered by chemical pollution, heat, or mechanical damage to erythrocytes from blocked hemodialysis lines (1-7).

Lactate dehydrogenase, often known as LDH, is an intracellular enzyme that converts pyruvate to lactate to provide energy in the absence of oxygen. The breakdown of tissue is the major cause of elevated blood LDH levels (8,9). Multiple clinical conditions, particularly hemolytic diseases (10-15), are associated with high LDH levels in the blood.

AsahiKASEI is the manufacturer of both the Rexeed (Japan) and the Leoceed (Japan) dialyzers. The construction and permeability of the membranes were same, but the angle at which blood entered the chamber, chamber length, and number of holes varied (Figure 1).

There have been cases of hemolysis resulting from improperly made or kinked blood lines. This study aims to determine whether or not the design of a dialyzer influences hemolysis.

Materials and Methods

This study comprised 142 patients who received chronic hemodialysis treatment at the Rentek Hemodialysis Center for a total of 12 hours per week. During separate hemodialysis sessions, the pre-HD and post-HD LDH levels of those who had hemodialysis with both dialyzers were compared. Every patient was assessed to be in a stable clinical condition, and they were all getting bicarbonate low-flux HD treatment on a regular basis. Ineligibility criteria included: 1) six months of HD; 2) three weeks of dialysis; 3) a current, unresolved acute illness of any etiology; 4) acute cardiovascular events and major surgery in the last three months; and 5) the presence of hepatic disease. The study was approved by Istanbul Prof. Dr. Cemil Tascioglu City Hospital Clinical Research Ethics Committee (approval number: 3.11.2022/E-486707-514.99 and the study was carried out in accordance with the Helsinki Declaration of Principles. All of the patients agreed to participate in the trial.

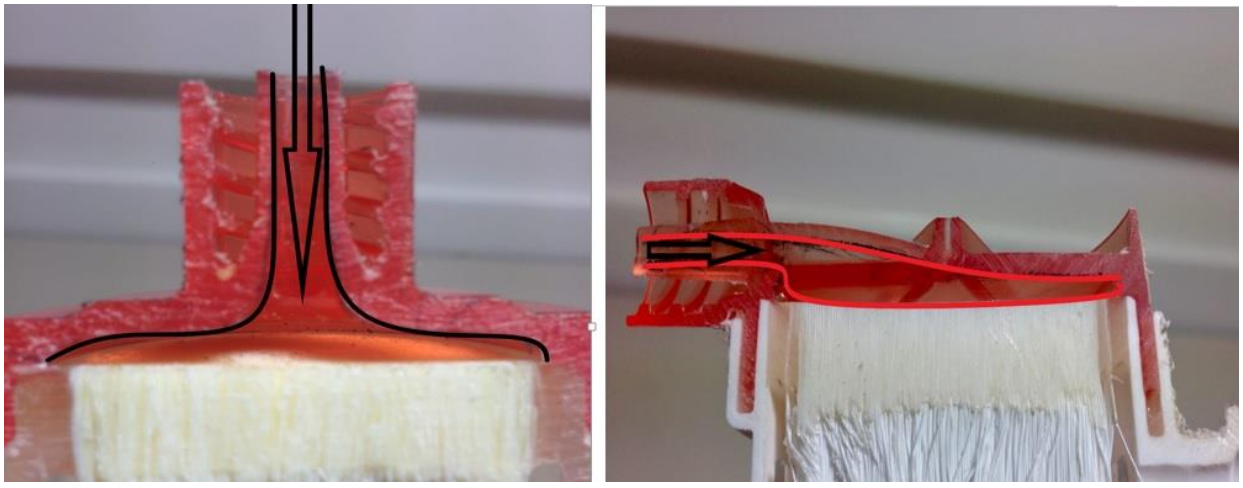


Figure 1. Dialyzers: Leoceed (left), Rexeed (right)

LDH Measurement

All of the blood samples for the laboratory tests were taken before and just after hemodialysis The samples were centrifuged at 3000 × g for 5 min, and then serum was used to analyze LDH level. LDH activity assay kit was used (sigma Aldrich) by colorimetric method. LDH difference was calculated by -post-dialysis LDH minus pre-dialysis LDH.

Statistical Analysis

SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. Normality distribution of the variables was analyzed using the Shapiro–Wilk test. The variables distributed normally are presented as mean± standard deviation. For normally distributed variables, comparisons between the two independent groups were performed using Student's t-test; Categorical variables were compared using the chi-square test. All of the reported P-values were 2-tailed, and those less than 0.05 were considered to be statistically significant.

Results

A hundred forty-two patients (63% female) on hemodialysis (HD) treatment were enrolled in the study. Twenty-eight patients (20%) had diabetes, 45 had hypertension (32%) and 16 had ischemic heart disease (11%) as a comorbid condition. Twenty-eight patients had diabetes (20%), 26 patients had hypertension (18%) and 18 (12%) patients had pyelonephritis as etiology of CKD. Eleven patients had polycystic kidney disease (8%), 35 of the patients had glomerulonephritis (25%) while in 24 patients (17%) etiology is unknown. (Table 1).

Table 1
Demographic Findings in Patient Group

Parameter	HD patients (n=142)
Age (years)	51.0±17.5
Gender (female, n, %)	89(63%)
Fistula (n, %)	117(82%)
Co-morbidities	
Diabetes (n, %)	28 (20%)
Hypertension (n, %)	45(32%)
Ischemic heart disease *(n, %)*	16 (11%)
Dialysis Vintage (months)	28.8±16.0
Cause of CKD (n, %)	
Diabetes	28 (20%)
Glomerulonephritis	35 (25%)
Hypertension	26 (18%)
Polycystic kidney disease	11(8%)
Chronic pyelonephritis	18 (12%)
Unknown	24 (17%)

When LDH difference is compared between groups Leoceed dialyzer group) had statistically significantly higher LDH difference when compared with Rexeed dialyzer group (49.1±20 U/l vs229.8±24.45 U/l; p=0.008) (Table 2).

Table 2
LDH Difference Between Two Dialyzers

Parameter	REXEED	LEOCEED	P
LDH(U/l)	29.8±24.45 U/l	49.1±20 U/l	0.008

When the patients are analyzed having diabetes or not: LDH tends to be higher in diabetic group but the difference was statistically insignificant (Table 3, Table 4).

Table 3
LDH Difference in Diabetic and Non-Diabetic Patients in REXEED Group

Parameter	DM (+)	DM (-)	P
LDH(U/l)	32.3±23.4 U/l	28.9±24.1	0.12

Table 4
LDH difference in diabetic and non-diabetic patients in LEOCEED group

Parameter	DM (+)	DM (-)	P
LDH(U/l)	52.4±24.4 U/l	48.3±23.1	0.1

Discussion

Hemolysis has been the subject of study in a variety of contexts. Hypoosmolality in the dialysate, the presence of hydrogen peroxide or formalin as a result of reuse, hypochlorite as a result of machine sterilization, copper as a result of pipe corrosion, and elevated temperatures are all possible causes of hemolysis. This situation may also be caused by a blocked pump, single-needle dialysis, catheter occlusion, or collapsed arterial line (1-7).

When the water supply has been contaminated, it is quite likely that the majority of patients receiving dialysis will display symptoms of hemolysis. Dialysate may include toxins in the form of bacteria, endotoxins, or disinfectants; nevertheless, it is uncommon for these toxins to cause hemolysis. The very unusual incidence of hemolysis in HD has been linked to the presence of kinks in HD blood lines.

When the Leocced dialyzer was used, the level of lactate dehydrogenase (LDH) in our patient group was dramatically and significantly elevated. Transporting the Leocced dialyzer has spurred the development of a novel packing solution. Moreover, they assert that less storage space is required. Instead of being exposed to nonphysiologically substantial pressures, the blood is harmed by the high shearing stresses caused as blood cells are driven through the limited flow channel of the tubing kink. This causes the blood to become compromised (16,17). Due to the angle at which the blood is linked to the dialyzer, shear stress equivalent to that which leads to tube kinking and hemolysis may be produced (figure 1). Because patients were treated with hemodialysis utilizing both dialyzers simultaneously, additional forms of hemolysis were inevitable.

A high LDH level in the blood is associated with a variety of clinical conditions, including inflammation, infection, and sepsis (18–23), hepatic diseases (24–26), and several oncologic pathologies (27–33). As a marker for cellular damage, LDH is sensitive but not specific for any particular kind of damage. Infected individuals, those with hepatic issues, and those with oncologic diseases were excluded from our analysis. As a result, we may infer that these various variables are not responsible for the varied LDH levels.

Despite the fact that this difference was not statistically significant, diabetes patients had considerably higher LDH levels than those without diabetes. Patients with diabetes, a well-known disease, have an increased chance of developing acute inflammation. LDH has been linked to various inflammatory markers

in the past, and prior research has shown that inflammatory cells may create LDH at serum-detectable quantities (20). LDH has also been linked to several inflammatory indicators (34-37). Diabetes may exacerbate inflammation, which may account for the increase.

Our patients exhibited a little amount of hemolysis. In addition, LDH levels may increase as a consequence of the dialysis operation. Due to the possibility of mechanical hemolysis in extracorporeal blood systems like dialysis, an increase in LDH may be seen and quantified (38, 39). (38, 39). In this regard, Vaziri et al. (41) observed that a single extracorporeal system transit increased overall serum LDH levels. It's probable that platelets contributed to this increase. In addition, Cheng et al. (41) found that patients with HD had higher LDH levels than those with ischemic heart disease and the healthy control group. This suggests that individuals with HD have a higher anaerobic metabolism and activity.

Conclusions

This is the first letter we are aware of reporting an increase in LDH and hemolysis due to a dialyzer. It is quite likely that the arrangement of the Leoceed dialyzer is one of the elements that contributes to the cell damage caused by the elevated serum LDH level. To do corrective research on dialyzer design, it would be advantageous to evaluate the effect of dialyzer design on cell damage using a larger patient sample size. This would provide a more precise evaluation of the influence of dialyzer design.

Ethics Committee Approval: The study was approved by Istanbul Prof. Dr. Cemil Tascioglu City Hospital Clinical Research Ethics Committee (approval number: 3.11.2022/E-486707-514.99 and the study was carried out in accordance with the Helsinki Declaration of Principles.

Informed Consent: Written consent was obtained from the participants or their legal guardians.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Author Contributions: Idea/Concept: G.Y., S.A.; Design: G.Y., S.A.; Supervision: S.A.; Materials: G.Y.; Data Collection/Processing: G.Y., S.A.; Analysis/Interpretation: G.Y., S.A.; Literature Review: G.Y., S.A.; Drafting/Writing: G.Y., S.A.; Critical Review: G.Y., S.A. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Abtahi M, Uzan M, Souid M. Hemolysis-induced acute pancreatitis secondary to kinked hemodialysis blood lines. Hemodial Int. 2007;11(1):38–41.
2. Pendergrast JM, Hladunewich MA, Richardson RM. Hemolysis due to inadvertent hemodialysis against distilled water: perils of bedside dialysate preparation. Crit Care Med. 2006;34(10):2666– 73.
3. Kuo KL, Chou YH, Tarng DC. Mechanical hemolysis in a hemodialysis patient with carotid-jugular arteriovenous fistula. Clin Nephrol. 2004;61(1):74–7.
4. Davidovits M, Barak A, Cleper R et al. Methaemoglobinaemia and haemolysis associated with hydrogen peroxide in a paediatric haemodialysis centre: a warning note. Nephrol Dial Transplant. 2003;18(11):2354–58.
5. Maduell F, NavarroV,Al´osMet al. Intradialysis hemolysis secondary to hypophosphatemia. Nefrologia. 2003;23(1):85–8.
6. Kitching AR, Ritchie D, Wong JK et al. Chloramine-induced hemolysis associated with neurological symptoms in a home hemodialysis patient. Clin Nephrol. 2001;55(3):259–60.
7. Yang MC, Lin CC. In vitro characterization of the occurrence of hemolysis during extracorporeal blood circulation using a mini hemodialyzer. ASAIO J. 2000;46(3):293–7.
8. Jurisic V, Radenkovic S, Konjevic G. The actual role of LDH as tumor marker, biochemical and clinical aspects. Adv Exp Med Biol. 2015;867:115–24.

9. Rossello X, Hall AR, Bell RMet al. Characterization of the Langendorff perfused isolated mouse heart model of global ischemia-reperfusion injury: Impact of ischemia and reperfusion length on infarct size and LDH release. J Cardiovasc Pharmacol Ther. 2016;21(3):286–95.
10. Gedik E, Yucel N, Sahin T et al. Hemolysis, elevated liver enzymes, and low platelet syndrome: Outcomes for patients admitted to intensive care at a tertiary referral hospital. Hypertens Pregnancy. 2017;36(1):21-29.
11. Hanna RM, Barsoum M, Vandross A et al. Atypical hemolytic uremic syndrome and complement blockade: Established and emerging uses of complement inhibition. Curr Opin Nephrol Hypertens. 2019;28(3):278-87.
12. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. Blood 2014;124(18):2804-11
13. Hill A, Hill QA. Autoimmune hemolytic anemia. Hematology Am Soc Hematol Educ Program. 2018;2018(1):382–9.
14. Artinger K, Hackl G, Schilcher G et al. The conundrum of postpartum thrombotic Microangiopathy: Case report and considerations for management. BMC Nephrol. 2019;20(1):91.
15. Meibody F, Jamme M, Tsatsaris V et al. Post-partum acute kidney injury: Sorting placental and non-placental thrombotic microangiopathies using the trajectory of biomarkers. Nephrol Dial Transplant. 2019;35(9):1538-46.
16. Yasuda T, Funakubo A, Miyawaki F, Kawamura T, Higami T, Fukui Y. Influence of static pressure and shear rate on hemolysis of red blood cells. ASAIO J. 2001;47(4):351-3.
17. Blackshear PL Jr., Dorman FD, Steinbach JH. Some mechanical effects that influence hemolysis. Trans Am Soc Artif Intern Organs. 1965;11:112–7.
18. Erez A, Shental O, Tchebiner JZ et al. Diagnostic and prognostic value of very high serum lactate dehydrogenase in admitted medical patients. Isr Med Assoc J. 2014;16(7):439-43.
19. Hernandez-Cardenas CM, Serna-Secundino H, Garcia-Olazaran JG et al. Acute respiratory distress syndrome secondary to influenza A(H1N1)pdm09: Clinical characteristics and mortality predictors. Rev Invest Clin. 2016;68(5):235-44.
20. Drent M, Cobben NA, Henderson RF et al. Usefulness of lactate dehydrogenase and its isoenzymes as indicators of lung damage or inflammation. Eur Respir J. 1996;9(8):1736-42.
21. Quist J, Hill AR. Serum lactate dehydrogenase (LDH) in Pneumocystis carinii pneumonia, tuberculosis, and bacterial pneumonia. Chest. 1995;108(2):415-8.
22. Knight JA, Dudek SM, Haymond RE. Early (chemical) diagnosis of bacterial meningitis–cerebrospinal fluid glucose, lactate, and lactate dehydrogenase compared. Clin Chem. 1981;27(8):1431-4.
23. Quaglia A, Karlsson M, Larsson M et al. Total lactate dehydrogenase in cerebrospinal fluid for identification of bacterial meningitis. J Med Microbiol. 2013;62(Pt 11):1772-3.
24. Connell LC, Boucher TM, Chou JF et al. Relevance of CEA and LDH in relation to KRAS status in patients with unresectable colorectal liver metastases. J Surg Oncol. 2017;115(4):480-7.
25. Yang Z, Ye P, Xu Q et al. Elevation of serum GGT and LDH levels, together with higher BCLC staging are associated with poor overall survival from hepatocellular carcinoma: A retrospective analysis. Discov Med. 2015;19(107):409-18.
26. Zhao P, Wang CY, LiuWWet al. Acute liver failure in Chinese children: A multicenter investigation. Hepatobiliary Pancreat Dis Int. 2014;13(3):276-80.
27. Tredan O, Ray-Coquard I, Chvetzoff G et al. Validation of prognostic scores for survival in cancer patients beyond first-line therapy. BMC Cancer. 2011;11:95.
28. You B, Tranchand B, Girard P et al. Etoposide pharmacokinetics and survival in patients with small cell lung cancer: A multicentre study. Lung Cancer. 2008;62(2):261-72.
29. Lossos IS, Intrator O, Berkman N et al. Lactate dehydrogenase isoenzyme analysis for the diagnosis of pleural effusion in haemato-oncological patients. Respir Med. 1999;93(5):338-41.
30. Sevinc A, Sari R, Fadillioglu E. The utility of lactate dehydrogenase isoenzyme pattern in the diagnostic evaluation of malignant and nonmalignant ascites. J Natl Med Assoc. 2005;97(1):79-84.

31. Fussenich LM, Desar IM, PetersME et al. A new, simple and objective prognostic score for phase I cancer patients. Eur J Cancer. 2011;47(8):1152-60.
32. Petrelli F, Cabiddu M, Coinu A et al. Prognostic role of lactate dehydrogenase in solid tumors: A systematic review and meta-analysis of 76 studies. Acta Oncol. 2015;54(7):961-70.
33. Dierksen J, Buja LM, Chen L. Clinicopathologic findings of hematological malignancy: A retrospective autopsy study. Ann Clin Lab Sci. 2015;45(5):565-73.
34. Nillawar AN, Bardapurkar JS, Bardapurkar SJ. High sensitive C-reactive protein as a systemic inflammatory marker and LDH-3 isoenzyme in chronic obstructive pulmonary disease. Lung India. 2012;29(1):24-9.
35. Song YJ, Kim A, Kim GT et al. Inhibition of lactate dehydrogenase A suppresses inflammatory response in RAW 264.7 macrophages. Mol Med Rep. 2019;19(1):629-37.
36. Yu SL, Xu LT, Qi Q et al. Serum lactate dehydrogenase predicts prognosis and correlates with systemic inflammatory response in patients with advanced pancreatic cancer after gemcitabine-based chemotherapy. Sci Rep. 2017;7:45194.
37. Miyoshi N, Tanigawa T, Nishioka S et al. Association of salivary lactate dehydrogenase level with systemic inflammation in a Japanese population. J Periodont Res. 2018;53(4):487-94.
38. Polaschegg HD. Red blood cell damage from extracorporeal circulation in hemodialysis. Semin Dial. 2009;22(5):524-31.
39. Yoon J, Thapa S, Chow RD et al. Hemolysis as a rare but potentially life-threatening complication of hemodialysis: A case report. BMC Res Notes. 2014;7:475.
40. Vaziri ND, Miyada DS, Kim I et al. Serum LDH and LDH isoenzymes in chronic renal failure: Effect of hemodialysis. Int J Artif Organs. 1990;13(4):223-7.
41. Cheng YC, Kuo WW, Wu CH et al. Iron status and cardiovascular risk factors in patients with haemodialysis versus patients with ischaemic heart disease. Nephrology (Carlton). 2009;14(1):65-9.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):98-104, doi:10.47493/abantmedj.1236292

Effect of Photochromic Senofilcon a Contact Lens on Total Aberrations of the Eye

Fotokromik Senofilcon A Kontakt Lensin Total Göz Aberasyonlarına Etkisi

Deniz KILIC [1*], Muhammed Raşit SİREM [1], Yunus Naci AZİZ [1], Semra KOCA [1], İbrahim TOPRAK [2]

[1] Ophthalmologist, Department of Ophthalmology, Kayseri City Education and Research Hospital, Kayseri, Türkiye

[2] Department of Ophthalmology, Pamukkale University Hospital, Denizli, Türkiye

Geliş Tarihi (*Received*): 16.01.2023 **Kabul Tarihi (*Accepted*):** 11.05.2023 **Yayın Tarihi (*Published*):** 01.08.2023

Abstract

Objective: To investigate the effect of newly designed photochromic Senofilcon-A lens (PCL) on optical aberrations of the eye (total (TA) and high-order-aberrations (HOA)) under ambient illumination conditions.

Materials and Methods: In this retrospective study, 40 eyes of 20 volunteers were fitted with a non-photochromic Senofilcon-A contact lens on the right eye, a PCL on left eye. Subjects were evaluated in terms of best-corrected visual-acuity. Aberrometric measurements were obtained at baseline(lens-free), with activated and deactivated PCL in 3 mm, 6 mm and maximum pupil size.

Results: In lens-free situation there was no difference in terms of TA and HOAs (for 3mm, 6mm and max-pupil-size, TA; p=0.456; p=0.687; p=0.899 and HOA; p=0.226; p=0.259; p=0.442 respectively).In all pupil diameters, in the PCL group compared to the standard lens group, there was a slight increase in total aberrations independent of lens activation, which was not statistically significant(for 3mm,6mm and max-pupil-size, activated lens situation; p=0.523; p=0.622; p=0.244 and deactivated lens situation; p=0.785; p=0.357; p=0.201, respectively). Contrary to total aberrations, higher order aberrations were non-significantly slightly decreased in the PCL group (for 3mm,6mm and max-pupil-size, activated lens situation; p=0.235; p=0.661; p=0.841 and deactivated lens situation; p=0.245; p=0.071; p=0.231, respectively).

Conclusion: The PCL produces similar TA and HOAs with the non-photochromic soft contact lens in both activated and deactivated situation. PCLs can be preferred for those who need uninterrupted vision in variable light conditions.

Keywords: Aberration, Contact Lens, Photochoromic, Ultraviolet

&

Öz

Amaç: Fotokromik Senofilcon-A kontakt lensin (FKL) ortam aydınlatma koşullarında gözün optik aberasyonları (toplam (TA) ve yüksek sıralı aberasyonlar (YSA)) üzerindeki etkisini araştırmak.

Gereç ve Yöntemler: Bu geriye dönük çalışmada, sağ gözlerine fotokromik olmayan Senofilcon-A kontakt lens (KL), sol gözlerine FKL takılan 20 gönüllü ele alındı. FKL aktif ve inaktif fazlarında ölçümler yapıldı. FKL'nin aktif fazına ulaşabilmek ultraviyole cihazı kullanıldı. Aberrometrik ölçümler 3 aşamada; lens takılmadan önce, FKL inaktifken ve FKL aktifken yapıldı. Ayrıca pupil boyutlarının aberasyonları etkileyebileceğinden aberasyonlar pupil çapları 3 mm, 6 mm ve maksimum genişlikte alındı.

Bulgular: Her iki göz için başlangıçta TA ve YSA'lar açısından fark yoktu (3 mm, 6 mm ve maksimum pupil boyutu için, TA; p=0,456; p=0,687; p=0,899 ve YSA; p=0,226; p=0,259; p=0,442). Tüm pupil çaplarında, FKL grubunda KL grubuna göre toplam aberasyonlarda lens aktivasyonundan bağımsız olarak istatistiksel anlamlı olmayan artış bulundu (3 mm, 6 mm ve maksimum pupil boyutu için, aktif lens durumu; p=0,523; p=0,622; p=0,244 ve inaktif lens durumu; p=0,785; p=0,357; p=0,201, sırasıyla). FKL grubunda, YSA'larda istatistiksel anlamlı olmayan azalma bulundu (3mm, 6mm ve maksimum pupil boyutu için, aktif lens durumu; p=0,235; p=0,661; p=0,841 ve inaktif lens durumu; p=0,245; p=0,071; p=0,231, sırayla).

Sonuç: FKL, hem aktif hem de inaktif durumda fotokromik olmayan yumuşak kontakt lens ile benzer TA ve YSA'lara sahip olduğu bulundu. Değişken ışık koşullarında FKL tercih sebebi olabilirler.

Anahtar Kelimeler: Aberasyon, Kontakt Lens, Fotokoromik, Ultraviyole

Atıf/Cite as: Kılıc D. , Sirem M. R. , Aziz Y. N. , Koca S. , Toprak İ. Effect of Photochromic Senofilcon A Contact Lens on Total Aberrations of the Eye. Abant Med J. 2023; 12(2): 2-3. doi: 10.47493/abantmedj.1236292

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*] **Sorumlu Yazar (Corresponding Author):** Deniz Kılıc, **e-mail**: dnz_kilic@hotmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

Contact lenses are an indispensable part of visual rehabilitation. Although they provide a spectacle-free life, some patients were complaining from being uncomfortable. These comfort and mechanic problems have been largely resolved due to the improvements in lens material and technology. However, the glare disability and light disturbance that occur in ambient illumination still continues. For this purpose, fixed-tinted lenses were developed (1). However, they affect vision adversely, especially in scotopic conditions by absorbing near the peak of visible light. (1,2) On the other hand, newly designed photochromic contact lenses (PCL) reduce visual disturbances such as halo, glare, and light scatter and improve photostress recovery by adjusting the light entering the eye (3). PCLs are activated by ultraviolet (UV) and high energy visible light and change their color depending on the wavelength and intensity of ambient light in the environment. This color change is relatively rapid, reversible, and dose-dependent. Under indoor and/or nighttime conditions, PCLs are colorless and provide optimal vision (3).

Although visual acuity is the hallmark of optimal vision and visual function, image quality deteriorates from the optical aberrations (2). The eye, as any other optical system, is far from perfect and also suffers from optic aberrations that affect optical quality. In the eye, the majority of the wavefront aberrations are caused by low-order aberrations (LOA), including refractive errors such as myopia (positive defocus), hyperopia (negative defocus), regular astigmatism, and other non-visually significant aberrations. Most of these aberrations are tolerated well and corrected with spectacles or contact lenses (2,4). High-order aberrations (HOA) reduce retinal image quality and cannot be corrected using conventional optical corrections.

Corneal topography and wavefront technology have allowed ophthalmologists to evaluate these aberrations and thus optical quality objectively and quantitatively. They helped ophthalmologists in deeper understanding the effect of aberrations on vision. The iDesign Advanced Wavescan system is a Hartmann-Shack aberrometer, which uses a Fourier mathematic reconstruction of the wavefront profile. This system provides precise detection of not only LOA but also HOA with better resolution and more detection points (2).

The effect of PCL on visual performance has been widely investigated (4-6). The studies were focused on especially visual acuity and the patients' visual qualities on outdoor activities. However, the investigations about the effect of PCLs on ocular aberrations still lacks. Thus, the aim of this retrospective study was to evaluate the effect of photochromic Senofilcon A lens on optical aberrations of the eye under ambient illumination conditions.

Materials and Methods

This retrospective cross-sectional single center study was conducted in the Cornea and Refractive Surgery Department of Kayseri City Hospital and organized in accordance with the ethical standards. The study was approved by the Ethics Committee of Kayseri City Hospital (date: 21.07.2022 and approval number: 2022/670). All the study procedures were performed in accordance with the Declaration of Helsinki. Informed consent was obtained from patients or their legal guardians. Medical records of 40 eyes of 20 volunteers over the age of 18 years were included in this retrospective study. Subjects whose spherical equivalent is in the range of -0.75 to -3.50 D in each eye and whose best contact lens corrected visual acuity was 20/20 were included in the study. The exclusion criteria are as follows: presence of ocular surface diseases (dry eye, active ocular infection, allergic conjunctivitis, herpetic keratitis, corneal scar or opacities, corneal neovascularization), eyelid problems, such as ectropion and entropion, contact lens wearing in the past three weeks, history of cataract, uveitis, glaucoma and retinal disease, history of ocular trauma and ocular surgery, smoking, any systemic disease, pregnancy, use of systemic or ocular medication known to affect visual acuity and quality.

All cases were evaluated for manifest and subjective refraction, best corrected visual acuity, preliminary slit-lamp biomicroscopy and aberrometry scans before contact lens insertion. Refraction measurements were recorded as spherical equivalents (SE).

Contact Lenses

The lenses fitted were Acuvue Oasys (Johnson & Johnson Vision Care Inc., Jacksonville, Florida) in the right eyes and Acuvue Oasys with Transition (Johnson & Johnson Vision Care Inc., Jacksonville, Florida) in the left eyes. In both lenses the lens material was Senofilcon A, which has a Dk/t of 147 and 38% water content. The total diameter is 14.0 mm, the base curve is 8.4 mm and refractive power is available ranging -12.0 to +8.0 diopter (D) in 0.25 D steps.

Acuvue Oasys with Transition Light Intelligent Technology soft contact lens was approved by The U.S. Food and Drug Administration in 2018. (3)

This contact lens contains naphthopyran monomers, which can darken in 45 seconds when exposed to UV and high energy visible light and transmit 35%±5% of 380-780 nm visible light. When removed from direct sunlight, the lens rapidly fades in 90 seconds and transmits 85%±5% of visible light. (4)

In this study PCLs were activated by using a Light-Link CXL Crosslinking System (Lightmed, Taiwan) emitting 355±5 nm wavelength. After five minutes of exposure to the UV light of the machine, lenses were fitted to the patients and the activation of PCL was confirmed with a slit lamp biomicroscopic examination (Figure 1).

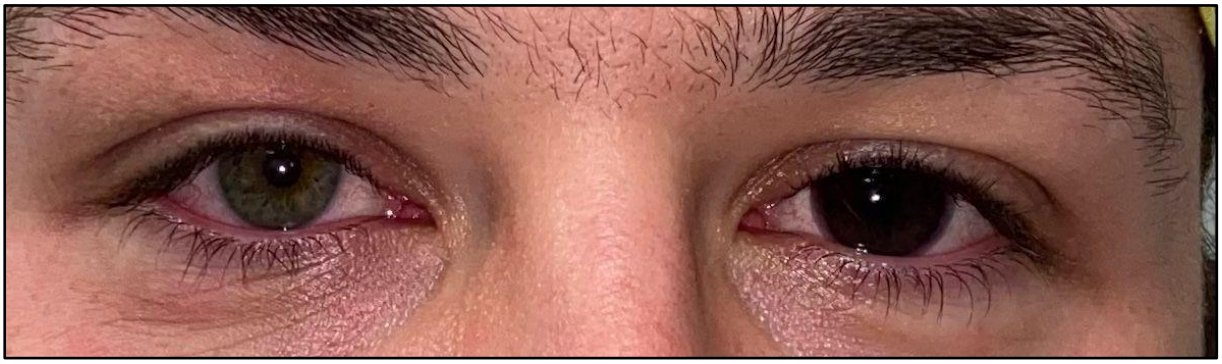


Figure 1. Subject has Senofilcon-A lens in the right eye and activated photochromic Senofilcon-A contact lens in the left eye.

Aberration Measurements

Before fitting a lens all patients were scanned with the iDesign Advanced Wavescan (Abbott Medical Optics, Santa Ana, CA) device to measure the total aberrations (TA) and HOA. Afterwards, subjects were asked to wear Senofilcon A soft contact lens (Group 1, Acuvue Oasys (Johnson & Johnson Vision Care Inc., Jacksonville, Florida)) in the right eye and the active photochromic Senofilcon A soft contact lens (Group 2, Acuvue Oasys with Transitions™ (Johnson & Johnson Vision Care Inc., Jacksonville, Florida)) in the left eye. Lens fit, vertical and horizontal alignment, and 0.5-1 mm movement with each blink were confirmed.

Total aberrations and HOA measurements were repeated. The subjects were kept in room light (200 Lux) for 15 minutes for the inactivation of the PCL and inactivation of the lens was confirmed with a slit lamp biomicroscopy. Measurements of aberrations were then repeated with the inactivated lens.

All aberrometric measurements were evaluated at least three times for each eye at baseline (lens-free), with activated PCL and deactivated PCL by an experienced ophthalmologist (DK). The image with best wavefront quality was selected for further statistical analysis. Root mean square (RMS) of the total and HOAs at 3 mm, 6 mm, and maximum pupil size were recorded. The maximum pupil size is the largest

measurable pupil diameter. Maximum wavefront diameter is 8.5 mm. Total and HOA measurements of both eyes in three examinations (lens-free, PCL activated and deactivated) were compared.

Statistical Analysis

Statistical analysis of the data was evaluated using the SPSS version 24.0 (IBM Corporation, Armonk, NY, USA) software program. The mean, standard deviation, minimum and maximum values of the numerical variables were calculated. Shapiro Wilk test was used to evaluate the normal distribution of variables. In addition, the variables with kurtosis and skewness values in the range of -2, +2 were considered to have a normal distribution. Paired T test was used if groups showed normal distribution in pairwise comparisons, and Wilcoxon test was used if groups did not provide normal distribution. A p value of < .05 was considered statistically significant.

Results

Forty eyes of 20 subjects with a mean age of 29.95±5.23 (range, 25-44) years were included in the study. The study group consisted of 13 (65%) males and 7 (35%) females. The mean SE in the standard contact lens group was -2.36±1.12 D, whereas that in the PCL group was 2.26±1.04 D, exhibiting no significant difference (p=0.777). The eyes were all asymmetrical in biometrical features. After fitted a contact lens, both groups were not different in mean SE (-0.25±0.12 in standard CL vs -0.22±0.20 in PCL, p=0.856). Groups were equal in best corrected visual acuity (BCVA) in Snellen tests (0.98±0.10 in standard CL and 0.97±0.13, p=0.899). Comparison of total and HOAs between the two groups with lens-free, PCL activated and deactivated was shown in Table 1. In lens-free situation there was no statistically significant difference in terms of total and HOAs in all pupil size. Total aberrations were slightly higher in Group 2 compared to Group 1 in all three lens situations, but the differences were not statistically significant. Contrary to total aberrations, there was a slight decrease in Group 2 compared to Group 1 in HOAs, which was not significant (except HOAs measured at maximum pupil size in PCL activated).

Table 1
Comparison of total and high order aberrations between the two groups with lens-free, PCL activated and deactivated.

	Total aberrations			HOAs		
	Group 1	**Group 2**	**P**	**Group 1**	**Group 2**	**P**
3 mm pupil size						
Lens-free	0.78±0.47	0.79±0.22	0.456	0.08±0.17	0.07±0.12	0.226
Activated	0.31±0.34	0.34±0.28	0.523	0.15±0.15	0.11±0.17	0.235
Deactivated	0.33±0.37	0.34±0.22	0.785	0.14±0.12	0.10±0.12	0.245
6 mm pupil size						
Lens-free	30.36±10.33	30.21±10.11	0.687	0.29±0.12	0.26±0.6	0.259
Activated	0.93±0.41	10.02±0.63	0.622	0.32±0.14	0.30±0.13	0.661
Deactivated	0.89±0.34	10.03±0.55	0.357	0.30±0.13	0.23±0.09	0.071
Maximum pupil size						
Lens-free	40.37±10.88	40.30±10.47	0.899	0.45±0.21	0.40±0.13	0.442
Activated	10.14±0.51	10.38±0.71	0.244	0.41±0.23	0.42±0.15	0.841
Deactivated	10.12±0.44	10.37±0.75	0.201	0.44±0.19	0.37±0.15	0.231

HOAs: High-order aberrations

Discussion

Acuvue® Oasys with Transitions™ is a relatively new PCL and there is no study in the literature investigating the effect of PCLs on wavefront aberrations. This comparative study has shown that there is no significant difference on total and HOAs between Oasys CL and Oasys with Transition PCLs.

Contact lenses are mostly transparent to visible light. In recent years, the contact lens industry has advanced remarkably with the design of PCL, which adapt to intensity and wavelength of light. PCLs may be useful for improving visual performance and reducing ocular fatigue, especially for drivers, artists, and athletes who are exposed to variable illumination conditions. Erickson et al. reported better contrast discrimination, visual performance, and better speed of visual recovery in bright sunlight with sport-tinted contact lenses. (5) Recently, it has been reported that greater than 95% of subjects composed of neophyte population were successfully fitted with the PCL based on comfort and vision and it provides advantages among a variety of both indoor and outdoor situations. (4) Photochromic additive contact lenses reduce the extent of positive dysphotopsia compared to non- PCL regardless of lens activation.

In a randomized controlled trial, all visual functions including glare disability, glare discomfort, and photostress recovery time were significantly improved with the activated PCL versus the clear lens. The authors reported that the photochromic feature improves individuals' abilities to cope with intense and short wavelength light and provides a rapid visual recovery after photo stress. (6) Studies have shown that PCL not only improved visual performance in the outdoors and in bright light conditions, but also improved visual functions including photostress recovery, glare disability, glare discomfort, and chromatic contrast in the indoors. (7) It has been shown that the effect of PCLs on nighttime and daytime driving visual performance is non-inferior to non-photochromic soft contact lens and plano photochromic spectacle lenses. (8)

The close relationship between ocular aberrations and visual performance has been investigated and well-known. The effect of soft contact lenses on visual acuity and contrast sensitivity was investigated and it was observed that visual performance was worse than rigid-gas permeable contact lenses. This situation may be associated with induced wavefront aberrations. (9,10) High-order aberrations were found to be significantly increased in the wavefront analysis in myopic soft contact lens wearers.(11) Decentration of soft contact lens from pupil center, ocular surface deformation and interaction between tear film and contact lens may induce wavefront aberrations. (12) In many studies tinted soft contact lenses have been shown to reduce contrast sensitivity, lead night vision disturbances and visual field problems. (13,14) Cosmetically, tinted soft contact lenses also increase HOAs and induce a reduction in optic quality under both photopic and mesopic conditions. (15,16) Besides, it is well known that BCVA is a prognostic factor for abberrations.(15) However, in this study it was found that both groups were similar in BCVA.

It is considered that structural deformations at the junctional zone between clear pupillary area and tinted area may cause an increase in HOAs. (17) In the present study, we found that total wavefront aberrations in all pupil size were not different in the PCL group compared to the non-photochromic soft contact lens group. PCLs ensure a slight reduction in HOAs that were not statistically significant regardless of lens activation. The inability of PCLs in both activated and deactivated situation to induce total and HOAs can provide continuous clear vision in varying lighting conditions.

In a recent study by Recep et al. (18) have assessed the change in ocular aberrations after fitting a FCL. They found that FCL did not influence ocular aberration in both phases (activated-inactivated.). This recent study is different than their study. The two lenses with the same material but a photochromic feature in one were compared. It is therefore valuable and is first to investigate the aberrations in the same material, but a photochromic lens and we believe that its contribution to the literature is important. As ophthalmologists know, there are great individual variations in ocular aberrations. The confounding effect of individual differences was eliminated by comparing the two eyes of subjects. The comparison with the non-photochromic soft contact lens with same material (Senofilcon A) enabled the study to better evaluate

the effect of the photochromic feature. This study also has some limitations, such as the relatively small sample size, and not evaluating the visual performance with objective or subjective methods.

Conclusions

In sum, in both the activated and deactivated situation, the PCL produces similar total and HOAs with the non-photochromic soft contact lens. Therefore, PCLes may be preferred by individuals such as athletes, artists, and drivers who work under bright lights or who need to maintain their visual performance uninterruptedly in ambient illumination. Future large-sampled clinical studies will be needed to better reveal the effect of PCL on ocular aberrations and visual performance.

Ethics Committee Approval: The study was approved by the Ethics Committee of Kayseri City Hospital (date: 21.07.2022 and approval number: 2022/670).

Informed Consent: Written consent was obtained from the participants or their legal guardians.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Author Contributions: Idea/Concept: D.K., S.K., M.R.S., Y.N.A., I.T.; Design: D.K., S.K., M.R.S., Y.N.A., I.T.; Supervision: D.K., S.K., M.R.S., Y.N.A., I.T.; Funding: D.K., S.K., M.R.S., Y.N.A., I.T.; Materials: D.K., S.K., M.R.S., Y.N.A., I.T.; Data Collection/Processing: D.K., S.K., M.R.S., Y.N.A., I.T; Analysis/Interpretation: D.K., S.K., M.R.S., Y.N.A., I.T.; Literature Review: D.K., S.K., M.R.S., Y.N.A., I.T; Drafting/Writing: D.K., S.K.; Critical Review: D.K., S.K., M.R.S., Y.N.A., I.T. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Lee JE, Stein JJ, Prevor MB, Seiple WH, Holopigian K, Greenstein VC, et al. Effect of variable tinted spectacle lenses on visual performance in control subjects. CLAO J. 2002;28(2):80–2.
2. Manche E, Roe J. Recent advances in wavefront-guided LASIK. Curr Opin Ophthalmol. 2018;29(4):286–91.
3. (FDA) USF and DA. ACUVUE (Senofilcon a) soft contact lens with photochromic additive. 510(k) premarket notification [Internet]. Johnson & Johnson vision care, Inc. 2020. Available from: https://www.accessdata.fda.gov/cdrh_docs/ pdf18/K180299.pdf
4. Buch JR, Sonoda L, Cannon JL. Lens fitting and subjective acceptance of senofilcon A with photochromic additive on a neophyte population. Cont Lens Anterior Eye. 2021;44(4):101369.
5. Erickson GB, Horn FC, Barney T, Pexton B, Baird RY. Visual performance with sport-tinted contact lenses in natural sunlight. Optom Vis Sci. 2009;86(5):509–16.
6. Renzi-Hammond LM, Hammond BRJ. The effects of photochromic lenses on visual performance. Clin Exp Optom. 2016;99(6):568–74.
7. Renzi-Hammond LM, Buch JR, Hacker L, Cannon J, Hammond BRJ. The Effect of a Photochromic Contact Lens on Visual Function Indoors: A Randomized, Controlled Trial. Optom Vis Sci. 2020;97(7):526–30.
8. Buch JR, Toubouti Y, Cannon J. Randomized Crossover Trial Evaluating the Impact of Senofilcon A Photochromic Lens on Driving Performance. Optom Vis Sci. 2020;97(1):15–23.
9. Bauer GT. Longitudinal spherical aberration of modern ophthalmic lenses and its effect on visual acuity. Appl Opt. 1980;19(13):2226–34.
10. Cox I, Holden BA. Soft contact lens-induced longitudinal spherical aberration and its effect on contrast sensitivity. Optom Vis Sci. 1990;67(9):679–83.
11. Roberts B, Athappilly G, Tinio B, Naikoo H, Asbell P. Higher order aberrations induced by soft contact lenses in normal eyes with myopia. Eye Contact Lens. 2006;32(3):138–42.

12. Lu F, Mao X, Qu J, Xu D, He JC. Monochromatic wavefront aberrations in the human eye with contact lenses. Optom Vis Sci. 2003;80(2):135–41.
13. Spraul CW, Roth HJ, Gäckle H, Lang GE, Lang GK. Influence of special-effect contact lenses (Crazy Lenses) on visual function. CLAO J. 1998;24(1):29–32.
14. Ozkagnici A, Zengin N, Kamiş O, Gündüz K. Do daily wear opaquely tinted hydrogel soft contact lenses affect contrast sensitivity function at one meter? Eye Contact Lens. 2003;29(1):48–9.
15. Hiraoka T, Ishii Y, Okamoto F, Oshika T. Influence of cosmetically tinted soft contact lenses on higher-order wavefront aberrations and visual performance. Graefes Arch Clin Exp Ophthalmol. 2009;247(2):225–33.
16. Watanabe K, Kaido M, Ishida R, Dogru M, Negishi K, Tsubota K. The effect of tinted soft contact lens wear on functional visual acuity and higher-order aberrations. Cont Lens Anterior Eye. 2014;37(3):203–8.
17. Schanzer MC, Mehta RS, Arnold TP, Zuckerbrod SL, Koch DD. Irregular astigmatism induced by annular tinted contact lenses. CLAO J. 1989;15(3):207–11.
18. Recep ÖF, Kocabas DO, Kiziltoprak H, Ozulken K. Effects on Wavefront Aberration after Short-term Wear of Senofilcon A Photochromic Contact Lens. Klin Monbl Augenheilkd. 2022.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):105-113, doi: 10.47493/abantmedj.1246500

Radyolojik Olarak Covid-19 Pnömonisi Düşünülen Hastalarda Antikor Düzeylerinin Değerlendirilmesi

Evaluation of Antibody Levels in Patients Radiologically Considered to Have Covid-19 Pneumonia

Gözde ÖKSÜZLER KIZILBAY [1*], Serap ARGUN BARIŞ [1], Emel AZAK KARALİ [1], Aynur KARADENİZLİ [1], Hüseyin UZUNER [1], Sevtap DOĞAN [1], Haşim BOYACI [1], İlknur BAŞYİĞİT [1]

[1] Kocaeli Üniversitesi, Tıp Fakültesi, Göğüs Hastalıklar Anabilim Dalı, Kocaeli, Türkiye

Geliş Tarihi (*Received*): 02.02.2023 **Kabul Tarihi (*Accepted*):** 25.04.2023 **Yayın Tarihi (*Published*):** 01.08.2023

Öz

Amaç: Bu çalışmanın amacı, üst solunum yolu örneklerinde COVID-19 RT-PCR tetkiki negatif bulunan fakat tipik radyolojik bulguları nedeniyle COVID-19 pnömonisi olarak kabul edilen hastalarda COVID-19 antikor tetkiki sonuçlarının değerlendirilmesidir.

Gereç ve Yöntemler: Hastanemizde yatırılan COVID-19 pnömonisi açısından tipik bulguları olan 28 hasta retrospektif olarak taranarak periferik kanda ELISA yöntemi ile SARS-CoV2 Total (IgM + IgG) ve IgG antikor düzeylerinin çalışıldı. 10 hastanın yatış sırasında PCR tetkiki pozitif (kesin COVID-19 pnömonisi), 18 hastanın ise PCR tetkiki negatif (olası COVID-19 pnömonisi) olduğu görüldü. Kontrol grubu olarak Kasım 2019-Mart 2020 tarihleri arasında, ülkemizde ilk COVID-19 hastası tespit edilmeden önce yatırılan ve radyolojik bulguları COVID-19 pnömonisi ile uyumlu olarak değerlendirilen 10 hasta alındı (kontrol grubu).

Bulgular: Kontrol grubu olarak alınan hastaların hiçbirinde COVID-19 antikoru tespit edilmezken, radyolojik olarak COVID-19 pnömonisi tanısı alan 28 hastanın 22 tanesinde (%78,6) antikor pozitif bulundu. Kesin COVID-19 pnömonisi olan hastaların sadece 1 tanesinde antikor negatif bulundu. Bu hastanın yaygın Non-Hodgkin Lenfoma tanısı ile halen kemoterapi almakta olduğu tespit edildi. Olası COVID-19 pnömonisi grubunda 5 hastada antikor tespit edilmedi (%27,7). Bu hastaların ikisinin multipl miyelom tanılı olduğu, üç hastanın ise 75 yaş üzeri olduğu dikkati çekti. Kesin ve olası COVID-19 grupları arasında ortalama total ve IgG antikor düzeyleri açısından anlamlı fark tespit edilmedi (sırasıyla total antikor düzeyleri 79,21±32,4 ve 72,98±36,95, p>0,05; IgG antikor düzeyleri 2,57±1,08 ve 2,84 ± 0,9, p=0,6).

Sonuç: Pandemi döneminde radyolojik olarak COVID-19 pnömonisi düşünülen hastalarda geçirilmiş COVID enfeksiyonu tanısı için COVID-19 antikor düzeyleri kullanılabilir. Fakat, yaşlı ve hematolojik malignite başta olmak üzere immunsupresyonu olan hastalarda yeterli antikor yanıtı oluşmayabileceği, bu nedenle geçirilmiş enfeksiyonu göstermenin güç olabileceği akılda tutulmalıdır.

Anahtar Kelimeler: COVID-19, Antikor, Tanı

&

Abstract

Objective: The aim of this study is to evaluate the results of the COVID-19 antibody test in patients with negative COVID-19 RT-PCR (real-time-polymerase chain reaction) tests but accepted as COVID-19 pneumonia due to typical radiological findings.

Materials and Methods: SARS-CoV2 Total (IgM + IgG) and IgG antibody levels were studied by ELISA method of 28 patients were screened retrospectively with typical findings in terms of COVID-19 pneumonia. 10 of them had positive PCR examination (definite COVID-19 pneumonia), 18 had negative PCR examination (possible COVID-19 pneumonia). As the control group, 10 patients before the first COVID19 patient was detected in our country whose radiological findings were evaluated as compatible with COVID-19 pneumonia were included.

Results: While no COVID-19 antibody was detected in any of the patients included in the control group. Antibody was negative in only 1 of the patients with definite COVID-19 pneumonia. It was determined that this patient was still receiving chemotherapy with the diagnosis of diffuse Non-Hodgkin Lymphoma. In the probable COVID-19 pneumonia group, no antibodies were detected in 5 patients (27.7%). Two of these patients were diagnosed with multiple myeloma, and three patients were over 75 years of age. There was no significant difference between the definite and probable COVID-19 groups in terms of mean total and IgG antibody levels (total antibody levels 79.21±32.4 and 72.98±36.95, p>0.05; IgG antibody levels 2.57±1.08 and 2.84 ± 0.9, p=0.6 respectively).

Conclusion: COVID-19 antibody levels can be used for the diagnosis of COVID-19 infection in patients with radiologically suspected COVID-19 pneumonia. However, it should be kept in mind that adequate antibody response may not occur in elderly and immunosuppressed patients, it may be difficult to show a previous infection.

Keywords: COVID-19, Antibody, Diagnosis

Atıf/Cite as: Öksüzler Kızılbay G. , Argun Barış S. , Azak Karali E. , Karadenizli A. , Uzuner H. , Doğan S. , Boyacı H. , Başyiğit İ. Radyolojik Olarak Covid-19 Pnömonisi Düşünülen Hastalarda Antikor Düzeylerinin Değerlendirilmesi. Abant Med J. 2023; 12(2): 3-4. doi: 10.47493/abantmedj.1246500

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

*Sorumlu Yazar (Corresponding Author): Dr. Gözde Öksüzler Kızılbay, e-mail: gozdeoksuzler@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Giriş

Severe Acute Respiratory Syndrom-Coronavirus-2 (SARS-CoV-2), Aralık 2019'da Çin'in Wuhan kentinde ortaya çıkan ve 11 Mart 2020'de tüm dünyada Koronavirüs hastalığı 2019 (COVID-19) pandemisi ilan edilmesine yol açan bir virüstür (1). Eylül 2022 tarihine kadar 606.459.140 vaka doğrulanmış ve 6.495.110 ölüm rapor edilmiştir (2). Virüsün insan vücudundaki inkübasyon süresi 2-14 gün arasında olmakla birlikte genelde ilk haftada bulaşıcılık göstermektedir (3). En sık görülen semptomlar ateş, öksürük, baş ağrısı, halsizlik, kas ağrısı, nefes darlığı karın ağrısı ve ishal olup asemptomatik seyredebildiği de bildirilmiştir (3–5). Üst solunum yolu tutulumundan pnömoni, sepsis ve Acute respiratory distress sendromuna (ARDS) uzanan klinik tabloda kendini gösteren virüsün laboratuar bulgularında lenfopeni, C-reaktif protein (CRP), prokalsitonin, d-dimer, ferritin, laktat dehidrogenaz (LDH), interlökin-6 (IL-6) gibi inflamatuar belirteçlerinde artış tespit edilmektedir (3,6). Tarif edilen klinik ve laboratuar belirteçler SARS-CoV-2'ye spesifik olmayıp diğer viral enfeksiyonlarda da görülebilmektedir.

COVID-19 pnömonisinde erken dönemde akciğer grafisi normal bulunabildiği için, toraks bilgisayarlı tomografi (BT) daha duyarlı bir yöntem olarak pandemi boyunca şüpheli hastalarda uygulanmıştır (3). COVID-19 Revers-Transkriptaz Polimeraz Zincir Reaksiyonu (RT-PCR) pozitifliği olan hastalarda çekilen toraks BT'nin sensitivitesi %97 olup, RT-PCR sonucu negatif olan hastalarda %75 oranında COVID-19 pnömonisi düşündürür bulgular saptanmıştır (7). Düşük doz ve kontrast vermeden çekilen toraks BT görüntülerinde sıklıkla bilateral, periferal yerleşimli posterior ve bazal segmentlerde daha yoğun olmak üzere yamalı tutulumlu buzlu cam dansitesinde lezyonlar izlenmiş olup hava bronkogramı içeren konsolidasyon ve kaldırım taşı manzarası da görülebilmektedir (7,8). Ciddi COVID-19 pnömonisi vakalarında akciğerin tüm loblarını etkileyip yaygın alveolar hasar ile karşımıza çıkmaktadır (3,9). Pnömoninin iyileşme safhasında ise ters halo bulgusu ve fibrotik bantlar görülebilir (3). Akciğer görüntülemesindeki bu bulgular SARS, Middle East Respiratory Sendrom (MERS) gibi diğer coronavirüs tiplerinde, influenza, parainfluenza, adenovirüs, RSV'de (Respiratuar sinsityal virüsü), pnömokok, mikoplazma türlerinde karşımıza çıkabilmekte olup pulmoner ödem, ARDS, organize pnömoni, alveolar hemoraji, interstisyel akciğer hastalarında da görülebilmektedir (10,11). Dolayısıyla hem klinik ve laboratuvar hem de radyolojik bulgular COVID-19 pnömonisi ile benzerlik göstermekte olup hastalığın kesin tanısında moleküler testler ile birlikte değerlendirilmektedir.

Real time nükleik asit zincir reaksiyonu (RT-PCR) COVID-19 tanısı için standart moleküler tanı yöntemi olarak kullanılmaktadır (12). Nazofarenks ve üst solunum yollarında pozitifliği gösterme oranı %32-93 olarak gösterilmiş olup hastalardan kombine burun/boğaz sürüntüsü rutin olarak uygulanmaktadır (13). Fakat RT-PCR testinin doğruluğu numunenin türüne, alınma şekline, hastalığın evresine göre değişmektedir (14,15). Radyolojik görüntüleme bulguları tipik akciğer tutulumu ile uyumlu bulunan COVID-19 hastalarında RT-PCR sürüntü örneklerinin yanlış negatif olarak sonuçlanabildiği bilinmektedir ve tekrarlayan örnek alımlarında COVID-19 RT-PCR pozitifliği tespit edilmektedir (1,16). Bu nedenle RT-PCR yönteminin dışında hastanın SARS-CoV-2 spesifik antikor düzeylerinin belirlenmesiyle tanıya yardımcı olunması amaçlanmıştır. Enzyme-Linked ImmunoSorbent Assay (ELISA), immünokromatografik, lateral akış immünoassay, kemilüminesans mikropartikül immunoassay yöntemleriyle Serum IgG (immünoglobulin) ve IgM düzeyleri tespit edilmiş ve geçirilmekte olan COVID-19 ve geçirilmiş COVID-19 hastalarını belirlemekte kullanılmıştır (12,13).

Yapılan çalışmalarda IgG, IgM düzeyleri ile RT-PCR ve radyolojik bulgular birlikte değerlendirildiğinde COVID-19 tanısının konmasında çok daha yüksek oranlara ulaşılabildiği gösterilmiştir (1,12).

Bu çalışmanın amacı, üst solunum yolu örneklerinde COVID-19 RT-PCR tetkiki negatif bulunan fakat tipik radyolojik bulguları nedeniyle COVID-19 pnömonisi olarak kabul edilen hastalarda COVID-19 antikor tetkiki sonuçlarının değerlendirilmesidir.

Gereç ve Yöntemler

Çalışma Popülasyonu

Çalışmada Kocaeli Üniversitesi Tıp Fakültesi Göğüs Hastalıkları servisinde kesin veya olası COVID-19 pnömonisi tanısı ile yatırılan hastaların verileri retrospektif olarak değerlendirildi. İlk grup hasta klinik ve radyolojik bulguları COVID-19 pnömonisi ile uyumlu ve nazofarengeal sürüntü ile alınan COVID-19 RT-PCR testleri pozitif bulunan hastalardı (kesin COVID-19 pnömonisi). İkinci grup hasta klinik ve radyolojik bulguları COVID-19 pnömonisi ile uyumlu fakat rekürren alınan COVID RT-PCR testleri negatif sonuçlanan hastalardı (olası COVID-19 pnömonisi). Kontrol grubu ise COVID-19 pandemi dönemi öncesinde pnömoni tanısı ile yatan, retrospektif olarak değerlendirilen radyolojik bulguları COVID-19 pnömonisi tutulumuna benzeyen fakat nazofarengeal sürüntüde COVID-19 PCR bakılmamış hastalardan oluşturuldu (kontrol grubu).

Çalışma hakkında Helsinki İlkeler Deklarasyonuna uyularak sözlü bilgilendirme yapıldıktan sonra çalışmaya katılmayı kabul eden 28 hastadan yazılı aydınlatılmış onam formu alındı, olgu rapor formları doldurulduu. Çalışmamız Kocaeli Üniversitesi Etik Kurul'u tarafından onaylandıktan sonra veri toplama ve analiz etme süreci başlandı (GOKAEK- 2020/177).

Çalışmaya dahil edilmesi uygun görülen olası COVID-19 hastaları ile kesin COVID-19 hastaları tanı ve tedavi sürecinden en az 30 gün sonra olmak üzere tekrar hastaneye çağrılarak antikor düzeylerine bakılmak için kan örnekleri alındı. Kontrol grubu olarak belirlenen, pandemi ilan edilmeden önce hastanede yatarak tedavi gören viral pnömonili hastaların kan örnekleri tanı almalarından 3-4 ay sonrasına denk gelmekteydi. Bu 3 grup hastanın olgu rapor formunda yer alan demografik bilgileri, hastalık geçirme tarihleri ve diğer ulusal aşılama programındaki aşılar ve risk grubundaki hastaların pnömokok aşısı, grip aşısı bilgileri kaydedildi.

Antikor Ölçümü

Çalışmaya dahil olan hastalarda periferik kanda SARS-CoV-2 Total (IgG+IgM) ve IgG antikor düzeyleri çalışıldı. Total antikor düzeyleri Cobas (Roche) cihazında Elecsys® Anti-SARS-CoV-2 kiti kullanılarak, IgG antikoru düzeyleri ise SARS-CoV-2 Elisa kiti (Euroimmun) kullanılarak belirlendi.

Hastaların kanları viroloji laboratuarında 10 dakika 400xg'de santrifüj edildi ve serum ayrıştırıldı. Elde edilen serumlar mikrosantrifüj tüplerinde -80 santigrat derecede derin dondurucuda saklandı. Çalışma günü geldiğinde tüm numuneler oda ısısına getirildikten sonra seyreltilerek COVID-19 rekombinant proteinleri ile kaplanmış pleyt kuyucuklarına konuldu ve 30 dakika inkübe edildi. Sonrasında yıkama solüsyonu ile 5 kere yıkanarak HRP işaretli Anti-hIG Tracer antikor ilave edilerek tekrar inkübasyon ve yıkama aşamalarından geçti. Substrat ve stop solüsyon eklenerek ELISA pleyt okuyucusunda 450nm dalga boyunda 10 dakika içerisinde okuma yapıldı.

İstatiksel Analiz

Tüm istatistiksel analizler, IBM SPSS for Windows sürüm 16.0 (SPSS, Chicago, IL, ABD) kullanılarak yapıldı. Sürekli değişkenler ortalama ± standart sapma (SD), kategorik değişkenler sayım (yüzde) olarak ifade edildi. Sürekli değişkenlerin karşılaştırılmasında One Way ANOVA testi kullanıldı. Kategorik değişkenlerin gruplar arasında karşılaştırılması ki-kare testi ile yapıldı. İki taraflı p değerinin $p<0,05$ olması istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışmaya katılan, kontrol grubu olarak belirlediğimiz grup; ülkemizde ilk vakanın tespit edildiği 11 Mart 2020 tarihinden önce servisimizde yatarak pnömoni tedavisi görmüş, klinik ve radyolojik olarak COVID-19 pnömonisi ile benzerlik göstermiş olan 10 hastadan oluşmaktaydı. O dönemde COVID-19 RT-PCR örneği alınmamış olan bu hastaların hiçbirinde Total (IgG+IgM) ve IgG antikor pozitifliği saptanmadı.

Çalışmaya hasta grubu olarak dahil edilen toplam 28 kişiden 18 tanesi olası, 10 tanesi ise kesin COVID-19 pnömonisi olarak kabul edilen hastalardı. Olası COVID-19 pnömoni hasta grubunun yaş ortalaması 58±14 olarak saptanmış olup, 10 tanesi kadın, 8 tanesi erkekti. Kesin COVID-19 pnömoni hasta grubunun yaş ortalaması 48±14 ve 5 kadın, 5 erkek hastadan oluşmaktaydı. Hastaların demografik özellikleri ve komorbiditeleri Tablo 1'de gösterilmiştir.

Tablo 1
Demografik Özellikler

Demografik özellikler	Kesin COVID-19 grubu n=10	Olası COVID-19 grubu n=18
Yaş, ortalama, yıl	48±14	58±14
Cinsiyet		
Kadın	5	10
Erkek	5	8
Komorbiditeler		
DM	3	5
HT	2	7
KAH	0	5
KKY	0	2
KBY	0	2
Astım	2	1
Hematolojik malignite	1	2
Solid organ malignitesi	0	2

DM, Diabetes mellitus; HT, Hipertansiyon; KAH, Koroner arter hastalığı; KKY, Konjestif kalp yetmezliği; KBY, Kronik böbrek yetmezliği

Olası COVID-19 pnömonisi olarak kabul edilen 18 hastanın periferik kanda bakılan SARS-CoV-2 Total (IgG+ IgM) antikor pozitiflik oranı %72 (n=13) saptandı. Total antikor pozitifliği olan her hastanın IgG değeri pozitif olarak bulundu. 5 hastada Total ve IgG antikor düzeyi limit değerin altında saptanarak negatif olarak sonuçlandı. Bu hastaların 2si erkek, 3ü kadın idi. Total (IgG+IgM) antikor düzeyi negatif sonuçlanan 5 hastanın yaş ortalaması 69 olup, 3 hasta 75 yaş ve üzerindeydi. Olası COVID-19 pnömonili hasta grubunun antikor sonuçları Tablo 2 ve 3'te gösterilmiştir.

Tablo 2
Antikor Sonuçları

	Kesin COVID-19 pnömoni grubu (n=10)	Olası COVID-19 pnömoni grubu (n=18)	Kontrol grubu (n=10)
Total (IgG+IgM) pozitif	9	13	0
Total (IgG+IgM) negatif	1	5	10

Kesin COVID-19 pnömonisi olarak kabul edilen 10 hastanın 9 tanesinde Total (IgG+IgM) pozitif bulunmuş olup sadece 59 yaşındaki 1 erkek hastada antikor negatif olarak saptanmıştır. Bu hastanın komorbid hastalık olarak sadece Non-Hodgkin Lenfoma tanısı tespit edilmiştir. Kesin COVID-19 pnömonili hasta grubunun antikor sonuçları Tablo 2 ve 4'te gösterilmiştir.

Kesin COVID-19 pnömoni grubu ile olası COVID-19 pnömoni grubu arasında total ve IgG antikor seviyeleri açısından istatistiksel anlamlı bir fark tespit edilmedi (sırasıyla total antikor düzeyleri 79,21±32,4 ve 72,98±36,95, p>0,05; IgG antikor düzeyleri 2,57±1,08 ve 2,84 ± 0,9, p=0,6).

Tablo 3
Olası COVID-19 Pnömonili Hasta Grubu

			Antikor Sonucu			
			Total (IgG+IgM)		IgG	
Hasta Numarası	Yaş	Cinsiyet	Değer	Sonuç	Değer	Sonuç
Hasta 1	66	Erkek	50,56	Pozitif	3,285	Pozitif
Hasta 2	36	Kadın	62,38	Pozitif	1,703	Pozitif
Hasta 3	74	Erkek	0,081	Negatif	-	-
Hasta 4	41	Kadın	140,1	Pozitif	1,032	Pozitif
Hasta 5	84	Kadın	0,082	Negatif	-	-
Hasta 6	70	Kadın	108,9	Pozitif	-	-
Hasta 7	33	Erkek	108,1	Pozitif	2,526	Pozitif
Hasta 8	67	Erkek	105	Pozitif	3,616	Pozitif
Hasta 9	57	Erkek	40,79	Pozitif	3,509	Pozitif
Hasta 10	76	Kadın	0,098	Negatif	-	-
Hasta 11	65	Erkek	73,14	Pozitif	3,281	Pozitif
Hasta 12	54	Kadın	41,36	Pozitif	2,986	Pozitif
Hasta 13	36	Erkek	106,4	Pozitif	3,548	Pozitif
Hasta 14	55	Kadın	0,082	Negatif	-	-
Hasta 15	60	Erkek	0,086	Negatif	-	-
Hasta 16	69	Erkek	59,82	Pozitif	3,796	Pozitif
Hasta 17	48	Erkek	26,85	Pozitif	1,962	Pozitif
Hasta 18	60	Kadın	25,42	Pozitif	-	-

Total (IgG+IgM) antikor test sonucu negatif olan hastaların IgG antikor sonuçları çalışılmayıp (-) olarak gösterilmiştir.

Tablo 4
Kesin COVID-19 Pnömonili Hasta Grubu

			Antikor Sonucu			
			Total (IgG+IgM)		IgG	
Hasta Numarası	Yaş	Cinsiyet	Değer	Sonuç	Değer	Sonuç
Hasta 19	64	Kadın	21,6	Pozitif	3,583	Pozitif
Hasta 20	33	Kadın	126,1	Pozitif	1,196	Pozitif
Hasta 21	48	Erkek	78,21	Pozitif	3,026	Pozitif
Hasta 22	59	Erkek	0,091	Negatif	-	-
Hasta 23	36	Erkek	82,82	Pozitif	Negatif	Negatif
Hasta 24	45	Erkek	112,1	Pozitif	0,945	Borderline
Hasta 25	30	Kadın	39,2	Pozitif	2,51	Pozitif
Hasta 26	63	Kadın	77,81	Pozitif	3,783	Pozitif
Hasta 27	70	Erkek	82,72	Pozitif	3,427	Pozitif
Hasta 28	41	Kadın	92,36	Pozitif	2,078	Pozitif

Total (IgG+IgM) antikor test sonucu negatif olan hastaların IgG antikor sonuçları çalışılmayıp (-) olarak gösterilmiştir.

Tartışma

COVID-19 pnömonisinin tipik radyolojik bulguları tespit edilen fakat tanı anında RT-PCR negatif bulunan hastaların %72'sinde antikor pozitifliği tespit edilmiştir. Antikor negatif bulunan hastaların ileri yaş ve komorbiditelere sahip hastalar olduğu izlenmiş olup, pandemi döneminde, COVID-19 pnömonisi düşünülüp COVID RT-PCR negatif bulunan hastalarda tanı için radyoloji ve antikor düzeyleri değerlendirmelerinin oldukça yararlı olduğu düşünülmüştür.

COVID-19 pandemisi başladıktan sonra, hastalığın nazofarenks, orofarenks, balgam, derin trakeal aspirasyon, bronkoalveolar lavaj gibi bölgelerden sürüntü ile COVID RT-PCR bakılarak tanı konması fakat bu tetkiklerin sensitivite ve spesifite değerlerinin %100 olmaması tüm sağlık çalışanlarını alternatif ve destekleyici tanı yöntemlerinin araştırılması konusunda harekete geçirmiştir.

Bu yöntemlerden pandeminin başından beri destekleyici tanı yöntemi olabilmesi açısından SARS-CoV-2 total antikor (IgG+IgM), IgG ve IgM düzeyleri araştırılmış, korelasyon olup olmadığı incelenmiştir. Çalışmalar sonucu COVID RT-PCR sonucu pozitif saptanan hastalarda hastalığın ilk haftasında erken dönemde alınan serum örneklerinde antikor saptanamayıp yanlış negatif sonuç verme ihtimali varken total antikor, IgM ve IgG antikor oluşma medyan süresi, 11, 12 ve 14 gün olarak saptanmıştır (1,17). Antikor oluşumunun en erken 7-11 gün arasında başlaması tek başına tanı koymada bu antikorların kullanımını kısıtlayıp akut hastalık döneminde tek başına kullanılamayacağı ileri sürülmüştür (17). Fakat günler ilerledikçe antikor oluşma yüzdesi artarak geçirilmiş COVID-19 hastalığını gösterme oranı artmaktadır ve Total antikor pozitiflik oranı 15 gün içerisinde %100'e yükselip, IgG düzeyinin ortalama 30 gün sonra kanda en yüksek düzeye ulaştığı görülmüştür (1,18). IgG pozitifliğinin ne kadar süre devam ettiği ile ilgili net bilgi olmamakla birlikte incelenen çalışmalarda hastalık başlangıcından en geç 13 hafta sonrasında antikor düzeyi bakılarak hala pozitif olduğu görülmüştür (1). IgM'in ilk 3 haftada en yüksek düzeyine ulaşıp sonrasında düşüşe geçtiği ve 12. haftada kandan kaybolduğu saptanmıştır (18). 68 çalışmanın yer aldığı bir meta analizde, COVID-19 tanısını doğrulamak amacıyla bakılan IgG, IgM ve IgA antikorlarının tek veya ikili kombinasyonları incelenmiş; antikor testlerinin her birinin spesifite oranları %98-%100 arasında bulunmuştur (19). Antikor kombinasyonlarından en yüksek sensitivite oranına sahip olan grubun %79 ile tek başına IgG veya tek başına IgM pozitifliği olduğu tespit edilmiştir (19).

Hastalığın erken döneminde antikorlar henüz oluşmadığı için yanlış negatif sonuçlar görülebilirken; interferon, nonspesifik IgM ve romatoid faktör varlığında yanlış pozitif sonuçlara ulaşılabilmektedir (18,20).

Bu nedenle yaptığımız çalışmada olası ve kesin COVID-19 hasta grubundan hastalık başlangıcından en az 30 gün sonra alınan kandan Total SARS-CoV-2 antikor ve IgG antikor düzeyleri bakılmıştır.

Çalışmamızda; ilk COVID-19 vakası ortaya çıkmadan önce hastanede yatan kontrol grubunun hiçbirinde SARS-CoV-2 antikoru tespit edilemedi. Olası COVID-19 pnömonisi grubunda antikor düzeyleri negatif sonuçlanan 5 hastanın da DM (diabetes mellitus), HT (hipertansiyon), KAH (koroner arter hastalığı), KOAH (kronik obstrüktif akciğer hastalığı), KKY (konjestif kalp yetmezliği) gibi hastalıklardan en az 2 tanesine sahip olduğu, aralarından 2 tanesinin hematolojik malignite olarak multiple myelom tanısına sahip immünsüprese hasta olduğu görüldü. Kesin COVID-19 pnömonisi grubundan sadece 1 tanesinin antikor düzeyi negatif olarak sonuçlanmış olup bu hastanın Non-Hodgkin Lenfoma tanılı hasta olduğu, aktif kemoterapi alması nedeniyle immünsüprese olduğu tespit edildi.

Çalışmanın sonuçları incelendiğinde SARS-CoV-2 antikor saptanamayan hastalarda yanlış negatiflik sebepleri düşük antikor konsantrasyonu, IgM düzeylerinin düşmeye başlaması ve dolayısıyla Total (IgM+IgG) antikorda saptanamaması, ileri yaşta ve immünsüprese hastalar olmaları ve antikor oluşturma oranlarının azalması olarak söylenebilir.

Çalışmamızın bazı kısıtlılıkları mevcuttur. Bunların ilki çalışmanın retrospektif olması nedeniyle literatürdeki bazı çalışmalar gibi hastalığın başlangıcı ile ilerleyen günler arasındaki antikor düzey

farklarının, pik, plato ve düşüş günlerinin tespit edilememiş olmasıdır (21). Fakat çalışmanın amacının geçirilmiş COVID enfeksiyonunu göstermek ve diğer tanı yöntemleri ile korelasyonunu ortaya koymak olması nedeniyle antikor düzeylerinin ayrıntılı analizine ihtiyaç olmadığı düşünülmüştür.

Ayrıca SARS-CoV-2 virüsünün yapısındaki bazı proteinler SARS-CoV, MERS-CoV gibi diğer coronavirüs çeşitleriyle benzer yapıda olup ELISA yöntemi ile antikor düzeyleri bakılırken çapraz reaksiyona sebep olabileceği kanıtlanmıştır (22). Çalışmaya dahil edilen hastalara COVID RT-PCR bakılırken diğer solunum yolu coronavirüslerine yönelik tarama yapılmadığı için çalışmamızdaki olası yanlış pozitiflik oranları tespit edilememiştir. Bununla birlikte, pandemi döneminde toplumda COVID-19 enfeksiyon sıklığı oldukça yüksek seyrederken, RT-PCR pozitif bulunan hastaların diğer coronavirüslerden çok SARS-CoV-2 virüsü olma olasılığının yüksek olduğu da kabul edilmelidir.

Çalışmamızda bir diğer kısıtlayıcı faktör ise çalışmanın az sayıda hasta içermesi ve sadece hastanede yatış gerektiren hastaların dahil edilmesidir. Radyolojik olarak tipik COVID-19 pnömonisi olan hastalar dahil edildiği için hastaların tümü yatan hastalardan oluşmuştur.

Bu kısıtlılıkların yanında, çalışma yapılırken ülkemizde aşı uygulamalarının başlamamış olması nedeniyle antikor pozitifliklerinin geçirilmiş COVID-19 infeksiyonunu göstermek açısından daha değerli olduğu, aşı ile antikor sonuçlarının değişmemiş olması nedeniyle de bu üç tanı yöntemi karşılaştırmak açısından önemli olduğu düşünülmektedir.

Tanı yöntemlerinin birlikte kullanılmasının kesin tanı oranlarını artıracağı kesindir fakat yukarıda da ifade edildiği gibi antikor düzeyi değerlendirmenin erken dönemde hastalık tanısı açısından yararı kısıtlıdır. Bu dönemde radyoloji ve RT-PCR tetkiklerinin birlikte kullanılması tanı şansını artırmaktadır. Çalışmamızda RT-PCR negatif bulunan hastalarda radyolojik güvenirlik %72 olarak bulunmuştur. Radyoloji uyumlu bulunup antikor tespit edilmeyen hastaların da yaşlı ve immunsupresif bireyler olduğu dikkat çekmiştir. Bu nedenle, pandemi döneminde tipik COVID-19 pnömonisi radyoloji bulguları olan hastaların, RT-PCR negatif bulunsalar bile COVID-19 pnömonisi olarak kabul edilebilecekleri düşünülmektedir. Elbette, COVID-19 dışı viral pnömonilerin ve enfeksiyon dışı sebeplerin benzer radyolojik bulgulara sebep olabileceği unutulmamalıdır. Özellikle pandeminin şiddetinin azaldığı dönemlerde ve benzer radyolojik bulguları oluşturabilecek komorbid hastalığı olanlarda radyolojik bulgular daha dikkatle yorumlanmalıdır.

Sonuçlar

Sonuç olarak, pandemi döneminde tipik COVID-19 pnömonisi radyoloji bulguları olan hastaların, RT-PCR negatif bulunsalar bile COVID-19 pnömonisi olarak kabul edilebilecekleri düşünülmektedir. Pandemi döneminde radyolojik olarak COVID-19 pnömonisi düşünülen hastalarda geçirilmiş COVID-19 enfeksiyonu tanısı için COVID-19 antikor düzeyleri kullanılabilir. Bununla birlikte, yaşlı ve hematolojik malignite başta olmak üzere immunsupresyonu olan hastalarda yeterli antikor yanıtı oluşmayabileceği, bu nedenle geçirilmiş enfeksiyonu göstermenin güç olabileceği akılda tutulmalıdır.

Etik Kurul Onamı: Çalışma Kocaeli Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu tarafından 18 Haziran 2020 tarih ve 2020/177 sayılı karar ile onaylanmıştır.

Bilgilendirilmiş Onam: Katılımcılardan yazılı onam alınmıştır.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Yazar Katkıları: Fikir/konsept: İ.B., A.K., H.B.; Tasarım: S.A.B., E.A.K.; Süpervizyon: İ.B., S.D., H.B.; Materyal: H.U., E.A.K.; Veri toplama/işleme: G.Ö.K., H.U., S.A.B.; Analiz/yorumlama: H.U., S.D., A.K.;

Literatür tarama: G.Ö.K., İ.B., A.K.; Taslak oluşturma/makale yazımı: İ.B., G.Ö.K.; Eleştirel inceleme: G.Ö.K, S.A.B., E.A.K., A.K., H.U., S.D., H.B., İ.B. Yazarlar bu yazının tüm içeriğinin sorumluluğunu kabul etmiş ve yayınlanmak için gönderilmesini onaylamıştır.

Kaynakça

1. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody Responses to SARS-CoV-2 in Patients With Novel Coronavirus Disease 2019. Clin Infect Dis. 19 Kasım 2020;71(16):2027-34.
2. WHO Coronavirus (COVID-19) Dashboard [Internet]. [cited 22 November 2022]. Available from: https://covid19.who.int
3. El Homsi M, Chung M, Bernheim A, Jacobi A, King MJ, Lewis S, et al. Review of chest CT manifestations of COVID-19 infection. Eur J Radiol Open. 2020; 7:100239.
4. Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China. J Med Virol. 2020;92(9):1525-32.
5. Guan W jie, Ni Z yi, Hu Y, Liang W hua, Ou C quan, He J xing, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
6. Helmy YA, Fawzy M, Elaswad A, Sobieh A, Kenney SP, Shehata AA. The COVID-19 Pandemic: A Comprehensive Review of Taxonomy, Genetics, Epidemiology, Diagnosis, Treatment, and Control. J Clin Med. 2020;9(4):1225.
7. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. 2020;296(2):E32-E40.
8. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. 2020;295(1):202-7.
9. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. Eur Radiol. 2020;30(6):3306-9.
10. Kim H. Outbreak of novel coronavirus (COVID-19): What is the role of radiologists? Eur Radiol. 2020;30(6):3266-7.
11. Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A Novel Coronavirus Emerging in China — Key Questions for Impact Assessment. N Engl J Med. 2020;382(8):692-4.
12. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. J Med Virol. 2020;92(9):1518-24.
13. Imai K, Tabata S, Ikeda M, Noguchi S, Kitagawa Y, Matuoka M, et al. Clinical evaluation of an immunochromatographic IgM/IgG antibody assay and chest computed tomography for the diagnosis of COVID-19. J Clin Virol. 2020; 128:104393.
14. Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, et al. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. Radiology. 2020;296(1):172-80.
15. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020;382(12):1177-9.
16. Wang M, Wu Q, Xu W, Qiao B, Wang J, Zheng H, et al. Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan [Internet]. Infectious Diseases (except HIV/AIDS); [cited 29 November 2022]. Avaliable from: http://medrxiv.org/lookup/doi/10.1101/2020.02.12.20022327
17. Patel R, Babady E, Theel ES, Storch GA, Pinsky BA, St. George K, et al. Report from the American Society for Microbiology COVID-19 International Summit, 23 March 2020: Value of Diagnostic Testing for SARS–CoV-2/COVID-19. mBio. 2020;11(2):e00722-20.
18. Li G, Chen X, Xu A. Profile of Specific Antibodies to the SARS-Associated Coronavirus. N Engl J Med. 2003;349(5):508-9.
19. Chen M, Qin R, Jiang M, Yang Z, Wen W, Li J. Clinical applications of detecting IgG, IgM or IgA antibody for the diagnosis of COVID-19: A meta-analysis and systematic review. Int J Infect Dis. 2021; 104:415-22.

20. Zhong L, Chuan J, Gong B, Shuai P, Zhou Y, Zhang Y, et al. Detection of serum IgM and IgG for COVID-19 diagnosis. Sci China Life Sci. 2020;63(5):777-80.
21. Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020;26(6):845-8.
22. Okba NMA, Müller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, et al. Severe Acute Respiratory Syndrome Coronavirus 2−Specific Antibody Responses in Coronavirus Disease Patients. Emerg Infect Dis. 2020;26(7):1478-88.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):114-121, doi:10.47493/abantmedj.1284334

Demographic Analysis of Pediatric Patients Presenting to the Emergency Department with Head Trauma

Acil Servise Kafa Travmasi ile Başvuran Pediatrik Hastalarin Demografik Analizi

Faruk DANIŞ [1*], Ayşegül DANIŞ [2]

[1] Izzet Baysal Training and Research Hospital, Emergency Department, Bolu, Türkiye

[2] Izzet Baysal Training and Research Hospital, Pediatric Neurology Department, Bolu, Türkiye

Geliş Tarihi (*Received*): 16.04.2023 **Kabul Tarihi (*Accepted*):** 24.05.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Abstract

Objective: In this study, it was aimed to analyze the demographic characteristics, mortality rates, hospitalization rates, and causes of trauma in pediatric patients admitted to the emergency department with head trauma.

Materials and Methods: Pediatric patients admitted to a university hospital emergency department (tertiary emergency service) between 01.01.2015 and 31.12.2020 due to head trauma were included in this study. Demographic data of the patients, computed tomography reports of the heads, inpatient to departments or intensive care units, discharge status, Glasgow Coma Scores, and Glasgow Outcome Scores were evaluated retrospectively and statistically analyzed.

Results: 691 patients were included in the study. The median age of the patients was 7.7 years (IQR: 4.2-13.1). It was observed that the most common age range for head trauma was 10-14 years (early adolescence). The most common cause of head trauma was falling (n=501, 72.5%). According to GCS, the most common cause of severe trauma was traffic accidents (n=8, 72.7%).

Conclusion: In our study; Contrary to the literature, it has been determined that head trauma occurs most frequently in the 10-14 age group. In our study, we found that the most common cause of head trauma was falling, but the most common cause of death was traffic accidents.

Keywords: Craniocerebral Trauma, Emergency Service, Intracranial Hemorrhages, Trauma Centers, Pediatric Emergency Medicine

&

Öz

Amaç: Bu çalışmadan acil servise kafa travması nedeniyle başvuran pediatrik hastaların demografik özelliklerinin analizi, mortalite oranları, hastaneye yatış oranları ve travma nedenlerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu çalışmaya, 01.01.2015-31.12.2020 tarihleri arasında bir üniversite hastanesi acil servisine (üçüncü basamak acil servis) kafa travması nedeniyle başvuran pediatrik hastalar alındı. Hastaların demografik verileri, bilgisayarlı beyin tomografisi raporları, yattığı servis ya da yoğun bakımlar, taburculuk durumları, Glaskow Koma Skor'ları, Glaskow Sonuç Skor'ları geriye dönük değerlendirildi ve istatistiksel olarak analiz edildi.

Bulgular: Çalışmaya 691 hasta dahil edildi. Hastaların yaş ortancası 7,7 yıldı (IQR: 4,2-13,1). Kafa travmasının en sık görüldüğü yaş aralığının 10-14 yaş (erken adolesan) olduğu görüldü. Kafa travmasına en sık neden olan durumun düşme olduğu görüldü (n=501, %72,5). GKS'ye göre ağır travmaya en sık sebep olan nedenin trafik kazaları olduğu görüldü (n=8, %72,7).

Sonuç: Bizim çalışmamızda; literatürden farklı olarak kafa travmasının en sık 10-14 yaş grubunda meydana geldiği tespit edilmiştir. Çalışmamızda kafa travmasının en sık nedeninin düşme olduğunu fakat en sık ölüm nedeninin trafik kazaları olduğunu tespit ettik.

Anahtar Kelimeler: Kafa Travması, Acil Servis, Kafa İçi Kanama, Travma Merkezi, Pediatrik Acil Tıp

Atıf/Cite as: Danış F. , Danış A. Demographic Analysis of Pediatric Patients Presenting To the Emergency Department with Head Trauma. Abant Med J. 2023; 12(2): 4-5. doi:10.47493/abantmedj.1284334

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Faruk Danış, **e-mail**: farukdanis@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

Head traumas in the pediatric age group constitute an important part of admissions to emergency services. In the United States, approximately 600.000 patients aged 18 and under apply to emergency services each year. Approximately 60000 of these patients are hospitalized and 7400 children are lost because of this (1-3). According to the results of a recent study in England; between 2000 and 2011, there was a 10% increase in the number of patients with head trauma admitted to emergency services, but the number of patients who underwent surgery and had a traumatic brain injury (TBI) remained stable (4). It is thought that the number of patients admitted to the emergency services due to head trauma in the childhood age group is high in our country, causing serious mortality and morbidity. In a study conducted in Turkey in 2010, it was determined that most of the head traumas in childhood are simple traumas and the most common etiological factors are falling and traffic accidents (5).

Minor head injuries are common in childhood and do not require any medical or surgical treatment. However, head trauma in infancy and childhood is the single most common cause of death and permanent disability. Measurable deficits occur even after mild to moderate head injury but are significantly greater after a serious injury. It includes cognitive and motor disorders, impaired attention, and psychiatric disorders.

Early recognition and proper management of patients with severe head trauma by physicians are extremely important in terms of reducing morbidity and mortality. Most of the patients who are admitted to the emergency department have minor head traumas (MHT) that do not cause obvious clinical symptoms and signs. In contrast, a small proportion of many patients with MHT have intracranial pathology that requires surgical intervention. For this reason, the approach to head trauma for physicians working in the emergency department can be quite complex and sometimes challenging (6). For this reason, for patients who applied to the emergency department; the mechanism of the trauma should be evaluated in terms of clinical findings and intracranial pathologies to occur, whether patients need surgical treatment should be determined early and complications should be determined quickly. Detection of intracranial damage as soon as possible in patients with head trauma depends on the good determination of risk factors that may cause intracranial damage. In patients with intracranial damage, not being able to make a diagnosis immediately may cause problems, and also multiple laboratory and imaging studies may delay the diagnosis of other life-threatening organ injuries, causing time loss and unnecessary expenses (7).

Emergency departments are where the first evaluation of traumatized children is performed. For this reason, it is important that standard trauma protocols are accepted and that the emergency team evaluates the traumatized child with these protocols. The lack of knowledge of the anatomical and physiological differences between pediatric patients and adults and the lack of clinical experience in emergency management are the two main problems in the approach to pediatric head trauma patients' management. These existing problems may cause permanent disability and death due to inadequate diagnosis and treatment. So, it is important that standard trauma protocols are accepted and that the emergency team evaluates the traumatized child with these protocols. Determining the demographic characteristics of the patients who applied to the emergency service is an important step in creating these protocols.

The primary outcome of the related study is to determine the demographic characteristics and mortality rates of pediatric patients brought to a university hospital emergency department due to head trauma. The secondary outcome is to reveal the computed tomography results, hospitalization rates (intensive care and service admission), operation rates, and Glasgow Outcome Scores of the patients included in the present study.

Materials and Methods

Study Design

The present study was carried out with the permission of Bolu Abant İzzet Baysal University Faculty of Medicine Ethics Committee (Date:22/03/2022-Decision No:2022/75). The study was realized within the framework of the Helsinki Declaration principles and ethical rules.

Selection of the Participants

All patients with head trauma under the age of 18 who applied to İzzet Baysal Training and Research Hospital Emergency Department between 01.01.2016 - 31.12.2020 and were treated as outpatients or inpatients were included in the study. The cases were grouped as 0-2 years (infancy), 3-5 years (game child), 6-9 years (school child), 10-14 years (early adolescence), and 14-18 years (late adolescent).

Measurements and Outcomes

Demographic data, computed tomography of head (CTH) results, and clinical outcomes of the patients were evaluated retrospectively. Patients whose file data cannot be reached will be excluded from the study. Demographic information of the patients, comorbidities, if any, admission Glasgow Coma Scale (GCS), neurological examination results, mechanism of trauma, other system injuries, radiological imaging results, surgical interventions if performed, hospitalization, and outcomes of patients treated were collected.

Regarding the severity of the head trauma, the patients were classified as a mild head injury is defined as GCS score of 13-15, moderate head injury as GCS 9-12, and severe head injury as GCS 8 or less (8).

The Glasgow Outcome Score (GOS) is an outcome scale that classifies patients with brain injury according to the objective degree of recovery (9).

GOS;

1. Death: Severe injury or death without recovery of consciousness
2. Persistent vegetative state: Severe damage with a prolonged state of unresponsiveness and a lack of higher mental functions
3. Severe disability: Severe injury with permanent need for help with daily living
4. Moderate disability: No need for assistance in everyday life, employment is possible but may require special equipment.
5. Low disability: Light damage with minor neurological and psychological deficits.

Statistical Analysis

SPSS version 25.0 (SPSS Inc., Chicago, Illinois, USA) package program was used for data analysis in the present study. Descriptive data on the sociodemographic and clinical information of the patients are given as n and % or median, interquartile range (IQR) tables. The Kolmogorov-Smirnov test was performed to see if it was normally distributed. Frequency distributions and crosstabs were used as analysis methods. Later, these tables were converted to graphics in the same package program.

Results

A total of 782 patients were admitted to the emergency clinic during the study. 91 of these patients were excluded from the study due to incomplete data. As a result, 691 patients were included in the statistical analysis. Of the patients, 264 (38.2%) were female and 427 (61.8%) were male. The median age of the patients was 7.7 years (IQR: 4.2-13.1). Considering the age distribution of the patients included in the study; The most common age group for trauma was early adolescence with 203 patients (29.4%). The distribution of cases according to age groups is shown in Figure 1.

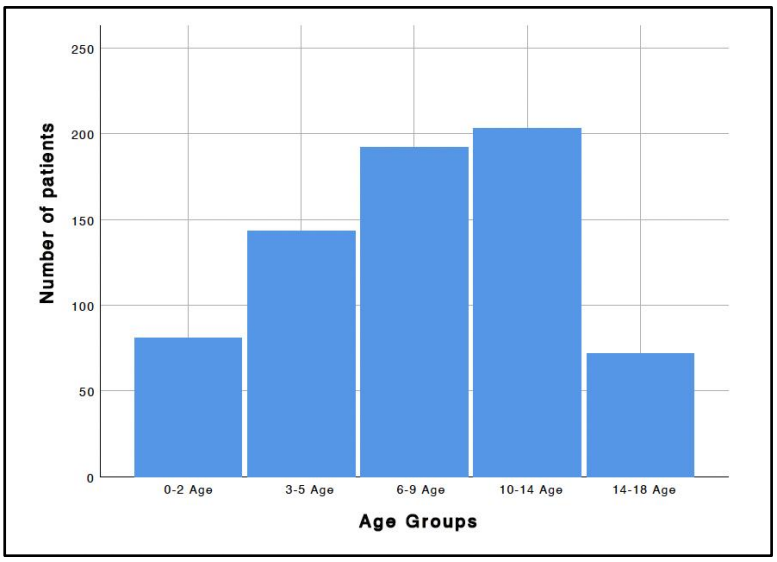


Figure 1. Distribution of the Number of Patients by Age Groups

When the CTH results of 691 patients included in the study were examined; It was determined that 367 (53.1%) patients underwent tomography. No traumatic findings were found in 635 (91.6%) of the patients who underwent CTH. Among the 56 (8.4%) patients who underwent CTH and found traumatic findings; Fractures were observed in 42 (6.1%) patients, intracranial hemorrhage in 29 (4.2%) patients, and contusion in 12 (1.7%) patients. The distribution of age groups according to the causes of trauma is shown in Table 1. The distribution of trauma causes according to GCS is shown in Table 2.

Table 1

Distribution of Age Groups by Causes of Trauma

	Trauma Mechanism				
Age Groups	**Fall n=501**	**Battered n=48**	**Penetrating Injury n=2**	**Traffic Accident n=97**	**Others n=43**
0-2 Age	74 (14.8 %)	0	0	1 (1.2%)	6 (7.4%)
3-5 Age	104 (20.8%)	2 (1.4%)	0	27 (18.9%)	10 (7%)
6-9 Age	155 (80.7%)	5 (2.6%)	0	18 (9.4%)	14 (7.3%)
10-14 Age	117 (57.6%)	32 (15.8%)	2 (1%)	43 (21.2%)	9 (4.4%)
14-18 Age	51 (70.8%)	9 (12.5%)	0	8 (11.1%)	4 (5.6%)

Table 2

Distribution of Trauma Causes by GCS

GCS	Trauma Mechanism					
	Fall	**Battered**	**Penetrating Injury**	**Traffic Accident**	**Others**	**Total**
Severe	2 (18.2%)	0	0	8 (72.7%)	1 (9.1%)	11 (100%)
Moderate	0	0	0	1 (100%)	0	1 (100%)
Mild	499 (73.5%)	48 (7.1%)	2 (0.3%)	88 (13%)	42 (6.2%)	679 (100%)
Total	501 (72.5%)	48 (6.9%)	2 (0.3%)	97 (14%)	43 (6.2%)	691 (100%)

It was determined that 62 (9%) of the patients were hospitalized in departments, 69 (10%) were hospitalized in intensive care units, 1 (0.1%) died in the emergency department, and 559 (80.9%) patients were discharged from the emergency department.

Looking at the Glasgow Outcome Score of patients with brain damage, it was determined that 6 patients got 1 point, 1 patient got 2 points, 5 patients got 3 points, 5 patients got 4 points, and 39 patients got 5 points. The distribution of Trauma Causes according to Glasgow Outcome Score is summarized in Table 3.

Table 3

Distribution of Trauma Causes by Glasgow Outcome Score.

Trauma Mechanism	Glaskow Outcome Scale					
	1	**2**	**3**	**4**	**5**	**Total**
Fall	2 (4.7%)	0	0	5 (11.6%)	36 (83.7%)	43 (100%)
Traffic Accidents	4 (44.4%)	1 (11.1%)	4 (44.4%)	0	0	9 (100%)
Others	0	0	1 25%	0	3 (75.0%)	4 (100%)
Total	6 (10.7%)	1 (1.8%)	5 (8.9%)	5 (8.9%)	39 (69.6%)	56 (100%)

It was determined that 1 of the 6 patients who died in total died in the emergency department and 5 of them died in the intensive care units. When the causes of mortality were examined, it was determined that 2 patients died due to falling and 4 patients died due to traffic accidents.

When the 6 patients who died were examined according to age groups, it was determined that 2 patients were between the ages of 0-2, 1 patient was between the ages of 3-5, 1 patient was between the ages of 6-9, and 2 patients were between the ages of 10-14.

Discussion

Head trauma is one of the most common socio-economic problems with its forensic and medical aspects (8). Despite efforts to reduce its incidence, it remains a major problem in pediatric patients. It is the most common childhood injury, resulting in more than 500.000 emergency room visits, 95.000 hospitalizations, and annual costs of $1 billion. It ranks third among the causes of mortality and morbidity in children (10). Mild head trauma, which is very common in childhood, is defined as a head injury that does not cause intracranial injury, has a GCS score of 14-15, and does not leave sequelae in the long term. Among the causes of head trauma, the first place is accidental falls, followed by traffic accidents and sports injuries.

In many studies, when children with head trauma are separated according to age groups, it has been seen that the group with the highest number of patients is children under 5 years old (11). However, in the present study, the highest number of patients were between the ages of 10-14. We think that this difference with the literature is because our hospital is a university hospital in the province, and mild cases mostly apply to the state hospital in the city center. In other studies, as in ours, there was a male gender predominance in all age groups (11, 12). Penetrating trauma was rare in each age group, both of the two patients were in the 10-14 age group.

Today, brain computed tomography (CT) is used as the main imaging method for the rapid detection of children with clinically severe TBI, especially those who need surgery, among the large number of patients admitted to the emergency department. However, it is noteworthy that there has been a significant increase in the number of patients undergoing brain CT imaging in recent years. Although many abnormal findings detected in brain CT do not appear to be an abnormality requiring urgent surgical intervention, the increase in the frequency of CT use continues. However, CT, which is known to increase the risk of cancer due to ionizing radiation, should be used with caution, especially in children. Although the risk of developing lethal cancer from CT in children decreases with age, its frequency varies between 1:1000 and 1:5000 (13). In the last decade, some studies are reporting clinical scores and clinical decision-making rules that help to determine the effective use of CBT in children with mild head trauma (14). Osmond et al. reported that of 3.866 children with mild head trauma, 52.8% had CCT, 4.1% had brain damage, and 0.6% had surgical intervention (15). For this reason, efforts are being made to reduce the frequency of CT use and, on the other hand, to establish guidelines for detecting TBI in the most accurate and precise way.

There is little research in the field of traumatic brain injury, particularly in the pediatric population. Because there are many differences between the brains of adults and the brains of children, the results obtained in studies on adult patients cannot be generalized to the pediatric population. Therefore, it is of great importance to conduct more specific studies from various aspects to obtain evidence-based guidelines for the diagnosis and treatment of pediatric head trauma.

Conclusions

Parent-oriented strategies and product and environmental regulations are the most effective methods for preventing childhood injuries. Changes to the child's environment, such as stair gates, window guards, smoke alarms, car seats, child protection covers for medication packages, wall-mounted lockers, and a fenced pool, are the most important tools to prevent injuries and head injuries.

Ethics Committee Approval: The study was approved by the Non-Interventional Research Ethics Committee of Bolu Abant Izzet Baysal University ((Date:22/03/2022 -Decision No:2022/75)

Informed Consent: Written informed consent was obtained from all patients' parents or legal guardians of the children included.

Conflict of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Financial Disclosure: Authors declared no financial support.

Acknowledgement: We thank the staff of the Emergency, Radiology, Pediatrics, and Neurosurgery Clinics who contributed to the diagnosis and treatment processes of the patients involved in the related study.

Author Contributions: Idea/Concept: F.D., A.D.; Design: F.D., A.D.; Data Collection/Processing: F.D., A.D.; Analysis/Interpretation: F.D., A.D.; Literature Review: F.D., A.D.; Drafting/Writing: F.D., A.D.; Critical Review: F.D., A.D. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Langlois JA, Rutland-Brown W, Thomas KE. Traumatic brain injury in the United States; emergency department visits, hospitalizations, and deaths. CDC Stacks. 2006.
2. McCaig LF, Nawar EW. National Hospital Ambulatory Medical Care Survey: 2004 emergency department summary. Adv Data. 2006;(372):1-29.
3. McCaig L, Nghi L. National Hospital Ambulatory Medical Care Survey: 2000 Emergency Department Summary. Advance data. 2002; (327):1-27.
4. Marlow R, Mytton J, Maconochie IK, Taylor H, Lyttle MD. Trends in admission and death rates due to paediatric head injury in England, 2000–2011. Archives of disease in childhood. 2015;100(12):1136-40.
5. Tuna IC, Akpinar AA, Kozaci N. Demographic analysis of pediatric patients admitted to emergency departments with head trauma/Acil servise basvuran pediatrik kafa travmali olgularin demografik analizi. Eurasian Journal of Emergency Medicine. 2012;11(3):151.
6. Babl FE, Lyttle MD, Bressan S, Borland M, Phillips N, Kochar A, et al. A prospective observational study to assess the diagnostic accuracy of clinical decision rules for children presenting to emergency departments after head injuries (protocol): the Australasian Paediatric Head Injury Rules Study (APHIRST). BMC Pediatr. 2014;14:148.
7. Davis T, Ings A. Head injury: triage, assessment, investigation and early management of head injury in children, young people and adults (NICE guideline CG 176). Arch Dis Child Educ Pract Ed. 2015;100(2):97-100.
8. Tabatabaei S, Seddighi A. Pediatric head injury. Iranian Journal of Child Neurology. 2008;2(2):7-13.
9. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet. 1975;1(7905):480-4.
10. ŞAHİN S, DOĞAN Ş, AKSOY K. Çocukluk çağı kafa travmaları. Uludağ Üniversitesi Tıp Fakültesi Dergisi. 2002;28(2):45-51.
11. Fylli C, Schipper IB, Krijnen P. Pediatric Trauma in The Netherlands: Incidence, Mechanism of Injury and In-Hospital Mortality. World Journal of Surgery. 2023;47(5):1116-28.
12. Çıtak Tuna İ, Açıkalın Akpınar A, Kozacı N. Demographic Analysis of Pediatric Patients Admitted to Emergency Departments with Head Trauma. Journal of Academic Emergency Medicine/Akademik Acil Tip Olgu Sunumlari Dergisi. 2012;11(3).
13. Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric CT. American journal of roentgenology. 2001;176(2):289-96.
14. Maguire JL, Boutis K, Uleryk EM, Laupacis A, Parkin PC. Should a head-injured child receive a head CT scan? A systematic review of clinical prediction rules. Pediatrics. 2009;124(1):e145-e54.

15. Osmond MH, Klassen TP, Wells GA, Correll R, Jarvis A, Joubert G, et al. CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. Cmaj. 2010;182(4):341-8.

Araştırma Makalesi / Research Article

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):122-130, doi:10.47493/abantmedj.1313791

Claudin 18.2 Expression in Gastric Adenocarcinomas in a Large Turkish Cohort

Geniş Bir Türk Kohortundaki Gastrik Adenokarsinomlarda Claudin 18.2 Ekspresyonu

Aynur IŞIK [1*,2], Güneş GÜNER [3], Can ZEYNELOĞLU [4]
Seçil DEMİRKOL CANLI [5,7], Hakki TASTAN [6], Aytekin AKYOL [1,3,5,7]

[1] Hacettepe University Transgenic Animal Technologies Research and Application Center, Sıhhiye, Ankara, Türkiye
[2] PhD student, Department of Biology, Faculty of Science, Gazi University, Ankara, Türkiye
[3] Department of Pathology, Hacettepe University Faculty of Medicine, Sıhhiye, Ankara, Türkiye
[4] Hacettepe University, Faculty of Medicine, Sıhhiye, Ankara, Türkiye
[5] Molecular Pathology Application and Research Center, Hacettepe University, Sıhhiye, Ankara, Türkiye
[6] Department of Biology, Faculty of Science, Gazi University, Ankara, Türkiye
[7] Division of Tumor Pathology, Hacettepe University Cancer Institute, Sıhhiye, Ankara, Türkiye

Geliş Tarihi (*Received*): 13.06.2023 **Kabul Tarihi (*Accepted*):** 02.08.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Abstract

Objective: Claudin 18.2 (CLDN18.2) is a tight junction protein expressed especially in gastric adenocarcinomas. The prognostic and clinicopathologic implications of CLDN18.2 expression is currently unknown. Zolbetuximab monoclonal antibody against CLDN18.2 is under investigation as a potential treatment for advanced gastric cancer (GC). We aimed to investigate the impact of CLDN18.2 expression in GC on prognosis and tumor features in a large Turkish cohort.

Materials and Methods: Seven tissue microarrays (TMAs) containing 263 cases of GC were constructed. Assessment of CLDN18.2 expression was performed by immunohistochemistry. The expression of CLDN18.2 was scored based on staining intensity and the percentage of staining. Staining intensity was classified as: 0, no reactivity; 1, weak; 2, moderate; and 3, strong. Percentage of staining was classified as: (0-39%), negative; (40-100%), positive. Cases with a percentage of staining score of (40-100%) with moderate to strong staining intensity (2 or 3) were defined as positive and cases with a percentage of staining score of (0-39%) with no to weak staining intensity (0 or 1) were defined as negative.

Results: 14.3% (37/258) of GCs were stained with anti-CLDN18.2 antibody. While 7.8% (20/258) of all cases were positive, 92.2% (238/258) were scored as negative. There was no statistically significant difference between the two groups in terms of patient features such as age or sex, tumor grade, TNM stage, histologic subtype, or overall survival.

Conclusion: CLDN18.2 expression was not associated with patient prognosis in the Turkish cohort. However, as this molecule is a potential therapeutic target, information about the impact of CLDN18.2 expression will be important in managing patients, therefore more studies are needed to learn more on the outcomes of CLDN18.2 expression on clinicopathologic features in GC.

Keywords: Gastric Cancer, CLDN18.2, Biomarker

&

Öz

Amaç: Claudin 18.2 (CLDN18.2) özellikle gastrik adenokarsinomlarda (GC) eksprese edilen bir sıkı bağlantı proteinidir. CLDN18.2 ekspresyonunun prognostik ve klinikopatolojik etkileri halen bilinmemektedir. CLDN18.2'yi hedef alan Zolbetuximab monoklonal antikoru, ileri evre gastrik adenokarsinomlar için potansiyel bir tedavi olarak değerlendirilmektedir. Bu çalışmada, gastrik adenokarsinomlarda CLDN18.2 ekspresyonunun prognoz ve tümör özelliklerini geniş bir Türk kohortunda araştırmayı amaçladık.

Gereç ve Yöntemler: 263 GC vakası içeren yedi tane doku mikro dizini (TMA) hazırlanmıştır. CLDN18.2 ekspresyonu immünohistokimyal boyama yöntemi ile tespit edilmiştir. CLDN18.2 ekspresyonu, boyanma yoğunluğu ve boyanma yüzdesine göre puanlanmıştır. Boyanma yoğunluğu 0, reaktivite yok; 1, zayıf; 2, orta ve 3; güçlü. Boyanma yüzdesi şu şekilde sınıflandırılmıştır: (%0-39), negatif; (%40-100), pozitif. Boyanma yüzdesi (%40-100) olan ve orta ila güçlü boyanma yoğunluğuna (2 veya 3) sahip vakalar pozitif, boyanma yüzdesi (%0-39) olan ve hiç reaktivite olmayan veya zayıf boyanma yoğunluğuna (0 veya 1) sahip vakalar negatif olarak tanımlanmıştır.

Bulgular: GC'lerin %14,3'ü (37/258) anti-CLDN18.2 antikoru ile boyanmıştır. Tüm vakaların %7,8'i (20/258) pozitif, %92,2'si (238/258) negatif olarak değerlendirilmiştir. İki grup arasında yaş veya cinsiyet, tümör derecesi, TNM evresi, histolojik alt tip veya genel sağkalım gibi hasta özellikleri açısından istatistiksel olarak anlamlı bir fark bulunamamıştır.

Sonuç: CLDN18.2 ekspresyonu Türk kohortundaki GC'li vakalarda prognoz ile ilişkili değildir. Bununla birlikte CLDN18.2 potansiyel bir terapötik hedeftir ve CLDN18.2 ekspresyonu ile ilgili bilgiler hastalık yönetiminde önemli olacaktır. GC'lerde CLDN18.2 ekspresyonunun klinikopatolojik özellikler üzerindeki etkilerini anlamak için daha fazla çalışmaya ihtiyaç vardır.

Sonuç: CLDN18.2 ekspresyonu Türk kohortundaki GC'li vakalarda prognoz ile ilişkili değildir. Bununla birlikte CLDN18.2 potansiyel bir terapötik hedeftir ve CLDN18.2 ekspresyonu ile ilgili bilgiler hastalık yönetiminde önemli olacaktır. GC'lerde CLDN18.2 ekspresyonunun klinikopatolojik özellikler üzerindeki etkilerini anlamak için daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Gastrik Kanser, CLDN18.2, Biomarker

Atıf/Cite as: Işık A. , Güner G. , Zeyneloğlu C. , Demirkol Canlı S. , Tastan H. , Akyol A. Claudin 18.2 Expression in Gastric Adenocarcinomas in a Large Turkish Cohort. Abant Med J. 2023; 12(2): 5-6. doi:10.47493/abantmedj.1313791

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Aynur Işık, **e-mail**: aynur.isik14@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

Gastric Cancer (GC) is one of the most common types of cancer worldwide, with high incidence and mortality rates (1). For decades, the standard treatment option for GCs has been perioperative and adjuvant chemotherapy/chemoradiation therapies. However, the 5-year disease survival rates' dramatic decline beyond Stage II, ranging from 61–63% for Stage IIIa to 30% – 35% for Stage IIIc, has led to the investigation and development of targeted treatments for advanced GCs (2). One of the first examples for targeted therapy in advanced GC is the use of the anti-HER2 antibody trastuzumab in patients bearing tumors with HER2 overexpression or amplification, which has been instituted in guidelines based on the results of the ToGA trial (3). Other targeted treatments used in the management of advanced GC include ramucirumab, a monoclonal antibody that targets the vascular endothelial growth factor receptor-2 (VEGF-R2) (4) and nivolumab/ pembrolizumab, immune checkpoint inhibitors that have shown benefit in clinical trials (5, 6).

Claudins are a family of 27 transmembrane proteins that form the major structural and functional components of tight junctions. Some subtypes of claudins are expressed in a tissue-specific manner (7). CLDN18.2 is a member of the claudin family and is specifically expressed in the stomach. It has been shown to be expressed in various types of cancers including GC, lung cancer, pancreatic cancer, ovarian and esophageal cancer (8). Targeting CLDN18.2 with zolbetuximab is a promising approach for treating advanced GC. Zolbetuximab was shown to significantly improve overall survival when added to standard chemotherapy, as investigated in the FAST trial (NCT03504397) (9). The initial results obtained from the global phase 3 study SPOTLIGHT(NCT03504397) were in concordance with the FAST trial. Currently, there are numerous clinical trials evaluating the efficacy of Zolbetuximab in addition to standard chemotherapy/immunotherapy regimens in locally advanced and metastatic gastric/gastroesophageal junction cancers (NCT 03504397, NCT03653507, NCT03505320) and one clinical trial studying the efficacy of Zolbetuximab in metastatic pancreatic adenocarcinoma (NCT03816163).

GC is a heterogeneous disease that shows significant differences in molecular characteristics among ethnic populations (10). The aim of this study was to evaluate the expression of CLDN18.2 in a large Turkish population with GC, and to compare it with prognostic parameters.

Materials and Methods

Patients and Gastric Cancer Tissue Microarrays

All cases diagnosed with GC at the Department of Pathology of Hacettepe University Faculty of Medicine between 2014-2022 were screened. Cases that received radiotherapy, chemotherapy before surgery, or any form of neoadjuvant therapy were excluded. The HE sections of total or partial gastrectomy materials of the cases were re-examined by two pathologists (AA, GG) and confirmed to be adenocarcinomas. The regions that best represented the tumor were identified in the HE sections. Recipient blocks necessary to create tumor microarrays (TMA) were prepared using a three mm Recipient Block Mold Kit (Quick Mold). One single core of 3 mm diameter Formalin-Fixed Paraffin-Embedded (FFPE) tissue sample was transferred to the recipient block for each case. A total of 7 tissue microarrays were prepared for 263 GC cases. Sections of 3.5-4.0 μm thickness were taken from the TMA blocks. Tumor foci were checked in the HE-stained sections. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University (GO 21/603).

Immunohistochemistry

Immunohistochemistry was performed on 4-micron-thick unstained sections obtained from seven TMA blocks which were first deparaffinized in an incubator at 75°C for 40 minutes then deparaffinized with xylene and rehydrated through a series of graduated alcohols. Antigen retrieval was performed by heating the tissue sections in Citrate buffer (pH 6.0) in a microwave oven for 10 minutes. Endogenous peroxidase activity was blocked by incubating the sections in 3% hydrogen peroxide and methanol solution for 10

minutes. CLDN18.2 primary antibody (clone EPR19202, Abcam, Cambridge) was incubated at a dilution of 1:250 in antibody diluent for 1 hour at room temperature. After, the sections were incubated with a biotinylated secondary antibody and streptavidin-peroxidase (UltraVision Detection System Large Volume Anti-Polyvalent, HRP, Thermo Fisher Scientific) for 30 minutes each at room temperature. The signal was visualized with diaminobenzidine (DAB) chromogen, using hematoxylin as a counterstain. Normal gastric mucosa was used as a positive control.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 23.0 for Windows (IBM Corp. Released 2015, Armonk, NY: IBM Corp.). Pearson chi-square test was used to determine the association between CLDN18.2 protein expression and other variables such as gender, age, T stage, N stage and Lauren phenotype. Survival curves were generated using the Kaplan-Meier method to assess the relationship between CLDN18.2 expression and survival. The log-rank test was employed to evaluate the difference between the survival curves of the groups. p values <0.05 were considered statistically significant.

Results

CLDN18.2 expression in Gastric Cancer Samples

CLDN18.2 antibody was used to stain 3 mm core TMA samples, and all 263 samples except for 5 that had technical issues were used. Initially, CLDN18.2 staining intensity was categorized into four groups: 0, no reactivity in membrane or cytoplasm; 1+, weak reactivity in membrane or cytoplasm; 2+, moderate reactivity in membrane or cytoplasm; and 3+, strong reactivity in membrane or cytoplasm. 14.3% (37/258) of all cases showed staining with CLDN18.2. Then, the classification system was modified using the FAST criteria (≥40% staining intensity in tumor cells is considered positive); subsequently, samples were categorized into negative (0-1+) or positive (2+-3+) groups based on staining intensity. Of the total 258 samples, 92.2% (n=238) were negative for CLDN18.2 expression and 7.8% (n=20) were positive. (Figure 1).

The clinicopathologic features of the gastric cancer cases are summarized in Table 1.

Overall survival was defined as the time from the operation to the last follow up for censored patients, and as the time from the operation to death from any cause for deceased patients. 7 patients who died within a month after the operation were excluded from the survival analysis due to high likelihood of surgery-related mortality. The median survival of patients in the CLDN18.2 negative and CLDN18.2 positive group were 33.0 and 65.3 months, respectively. Although patients with positive CLDN18.2 expression had a longer median overall survival, the prognostic difference between these groups was not statistically significant (p=0.144) (Figure 2). In addition to these findings, we noted that CLDN18.2 expression was not significantly related to gender, age, T stage, N stage and Lauren phenotype (Chi square p values >0.05 for all) (Table 2).

Discussion

In this study we aimed to investigate the implication of CLDN18.2 expression on prognosis and tumor characteristics in patients with gastric cancer from a Turkish cohort in a retrospective manner. This large cohort was obtained from a large tertiary health care center, with patients from all around the country. This might, to an extent, increase the generalizability of our results. None of our patients had received any type of treatment before applying to our hospital, which reduces any sort of selection bias.

We did not note statistically significant differences between cases with and without CLDN18.2 expression in terms of patient characteristics, tumor grade, TNM stage, histologic subtype per Lauren classification and overall survival. However, when the Kaplan-Meier survival graphs of the two groups are compared, a tendency of patients with CLDN18.2 expression towards longer survival can be noticed (Figure 2). Yet,

as mentioned before this difference was not deemed statistically significant. The reason behind this seemingly erratic tendency is currently unknown.

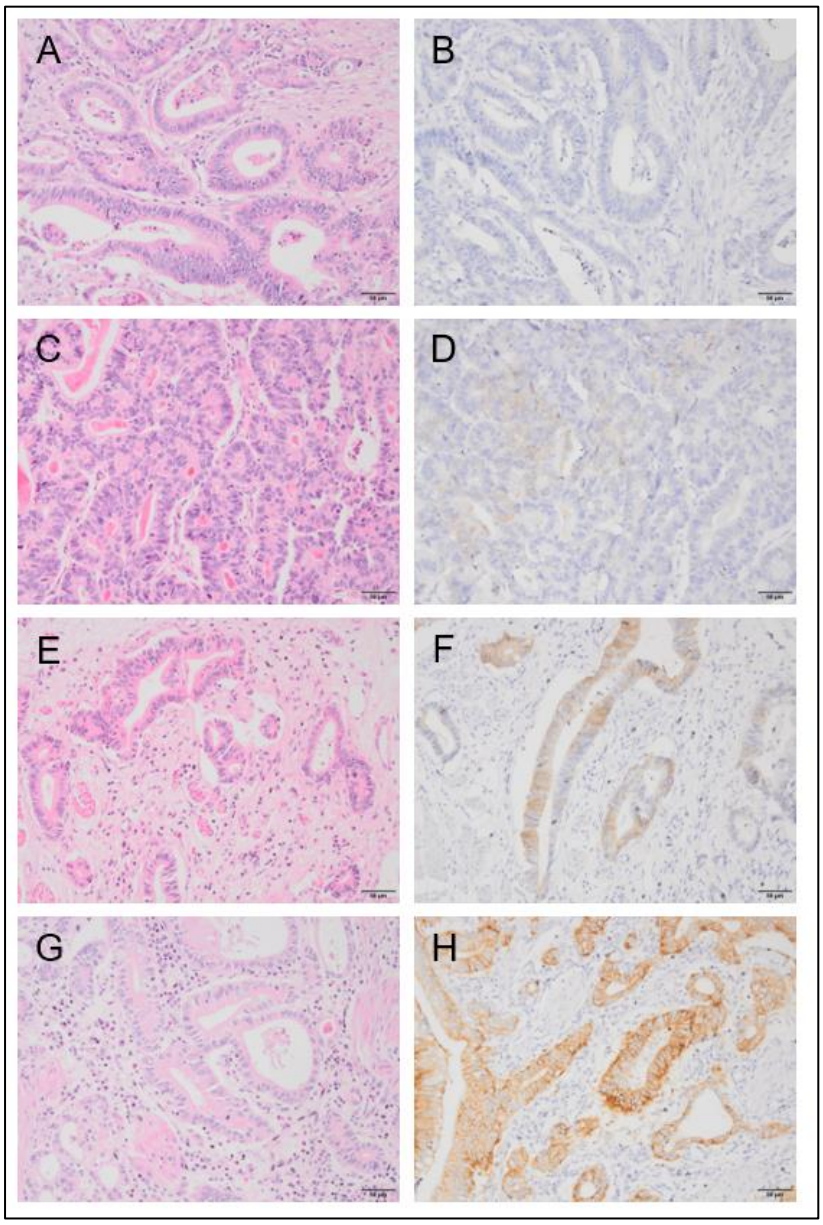


Figure 1. CLDN18.2 expression in gastric adenocarcinomas are demonstrated for negative (B), weak-focal (D), moderate (F) and strong (H) expression by immunohistochemistry (A, C, E, G; H&E staining images and B, D, F, H; CLDN18.2 immunohistochemistry of corresponding cases, respectively, scale bars: 50µm).

Previous studies conducted on the clinical implications of CLDN18.2 expression in GC have yielded conflicting results. The study conducted by Rohde et al. in 2019 found that CLDN18.2 was expressed in 87%, when the FAST criteria for positivity was applied this percentage dropped to 52%, of patients with GC in a Japanese cohort and CLDN18.2 expression was correlated with higher tumor grade and diffuse type GC per Lauren classification (10), Pelino et al. found that 45.1% of patients with advanced gastroesophageal cancers overexpressed CLDN18.2, in concordance with the FAST criteria. Although they found a correlation between lymph node metastasis, higher grade, peritoneal metastases and advanced stage, the overall survival between the two groups did not change (12). In another study, CLDN18.2

expression was higher in diffuse type GCs and HER-2 positive cancers, in a Korean cohort. However, they noted that the TNM stage and overall survival failed to differ according to CLDN18.2 expression (13).

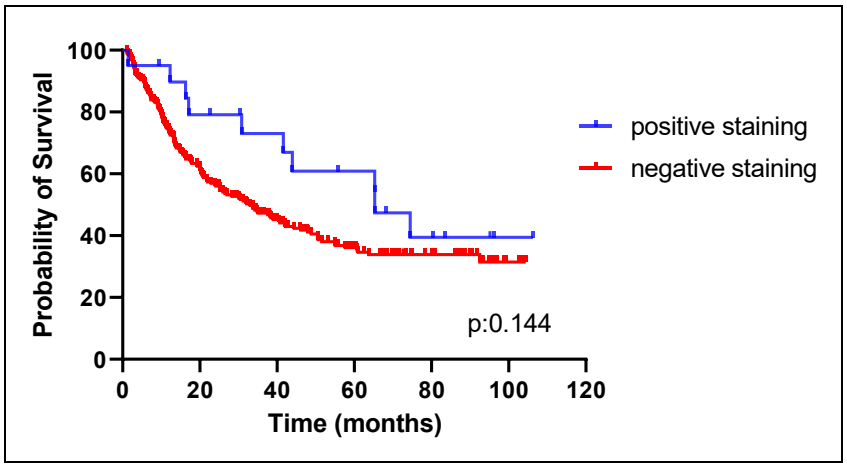


Figure 2. Kaplan-Meier curves depicting the postoperative survival of CLDN18.2 negative and positive gastric adenocarcinoma cases.

Table 1
Main Clinicopathological Characteristics of Patients with Gastric Adenocarcinoma Represented in Tissue Microarrays

Characteristics	**n (%)**
Age (years) [n=263], median (range)	62 (21-88)
Gender	
Female	97 (36.9)
Male	166 (63.1)
Histologic subtype	
Adenocarcinoma	123 (46.8)
Diffuse type carcinoma	62 (23.6)
Other/undetermined	78 (29.6)
Total	263
Size [mean (range)] (cm)*	6.4
*known for 255/263 cases (96.96%)	
Stage**	
**known for 262/263 cases (99.61%)	
I	1 (0.4)
II	26 (9.9)
III	56 (21.4)
IV	179 (68.3)
Status	
Alive	104 (39.5)
Deceased	159 (60.5)
CLDN18.2 immunostaining***	
***known for 258/263 cases (98.08%)	
Negative	221 (85.6)
Focal	17 (6.6)
Moderate	12 (4.7)
Strong	8 (3.1)

Table 2

Patient Characteristics and CLDN18.2 Expression

			CLDN18.2				
		Total	**Negative staining**	**Positive staining**	**% negative staining**	**% positive staining**	**p value**
Age	**≤60**	117	110	6	46.0	30.0	0.242
	>60	146	129	14	54.0	70.0	
Gender	**Male**	166	149	16	62.3	80.0	0.148
	Female	97	90	4	37.7	20.0	
T stage	**T1 or T2**	27	25	1	10.5	5.0	0.505
	T3 or T4	235	213	19	89.5	95.0	
N stage	**N0 or N1**	96	84	9	35.4	45.0	0.469
	N2 or N3	165	153	11	64.6	55.0	
Subtype	**Adenocarcinoma**	123	110	11	47.8	57.9	0.612
	Diffuse type carcinoma	62	56	3	24.3	15.8	
	Other/ undetermined	78	64	5	27.8	26.3	

Dottermusch et al., studied the clinicopathologic features of 481 GCs with and without CLDN18.2 expression in a Caucasian cohort. They showed that CLDN18.2 expression was not correlated with any clinical findings of patients, stage of tumor, Lauren phenotype or overall survival. Their results showed that when the FAST criterion for positivity was applied, the CLDN18.2 expression percentage failed to exceed 10%. Their studies also revealed a strongly positive correlation between EBV genome positivity and CLDN18.2 expression (14). A study done by Arnold et al. in 2020 also failed to show a correlation between tumor histologic subtype, tumor grade, stage or overall survival in a Caucasian cohort. After staining and analysis, 17.1% of gastric and esophageal adenocarcinomas showed overexpression of CLDN18.2, however there was no statistically significant correlation in clinical features of patients or overall survival with respect to CLDN18.2 expression (15). The works of Hong et al. in 2020, showed conflicting results with previous studies. They studied the characteristics of various tumor types with CLDN18.2 overexpression. Among 85 GC specimens, 12 showed CLDN18.2 expression, which approximates to 14%. Although they failed to show a difference in patient characteristics, EBV genome positivity, TNM stage, HER2 expression and overall survival between the two groups, they noticed that CLDN18.2 expression was higher in intestinal type of GCs when compared with diffuse type GCs per Lauren phenotype (16).

A meta-analysis done by Ungureanu et al. in 2021, which included only 6 studies due to the scarcity of studies, concluded that there was no correlation in histologic subtype, grade, TNM stage, HER2 expression between patients bearing tumors with or without CLDN18.2 expression. They also failed to find a difference between the overall survival rates of the two groups (17).

When the aforementioned studies are evaluated, the percentage of CLDN18.2 expression of GC differs considerably from one study to another. Though these conflicting results might seem counter-intuitive at first, there may be several reasons as to why they vary. The previous studies analyzed tumor samples from various different populations from distinct ethnic origins. The present study was done on a Turkish cohort,

which is largely of Caucasian origin, and yielded a CLDN18.2 overexpression percentage of 7.8%. Dottermusch et al. (14) also evaluated CLDN18.2 expression in GCs in a large Caucasian cohort, and their results were similar to ours, CLDN18.2 expression of 10% after applying the FAST eligibility criteria. However, when the works of Rohde et al. (10) and Baek et al. (13) are scrutinized, it is observed that the population they worked in is not of Caucasian but of Japanese and Korean origin, respectively. Although these two populations have different origins, they are closest to one another when compared with others (18). CLDN18.2 expression positivity in GCs from these two cohorts are much higher than in Caucasian cohorts; 52% for Rohde et al. and 29.4 % for Baek et al. The difference of CLDN18.2 expression might be explained by the varying genetic polymorphisms among populations.

Nonetheless, different ethnic origins do not suffice to explain the discrepancy among the results of the studies, since Pelino et al. also investigated a large Caucasian cohort and yielded a CLDN18.2 expression percentage of 45.1%. This might be attributed to the different antibodies used in the studies. As mentioned in the meta-analysis done by Unugaru et al., there are two major antibody kits used in the mentioned studies: The CLAUDETECT 18.2, which is not specific for claudin 18.2 but rather recognizes the C-terminal end of claudin 18, and the Anti-CLDN EPR19202 (Abcam, Cambridge), which is specific for 100 amino acids of the human claudin 18.2 isoform. Rohde et al. and Pelino et al. used the former whereas Dottermusch et al, Baek et al. and the current study used the latter, which might help to explain the higher CLDN18.2 expression positivity in the works of Rohde et al and Pelino et al.

A recent study done by Kayıkcıoglu et al. in a small Turkish cohort yielded a CLDN18.2 positivity of 73.8% (48/65). Although they also failed to show a correlation between clinicopathologic features of patients and CLDN18.2 expression, CLDN 18.2 expression was much higher than our study. Reason as to why, might be that the study only evaluated samples from patients with metastatic gastric adenocarcinomas excluding locally advanced gastric and gastroesophageal adenocarcinomas (19).

Claudins make up a crucial part of tight junctions which promote cell-cell adhesion. Loss of cell-cell adhesions have been well known to be an important part of the epithelial-mesenchymal transition which ultimately leads to invasion and metastasis. Matsuda et al. have validated this process in which they showed decreased expression of claudins in the invasive front of GCs when compared to the non-invasive front (20). This heterogenous expression of claudins may result in varying CLDN18.2 expression in samples taken from different parts of the tumor, even in the same patient, leading to discrepant results between studies.

Conclusions

As of now there is no consensus on the prognostic or clinicopathologic implications of CLDN18.2 expression in patients with GC. With the introduction of Zolbetuximab, a monoclonal antibody against CLDN18.2, as a therapeutic option for advanced GC, CLDN18.2 expression analysis may gain importance in clinical practice. As the data grows and more studies are conducted in different and larger cohorts, we might reveal the true face of CLDN18.2, when it comes to the prognosis of GC patients.

Ethics Committee Approval: The study was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University (GO 21/603).

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Acknowledgments: The authors received no specific grant for the research, authorship or publication of this article.

Author Contributions: Idea/Concept: A.A., A.I.; Design: A.A.; Supervision: A.A., H.T.; Materials: A.A.; Data Collection/Processing: A.I., G.G., C.Z., S.D.C.; Analysis/Interpretation: A.I., G.G., C.Z., S.D.C., H.T., A.A.; Literature Review: A.I., C.Z., A.A.; Drafting/Writing: A.I., C.Z., A.A.; Critical Review: A.I., G.G., C.Z., S.D.C., H.T., A.A. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Collaborators GBDSC. The global, regional, and national burden of stomach cancer in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease study 2017. Lancet Gastroenterol Hepatol. 2020;5(1):42-54.
2. Li K, Zhang A, Li X, Zhang H, Zhao L. Advances in clinical immunotherapy for gastric cancer. Biochim Biophys Acta Rev Cancer. 2021 Dec;1876(2):188615.
3. Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki A, et al.; ToGA Trial Investigators. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010;376(9742):687-97.
4. Javle M, Smyth EC, Chau I. Ramucirumab: successfully targeting angiogenesis in gastric cancer. Clin Cancer Res. 2014;20(23):5875-81.
5. Kang YK, Boku N, Satoh T, Ryu MH, Chao Y, Kato K, et al. Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2017;390(10111):2461-71.
6. Shitara K, Kawazoe A, Hirakawa A, Nakanishi Y, Furuki S, Fukuda M, et al. Phase 1 trial of zolbetuximab in Japanese patients with CLDN18.2+ gastric or gastroesophageal junction adenocarcinoma. Cancer Sci. 2023 Apr;114(4):1606-15.
7. Kyuno D, Takasawa A, Takasawa K, Ono Y, Aoyama T, Magara K, et al. Claudin-18.2 as a therapeutic target in cancers: cumulative findings from basic research and clinical trials. Tissue Barriers. 2022;10(1):1967080.
8. Tureci O, Koslowski M, Helftenbein G, Castle J, Rohde C, Dhaene K, et al. Claudin-18 gene structure, regulation, and expression is evolutionary conserved in mammals. Gene. 2011;481(2):83-92.
9. Sahin U, Tureci O, Manikhas G, Lordick F, Rusyn A, Vynnychenko I, et al. FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma. Ann Oncol. 2021;32(5):609-19.
10. Rohde C, Yamaguchi R, Mukhina S, Sahin U, Itoh K, Tureci O. Comparison of Claudin 18.2 expression in primary tumors and lymph node metastases in Japanese patients with gastric adenocarcinoma. Jpn J Clin Oncol. 2019;49(9):870-6.
11. Xu B, Liu F, Liu Q, Shi T, Wang Z, Wu N, et al. Highly expressed Claudin18.2 as a potential therapeutic target in advanced gastric signet-ring cell carcinoma (SRCC). J Gastrointest Oncol. 2020;11(6):1431-9.
12. Pellino A, Brignola S, Riello E, Niero M, Murgioni S, Guido M, et al. Association of CLDN18 Protein Expression with Clinicopathological Features and Prognosis in Advanced Gastric and Gastroesophageal Junction Adenocarcinomas. J Pers Med. 2021; 11(11):1095.
13. Baek JH, Park DJ, Kim GY, Cheon J, Kang BW, Cha HJ, et al. Clinical Implications of Claudin18.2 Expression in Patients with Gastric Cancer. Anticancer Res. 2019 Dec;39(12):6973-9.
14. Dottermusch M, Kruger S, Behrens HM, Halske C, Rocken C. Expression of the potential therapeutic target claudin-18.2 is frequently decreased in gastric cancer: results from a large Caucasian cohort study. Virchows Arch. 2019;475(5):563-71.
15. Arnold A, Daum S, von Winterfeld M, Berg E, Hummel M, Rau B, et al. Prognostic impact of Claudin 18.2 in gastric and esophageal adenocarcinomas. Clin Transl Oncol. 2020;22(12):2357-63.

16. Hong JY, An JY, Lee J, Park SH, Park JO, Park YS, et al. Claudin 18.2 expression in various tumor types and its role as a potential target in advanced gastric cancer. Transl Cancer Res. 2020;9(5):3367-74.
17. Ungureanu BS, Lungulescu CV, Pirici D, Turcu-Stiolica A, Gheonea DI, Sacerdotianu VM, et al. Clinicopathologic Relevance of Claudin 18.2 Expression in Gastric Cancer: A Meta-Analysis. Front Oncol. 2021;11:643872.
18. Wang CC, Yeh HY, Popov AN, Zhang HQ, Matsumura H, Sirak K, et al. Genomic insights into the formation of human populations in East Asia. Nature. 2021;591(7850):413-9.
19. Kayikcioglu E, Yuceer RO, Cetin B, Yuceer K, Karahan N. Prognostic value of claudin 18.2 expression in gastric adenocarcinoma. World J Gastrointest Oncol. 2023;15(2):343-51.
20. Matsuda Y, Semba S, Ueda J, Fuku T, Hasuo T, Chiba H, et al. Gastric and intestinal claudin expression at the invasive front of gastric carcinoma. Cancer Sci. 2007;98(7):1014-9.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):131-139, doi:10.47493/abantmedj.1341855

The Role of Uric Acid to HDL Cholesterol Ratio in Predicting Myocardial Ischemia in Myocardial Perfusion Scintigraphy in Diabetic Patients

Diyabetli Hastalarda Miyokard Perfüzyon Sintigrafisinde Miyokard İskemisini Öngörmede Ürik Asit-HDL Kolesterol Oranının Rolü

Hamdi AFŞİN [1*]

[1] Department of Nuclear Medicine, Abant Izzet Baysal University Hospital, Bolu, Türkiye

Geliş Tarihi (*Received*): 12.08.2023 **Kabul Tarihi (*Accepted*):** 23.08.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Abstract

Objective: Diabetes Mellitus (DM) is a significant risk factor for cardiovascular diseases, particularly myocardial ischemia. Both diabetes mellitus type 2 and cardiovascular conditions are characterized by a high burden of inflammation. The uric Acid to High-Density Lipoprotein cholesterol ratio (UHR) has been suggested as a novel marker of metabolic and inflammatory diseases. Hence, this study investigated the predictive role of the Uric Acid to High-Density Lipoprotein cholesterol ratio (UHR) in myocardial ischemia detected by Myocardial Perfusion Scintigraphy (MPS) in diabetic patients.

Materials and Methods: This study included patients who underwent MPS between January 2022 and March 2023 at the Nuclear Medicine Department of Abant Izzet Baysal University Hospital. Based on the MPS results, the participants were divided into normal perfusion and myocardial ischemia. Variables such as age, sex, leukocyte count, hemoglobin, hematocrit, platelet count, serum uric acid, urea, creatinine, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, transaminase, blood fasting glucose, C-reactive protein, and serum albumin were recorded and compared between the groups.

Results: Among the 73 diabetic patients, 37 had myocardial ischemia, and 36 had normal MPS. Serum uric acid levels were higher in the ischemic group (6.3 ± 1.5 mg/dL) than in the normal group (5.1 ± 1.8 mg/dL) ($p<0.05$). The UHR in the ischemic group was significantly higher (0.15 ± 0.05) than that in the normal MPS group (0.11 ± 0.04). Serum UHR was significantly positively correlated with myocardial ischemia ($r=0.36$, $p=0.002$). With a cut-off value of ≥ 0.11, UHR exhibited 76% sensitivity and 58% specificity in detecting myocardial ischemia ($p<0.05$).

Conclusion: High UHR is an independent predictor and diagnostic tool for myocardial ischemia in patients with diabetes and coronary artery disease. Routine use of UHR as an independent predictive marker is recommended for diabetic patients with myocardial ischemia who undergo MPS.

Keywords: Uric Acid to High-Density Lipoprotein cholesterol ratio (UHR), Myocardial Ischemia, Myocardial Perfusion Scintigraphy, Diabetes Mellitus, Biomarkers

&

Öz

Amaç: Diabetes Mellitus (DM) başta miyokardiyal iskemi olmak üzere kardiyovasküler hastalıklar için önemli bir risk faktörüdür. Hem diabetes mellitus tip 2 hem de kardiyovasküler durumlar, yüksek bir inflamatuar yük ile karakterizedir. Ürik Asit -Yüksek Yoğunluklu Lipoprotein kolesterol oranı (UHR), metabolik ve enflamatuar hastalıkların yeni bir belirteci olarak önerilmiştir. Bu nedenle, bu çalışma diyabetik hastalarda Miyokard Perfüzyon Sintigrafisi (MPS) ile saptanan miyokard iskemisinde Ürik Asidin Yüksek Yoğunluklu Lipoprotein kolesterol oranının (UHR) öngörmedeki rolünü araştırmıştır.

Gereç ve Yöntemler: Bu çalışmaya Ocak 2022 ile Mart 2023 tarihleri arasında Abant İzzet Baysal Üniversitesi Hastanesi Nükleer Tıp Anabilim Dalı'nda MPS uygulanan hastalar dahil edildi. MPS sonuçlarına göre katılımcılar normal perfüzyon ve miyokard iskemisi olarak iki gruba ayrıldı. Gruplar arasında yaş, cinsiyet, lökosit sayısı, hemoglobin, hematokrit, trombosit sayısı, serum ürik asit, üre, kreatinin, total kolesterol, LDL-kolesterol, HDL-kolesterol, trigliserit, transaminaz, kan açlık glikozu, C-reaktif protein ve serum albümini gibi değişkenler kaydedildi ve karşılaştırıldı.

Bulgular: Diyabetli 73 hastanın 37'sinde miyokardiyal iskemi, 36'sında normal MPS mevcuttu. Serum ürik asit düzeyleri iskemik grupta (6,3 ± 1,5 mg/dL) normal gruba (5,1 ± 1,8 mg/dL) göre daha yüksekti ($p<0,05$). İskemik gruptaki UHR, normal MPS grubundakinden (0,11 ± 0,04) anlamlı derecede yüksekti (0,15 ± 0,05). Serum UHR, miyokard iskemisi ile anlamlı olarak pozitif korelasyon gösterdi ($r=0,36$, $p=0,002$)). Cut off değeri ≥ 0,11 olan UHR, miyokard iskemisini saptamada %76 duyarlılık ve %58 özgüllük sergiledi ($p<0,05$).

Sonuç: Yüksek UHR, diyabetli ve koroner arter hastalığı olan hastalarda miyokard iskemisi için bağımsız bir prediktör ve tanı aracıdır.

Anahtar Kelimeler: Ürik Asit/Yüksek Yoğunluklu Lipoprotein kolesterol oranı (UHO), Miyokardiyal İskemi, Miyokard Perfüzyon Sintigrafisi, Diabetes Mellitus, Biyobelirteçler

Atıf/Cite as: Afşin H. The Role of Uric Acid to HDL Cholesterol Ratio in Predicting Myocardial Ischemia in Myocardial Perfusion Scintigraphy in Diabetic Patients. Abant Med J. 2023; 12(2): 6-7. doi:10.47493/abantmedj.1341855

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Hamdi Afşin, **e-mail**: hamdiafsin@hotmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

Diabetes Mellitus (DM) may affect carbohydrate metabolism, resulting in chronic hyperglycemia, which is associated with abnormalities in protein, lipid, and carbohydrate metabolisms. This condition is a key driver of crucial atherosclerosis, a significant cause of cardiovascular diseases. Altered lipid metabolism, a characteristic of atherosclerosis, intensifies cardiovascular risk, while chronic inflammation forms the fundamental link between DM and atherosclerosis, an inflammatory disorder of the arterial wall that can lead to serious health deterioration and even death (1).

Chronic hyperglycemia, a characteristic of DM, contributes to long-term dysfunction and damage to several organs. The complications associated with diabetes pose significant health risks, including retinopathy, nephropathy, peripheral neuropathy, and cardiovascular symptoms. Diabetic patients exhibit more atherosclerosis-related cardiovascular, peripheral arterial, and cerebrovascular diseases than the general population (2).

Coronary artery disease (CAD) is a significant cause of global mortality and morbidity, with over 90% of myocardial ischemia cases caused by coronary artery obstruction. Multiple factors contribute to the development of atherosclerosis, leading to CAD, including dyslipidemia, hypercoagulability, endothelial dysfunction, oxidative stress, inflammation, and infection (3).

Diabetes mellitus (DM) is a significant risk factor for CAD. The diagnostic methods include stress electrocardiography, stress echocardiography, and Gated and MPS SPECT to evaluate myocardial ischemia due to suspected CAD (4). Atherosclerosis involves lipid accumulation in arteries, leading to macrophage infiltration and the formation of cholesterol-rich foam cells (5).

Diabetes increases the risk, progression rate, and severity of CAD. Diabetic patients without previous myocardial infarction (MI) exhibit an MI risk similar to non-diabetic patients with an earlier history of MI (6).

High-Density Lipoprotein (HDL) cholesterol plays a pivotal role in cardiovascular diseases, as it transports excess cholesterol to the liver. It also supports vascular endothelial cells and reduces oxidative reactions in blood. Hyperuricemia can predict cardiovascular mortality and morbidity, causing gout, insulin resistance, high blood pressure, and deterioration of renal function. Uric acid is the final product of purine metabolism, and its increase leads to vascular endothelial dysfunction and stimulates oxidative stress (7).

Uric acid and HDL cholesterol disorders are important risk factors for CAD. Previous studies have reported that the Uric Acid to High-Density Lipoprotein cholesterol ratio (UHR) is associated with hypertension, liver steatosis, cardiovascular mortality, and thyroiditis. Some studies have revealed that high uric acid and low HDL cholesterol levels can cause endothelial oxidative damage and insulin resistance, leading to the deterioration of the cardiovascular system. Serum UHR is emerging as a novel superior biomarker for interpreting inflammatory and anti-inflammatory substances and the severity of CAD (8).

Both diabetes mellitus type 2 and cardiovascular conditions are characterized by a high burden of inflammation. The uric Acid to High-Density Lipoprotein cholesterol ratio (UHR) is suggested as a novel marker of metabolic and inflammatory diseases. The study significantly contributes to refining the diagnostic protocols for myocardial ischemia, particularly in the diabetic patient population. Our ultimate goal was to enhance early detection and subsequent management of myocardial ischemia, thereby improving patient outcomes.

The central aim of our study was to investigate the potential role of UHR in predicting myocardial ischemia in MPS. This ratio is gaining recognition as an emergent biomarker in cardiovascular health, and we intend to examine its effectiveness and predictive power in a specific clinical context.

Materials and Methods

Design and Setting

This study examined patients with diabetes who underwent MPS between January 2022 and March 2023 at the Nuclear Medicine Department of Abant Izzet Baysal University Hospital. Comprehensive patient demographics and laboratory data were obtained from institutional databases and individual patient files. Based on the MPS results, patients were divided into CAD and normal groups. Based on our MPS results, the subjects were systematically categorized into two groups: those exhibiting myocardial ischemia and those with normal perfusion. A wide range of parameters was recorded for each participant, including age, sex, blood leukocyte count (WBC), hemoglobin, hematocrit, platelet count, serum uric acid, blood urea, creatinine, total cholesterol, Low Density Lipoprotein (LDL)-cholesterol, HDL-cholesterol, triglycerides, aspartate, and alanine transaminase, fasting blood glucose, C-reactive protein, and serum albumin. A comparative analysis was performed between the myocardial ischemia and normal perfusion groups.

Inclusion/Exclusion Criteria

The eligibility criteria for the study were carefully defined. The study did not include patients presenting with active infections or inflammatory diseases, pregnant women, cancer patients, and individuals younger than 18 years.

Ethics Approval

We obtained informed consent from all participants, and the research protocol was approved by the local Ethics Committee of Abant Izzet Baysal University (Approval Number: 2023/101, Date: 11.04.2023).

Myocardial Perfusion Scintigraphy Imaging and Application Protocol

The MPS imaging procedures were carefully delineated. Stress perfusion alone was deemed sufficient for patients with normal perfusion no resting study was required. However, patients with abnormal perfusion during the stress study underwent a resting separate survey, typically the following day. Resting research was conducted within a week, depending on the patient's or department's circumstances. Exercise stress tests were performed using the Modified Bruce Protocol. Upon reaching the target heart rate (220-age) x 0.85, an intravenous injection of 20 mCi Tc99m-Sestamibi was administered, and the patient was asked to continue exercising for an additional minute. Imaging commenced 30-45 minutes post-exercise.

Patients who could not perform exercise stress tests for neurological or orthopedic reasons or non-diagnostic exercise tests were subjected to pharmacological stress tests using adenosine. Adenosine was intravenously administered at 140 µg/kg/min over six minutes. At the end of the third minute, at peak coronary hyperemia, a 20 mCi Tc99m-Sestamibi intravenous injection was administered, and the adenosine injection continued until the end of the sixth minute. İmaging began 30-45 minutes after adenosine injection.

Patients were administered milk and chocolate after stress (exercise or adenosine) and rest radiopharmaceutical injections to enhance cardiac imaging and reduce abdominal activity. The remaining stress images were deemed unnecessary for patients with normal perfusion. However, patients with suspected perfusion defects or hypoperfusion in stress images were administered a 20 mCi Tc99m-Sestamibi IV injection at rest, followed by rest imaging after 30-45 minutes. MPS is a less invasive method than coronary angiography for detecting coronary vascular diseases.

Radiophamaceuticals given for MPS imaging and their doses, adenosine dose and duration as well as procedures were performed according to the Turkish Nuclear Medicine Association Myocardial Perfusion SPECT Procedure Guideline published in 2020 (9).

MPS imaging was performed using a high-resolution dual-headed gamma camera (Siemens Symbia, Germany) covering a 180° angle between the 45° right anterior oblique view and the 45° left posterior oblique view. Images were acquired in a 64 × 64 matrix at 3° intervals with 60 projections. Each image had

a duration of 18 s, and a 20% energy window centered on the 140 keV Tc 99m photon peak was utilized. Patients were placed supine with their arms raised and immobile during image acquisition.

Statistical Analyses

All statistical analyses were performed using the SPSS software package (SPSS 20.0, IBM Corp., Armonk, NY, USA). The normality of the data was assessed using the Kolmogorov-Smirnov test. Variables that followed a normal distribution were expressed as means and standard deviations, and differences between groups were evaluated using an independent sample t-test. Non-normally distributed variables were presented as medians and interquartile ranges (IQR), and comparisons between groups were made using the Mann-Whitney U test.

The interrelationships between the study parameters were examined using Pearson's correlation test. Receiver operating characteristic (ROC) curve analysis was used to ascertain the sensitivity and specificity of UHR for detecting myocardial ischemia. The area under the curve (AUC) and 95% confidence interval (CI) values were calculated during the ROC analyses. The level of statistical significance was set at a p-value less than 0.05.

Results

The study population comprised 73 patients, 37 in the myocardial ischemia group and 36 in the normal MPS group. The median ages of the normal MPS and ischemia groups were 68 (39-81) years and 68 (41-82) years, respectively (p=0.41). There were 24 women and 12 men in the normal MPS group and 14 women and 23 men in the myocardial ischemia group (p=0.01) (Table 1).

No statistical differences between normal MPS and myocardial ischemia were reported in terms of WBC (p=0.13), Hb (p=0.28), Htc (p=0.78), Plt (p=0.68), total cholesterol (p:0.06), triglyceride (p=0.56), AST (p=0.98), ALT (p=0.84), GGT (p=0.37), fasting glucose (p=0.19), urea (p=0.30), creatinine (p=0.11), albumin (p=0.52), and CRP (p=0.67) levels (Table 1).

Serum uric acid levels of the diabetic patients with normal MPS and myocardial ischemia were 5.1 ± 1.8 mg/dL and 6.3 ± 1.5 mg/dL, respectively. The serum uric acid level of the ischemic diabetic subjects was higher than that of the diabetic patients with normal MPS (p=0.004). LDL cholesterol levels in diabetic patients with normal MPS and myocardial ischemia were 121 ± 35 mg/dL and 100 ± 39 mg/dL, respectively. LDL cholesterol levels were lower in ischemic diabetic subjects than in diabetic patients with normal MPS (p=0.02) (Table 1).

The mean UHR of diabetic patients with myocardial ischemia was 0.15 ±0.05 and was higher than that in the normal MPS group (0.11 ± 0.04). The difference between ischemia and normal MPS groups was statistically significant (p=0.001) (Table 1).

Serum UHR was significantly positively correlated with myocardial ischemia in patients with diabetes (r=0.36, p=0.002).

A UHR level higher than 0.11 have 76% sensitivity and 58% specificity in detecting myocardial ischemia in diabetic patients [AUC (Area under curve):0.71, p=0.002, 95% CI (confidence interval):0.59-0.83] (Figure 1).

Discussion

Our investigation revealed several key findings: (I) UHR can be positively associated with myocardial ischemia in diabetic patients, (II) an elevated UHR level significantly correlates with the onset of myocardial ischemia in individuals with type 2 diabetes mellitus, and (III) high UHR levels exhibit high sensitivity and moderate specificity for the detection of myocardial ischemia. This study represents a pioneering effort to elucidate the connection between elevated UHR levels and myocardial ischemia in diabetic patients who underwent MPS.

Table 1.

Laboratory and Demographic Data of Diabetic Patients According to MPS Results

	Normal Myocardial Perfusion	Myocardial Ischemia	p value
Gender			**0.01**
Male	12 (33%)	23 (62%)	
Female	24 (67%)	14 (38%)	
	Median (min-max)	**Median (min-max)**	
Age (years)	68 (39-81)	68 (41-82)	0.41
WBC (k/mm³)	6.99 (4-11)	7.21 (5-11)	0.13
Urea (mg/dL)	32 (15-110)	41 (19-82)	0.30
Creatinine (mg/dL)	0.86 (0.63-2.69)	1.01 (0.57-3.07)	0.11
HDL Chol.(mg/dL)	48.60 (29-77)	41.80 (23-85)	0.28
Triglyceride (mg/dL)	155 (34-416)	133 (63-378)	0.56
ALT (U/L)	16 (11-49)	15 (9-48)	0.84
GGT (U/L)	22.30 (13-74)	26 (11-98)	0.37
CRP (mg/dL)	1.36 (0.1-15.1)	1.05 (0.1-57.5)	0.67
Albumin (g/dL)	4.1(3.8-5.3)	4.3 (2.4-5.1)	0.52
Fasting Glucose (mg/dL)	128 (77-287)	117(74-564)	0.19
	Mean ± SD	**Mean ± SD**	
UHR	0.11±0.04	0.15±0.05	**0.001**
Hb (g/dL)	13.1±1.3	15.7±1.5	0.28
Htc (%)	40.2±3.7	40.5±6	0.78
Plt (k/mm³)	254±83.5	246.8±65.6	0.68
Uric acid (mg/dL)	5.1±1.8	6.3±1.5	**0.004**
Total Cholesterol (mg/dL)	198±44.2	177.9±46.5	0.06
LDL Chol. (mg/dL)	121±35	100.±39	**0.02**
AST (U/L)	19.9±6.5	19.8±5.4	0.98

WBC: White Blood Cells, HDL: High-Density Lipoprotein, ALT: Alanine Transaminase, GGT: Gamma-Glutamyl Transferase, CRP: C-Reactive Protein, UHR: Uric Acid to HDL Ratio, Hb: Hemoglobin, Htc: Hematocrit, Plt: Platelets, LDL: Low-Density Lipoprotein.

Elevated UHR has been implicated in inflammatory and metabolic disorders, including Hashimoto thyroiditis, type 2 diabetes mellitus, metabolic syndrome, and non-alcoholic fatty liver disease. Elevated UHR has also emerged as a potential biomarker for diabetic nephropathy in type 2 diabetes mellitus, which triggers chronic and low-grade inflammation. Our findings resonate with these observations, corroborating that myocardial ischemia triggered by chronic inflammation in patients with diabetes is significantly associated with high UHR (10).

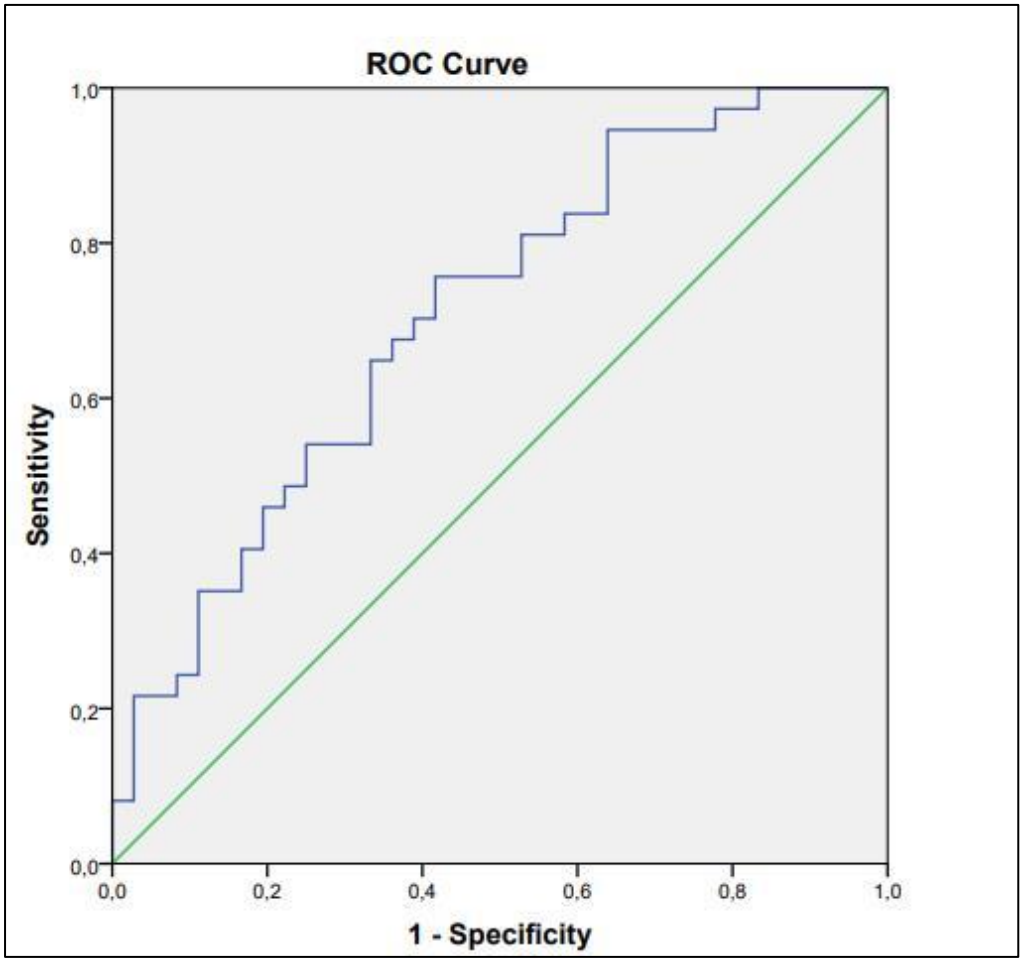


Figure1. ROC curve analysis of UHR in predicting myocardial ischemia, AUC of UHR for ischemia in diabetics: 0.71% 95 CI: 0.59-0.83; p<0.002; ROC: Receiver operating characteristics, AUC: Area under the curve, UHR: Uric Acid to HDL Ratio, CI: Confidence interval.

Furthermore, high uric acid levels have been implicated in many inflammatory conditions such as type 2 diabetes mellitus, metabolic syndrome, obesity, gout, and autoimmune thyroiditis (14,18,19). Kurtkulağı et al. delineated a substantial positive correlation between UHR and thyroid-stimulating hormone (TSH) and an inverse correlation with free T4 (FT4). The investigators underscored that elevated UHR is a robust and practical marker of Hashimoto's thyroiditis, an autoimmune disease in which chronic inflammation is instrumental in its clinical course (11). A high UHR could enhance the diagnostic utility of other markers for Hashimoto's thyroiditis. Our results are congruent with these findings, particularly in light of the substantial correlation between myocardial ischemia precipitated by persistent low-grade inflammation and increased UHR in our diabetic cohort.

Elevated serum uric acid levels are often associated with cardiovascular diseases, diabetes, hypertension, chronic kidney disease, and metabolic syndrome. Hyperuricemia is an independent risk factor for diabetes and positively correlates with diabetes-related complications. HDL cholesterol plays an integral role in cardiovascular health and metabolic syndrome, with the components of the metabolic syndrome being low HDL cholesterol, dyslipidemia, hypertriglyceridemia, hypertension, and impaired glucose tolerance. Notably, patients with diabetes exhibit decreased high-density lipoprotein (HDL) cholesterol levels. UHR, encompassing both uric acid and HDL cholesterol, is a robust indicator of metabolic deterioration, as shown in our study. The findings of this study underscore the significance of UHR as a diagnostic marker for diabetes and related metabolic disorders (12).

Type 2 diabetes mellitus and its consequential complications are often linked to inflammatory biomarkers such as neuregulin-4 (Nrg-4) and adipokines secreted by brown adipose tissue. Xuan et al. revealed a correlation between UHR and both macrovascular and microvascular complications of diabetes mellitus, in addition to a relationship between UHR and diabetic retinopathy, particularly in men and postmenopausal women. They advocated for monitoring and managing elevated UHR during diabetes follow-up, emphasizing its importance in preventing and mitigating diabetes-associated vascular complications. These results corroborate our findings, which showed a pronounced positive correlation between increased UHR and myocardial ischemia in diabetic patients with persistent inflammation (12).

Emerging studies have highlighted the predictive value of high UHR for inflammation in conditions such as metabolic syndrome (13), type 2 diabetes mellitus (14), non-alcoholic fatty liver disease, and liver steatosis (15). These insights underscore the potential utility of UHR as a predictive marker for diverse health conditions, supporting the findings of this study.

Uric acid, a product of purine catabolism, is primarily excreted through urine. Antigen cells exhibit sensitivity to uric acid owing to endogenous pro-inflammatory signaling; therefore, increased uric acid levels may induce inflammation. Conversely, a reduction in uric acid levels is related to a decrease in the overall inflammatory burden. Elevated uric acid levels have been associated with chronic low-level inflammatory conditions such as obesity, metabolic syndrome, and type 2 diabetes mellitus. Moreover, uric acid levels have been linked to glycated hemoglobin (HbA1c) levels and regulation of diabetes mellitus. Kosekli and colleagues suggested that high UHR levels could indicate hepatic steatosis in healthy individuals, proposing that UHR levels could be used for diagnostic and monitoring purposes in individuals with liver steatosis (15). Our findings resonate with these insights, suggesting that elevated UHR levels in patients with diabetes may potentially serve as a predictor of myocardial ischemia.

A recent large-scale population study highlighted a positive association between elevated UHR levels and reduced Glomerular Filtration Rate (GFR), which indicates a risk of chronic kidney disease. UHR is a sensitive and specific marker of kidney function. These findings and those of our research showed a consistent relationship between elevated UHR levels and the prediction of myocardial ischemia in MPS for diabetic patients (16).

Uric acid is a potential biomarker of diabetic nephropathy. An investigation by Kocak et al. showed that elevated uric acid levels correspond with the severity of diabetic kidney disease in patients with diabetes. These insights resonate with our findings, which indicate a correlation between high UHR levels and myocardial ischemia in patients (17).

HDL cholesterol has gained attention as an essential risk factor for cardiovascular diseases because it safeguards the vascular endothelium by promoting oxidative reactions in the bloodstream. Some studies have suggested a possible association between inflammatory conditions, such as diabetes mellitus, metabolic syndrome, various cancers, and low HDL cholesterol levels. Our study reaffirms this, as we observed that a decrease in HDL cholesterol tends to amplify UHR levels, further validating the use of UHR as a meaningful biomarker for predicting myocardial ischemia in patients with diabetes (20,21).

This is the first study to demonstrate the relationship between UHR and myocardial ischemia detected using MPS. While this study was rigorous in its approach, and the implications could potentially be significant, there were several limitations to note.

1. Sample size and selection bias: The study was conducted in a single hospital, and the sample size may not be sufficiently large to generalize the findings. The patients in this study may not represent the complete spectrum of patients with diabetes, leading to potential selection bias.

2. Cross-sectional design: Given that this was a cross-sectional study, it offers only a snapshot of the UA/HDL ratio and myocardial ischemia at a specific point in time. This design cannot capture the dynamic nature of these markers and the progression of myocardial ischemia.

3. Lack of a control group: Although the study compared patients with normal perfusion to those with myocardial ischemia, it did not include a non-diabetic control group. This omission restricts our ability to explore the role of diabetes in observed relationships.

4. Exclusion of confounding factors: While the study attempted to control for various confounding factors, there could be other unaccounted variables, such as lifestyle, dietary habits, and medication adherence, that could influence both UHR and myocardial ischemia.

5. Measurement error: There is always the potential for mistakes in measuring biochemical markers and interpreting MPS images, which could introduce bias into the study findings.

6. Reliance on existing data: This study utilized patient records and an institutional data-collection database. These records may contain inaccurate or missing information, affecting the results.

Future studies addressing these limitations may further increase our understanding of the role of UHR in predicting myocardial ischemia in MPS patients.

Conclusions

Based on the results of our study, we confirmed that high UHR serves as a crucial independent predictor and diagnostic tool for myocardial ischemia in patients with diabetes and CAD. UHR's ease of obtaining and cost-effectiveness of UHR significantly contributes to its potential as a routine diagnostic measure. We suggest that UHR can be routinely used as an independent predictive marker, particularly in diabetic patients suspected of having ischemia, who are candidates for MPS. These findings highlight the value of UHR in clinical practice for diagnosing CAD, thereby contributing to proactive treatment strategies and improving patient outcomes.

Ethics Committee Approval: The study was approved by the Ethics Committee of Bolu Abant Izzet Baysal University (date: 11.04.2023 and approval number: 2023/101).

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Author declared no conflict of interest.

Financial Disclosure: Author declared no financial support.

Acknowledgment: We would like to thank all the Bolu Training and Research Hospital researchers.

Author Contributions: Idea/Concept: H.A.; Design: H.A.; Materials: H.A.; Data Collection/Processing: H.A.; Analysis/Interpretation: H.A.; Literature Review: H.A.; Drafting/Writing: H.A.; Critical Review: H.A. The author has accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The Diabetes Mellitus-Atherosclerosis Connection: The Role of Lipid and Glucose Metabolism and Chronic Inflammation. Int J Mol Sci. 2020;21(5):1835.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011;34(Suppl 1):S62–9.

3. Koplay M, Erol C. Koroner arter hastalığı. Türk Radyoloji Seminerleri. 2013;1(1):57-69.
4. Efe SÇ, Özdemir Candan Ö, Gündoğan C, Öz A, Yüksel Y, Ayca B, et al. Value of C-reactive Protein/Albumin Ratio for Predicting Ischemia in Myocardial Perfusion Scintigraphy. Mol Imaging Radionucl Ther. 2020;29(3):112-7.
5. Maguire EM, Pearce SWA, Xiao Q. Foam cell formation: A new target for fighting atherosclerosis and cardiovascular disease. Vascul Pharmacol. 2019;112:54-71.
6. Baweja PS, Sandesara PB, Ashraf MJ. Asymptomatic coronary artery disease in type II diabetes. Mo Med. 2014;111(1):73-9.
7. Park B, Jung DH, Lee YJ. Predictive Value of Serum Uric Acid to HDL Cholesterol Ratio for Incident Ischemic Heart Disease in Non-Diabetic Koreans. Biomedicines. 2022;10(6):1422.
8. Li F, Zhao D, Li Q, Lin X, Sun H, Fan Q. Uric Acid to High-Density Lipoprotein Cholesterol Ratio is a Novel Marker to Predict Functionally Significant Coronary Artery Stenosis. J Interv Cardiol. 2022 Oct 13;2022:9057832.
9. Canbaz Tosun F, Özdemir S, Şen F, Demir H, Özdemir E, Durmuş Altun G. Miyokardiyal Perfüzyon SPECT Uygulama Kılavuzu. Nucl Med Semin. 2020;6:90-134.
10. Aktas G, Yilmaz S, Kantarci DB, Duman TT, Bilgin S, Balci SB, et al. Is serum uric acid-to-HDL cholesterol ratio elevation associated with diabetic kidney injury? Postgrad Med. 2023;135(5):519-23.
11. Kurtkulagi O, Tel BMA, Kahveci G, Bilgin S, Duman TT, Ertürk A, et al. Hashimoto's thyroiditis is associated with elevated serum uric acid to high density lipoprotein-cholesterol ratio. Rom J Intern Med. 2021;59(4):403-8.
12. Xuan Y, Zhang W, Wang Y, Wang B, Xia F, Zhang K, et al. Association Between Uric Acid to HDL Cholesterol Ratio and Diabetic Complications in Men and Postmenopausal Women. Diabetes Metab Syndr Obes. 2023;16:167-77.
13. Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Rev Assoc Med Bras (1992). 2019;65(1):9-15.
14. Aktas G, Kocak MZ, Bilgin S, Atak BM, Duman TT, Kurtkulagi O. Uric acid to HDL cholesterol ratio is a strong predictor of diabetic control in men with type 2 diabetes mellitus. Aging Male. 2020;23(5):1098-102.
15. Kosekli MA, Kurtkulagii O, Kahveci G, Duman TT, Tel BMA, Bilgin S, et al. The association between serum uric acid to high density lipoprotein-cholesterol ratio and non-alcoholic fatty liver disease: the abund study. Rev Assoc Med Bras (1992). 2021;67(4):549-54.
16. Cheng Y, Zhang H, Zheng H, Yin H, Wang Y, Wang H, et al. Association between serum uric acid/HDL-cholesterol ratio and chronic kidney disease: a cross-sectional study based on a health check-up population. BMJ Open. 2022;12(12):e066243.
17. Kocak MZ, Aktas G, Duman TT, Atak BM, Savli H. Is Uric Acid elevation a random finding or a causative agent of diabetic nephropathy? Rev Assoc Med Bras (1992). 2019;65(9):1155-60.
18. Khameneh Bagheri R, Najafi MN, Ahmadi M, Saberi M, Maleki M, Baradaran Rahimi V. Investigation of the association between serum uric acid levels and HEART risk score in patients with acute coronary syndrome. Physiol Rep. 2022;10(22):e15513.
19. Bao F, Wang Y, Ju SQ, Sun WJ, Li YH, Zhang YC, et al. [Correlation between serum uric acid and creatinine ratio and metabolic syndrome based on physical examination population in Nantong area]. Zhonghua Yu Fang Yi Xue Za Zhi. 2022;56(11):1630-5. Chinese.
20. Chang YC, Lin CJ, Yeh TL, Tsai MC, Hsu LY, Chien KL, et al. Lipid biomarkers and Cancer risk - a population-based prospective cohort study in Taiwan. Lipids Health Dis. 2021;20(1):133.
21. Reiner Z, Muacević-Katanec D, Katanec D, Tedeschi-Reiner E. Snizeni HDL-kolesterol--vazan cimbenik rizika od kardiovaskularnih bolesti [Low HDL-cholesterol--an important risk factor for cardiovascular diseases]. Lijec Vjesn. 2011;133(3-4):111-6. Croatian.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):140-145, doi:10.47493/abantmedj.1285603

Blaschko Çizgilerine Yerleşen Lineer Liken Planus: Olgu Sunumu

Linear Lichen Planus Located on Blaschko Lines: A Case Report

Tuna SEZER [1*], Feyza Nur ŞİMSEK [1], Eda Hilal İMAMOĞLU [2]

[1] Bolu Abant İzzet Baysal Üniversitesi Tıp Fakültesi Dermatoloji Ana Bilim Dalı, Bolu, Türkiye

[2] Bolu Abant İzzet Baysal Üniversitesi Tıp Fakültesi Patoloji Ana Bilim Dalı, Bolu, Türkiye

Geliş Tarihi (*Received*): 27.04.2023 **Kabul Tarihi (*Accepted*):** 06.07.2023 **Yayın Tarihi (*Published*):** 01.08.2023

Öz

Liken planus (LP) deride kaşıntılı, morumsu papüller karakterize olup saç, tırnak, mukoza tutulumu da yapabilen etiyolojisi tam olarak bilinmeyen kronik, inflamatuvar bir hastalıktır. Lezyonun şekline, morfolojisine ve anatomik lokalizasyonuna göre LP sınıflaması yapılmaktadır. Burada bu sınıflama içinde ender görülen Blaschko çizgilerine yerleşen Lineer LP olgusu sunmaktayız.

Anahtar Kelimeler: Blaschko, Lineer, Liken

&

Abstract

Lichen planus (LP) is a chronic, inflammatory disease of unknown etiology that is characterized by itchy, purplish papules on the skin and may involve hair, nails, and mucous membranes. LP classification is made according to the shape, morphology and anatomical localization of the lesion. Here, we present a case of Linear LP localized to Blaschko lines, which is rare in this classification.

Keywords: Blaschko, Linear, Lichen

Atıf/Cite as: Sezer T. , Şimsek F. N. , İmamoğlu E. H. Blaschko Çizgilerine Yerleşen Lineer Liken Planus: Olgu Sunumu. Abant Med J. 2023; 12(2): 7-8. doi:10.47493/abantmedj.1285603

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*] **Sorumlu Yazar (Corresponding Author):** Tuna Sezer, **e-mail**: tunasezer@yahoo.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Giriş

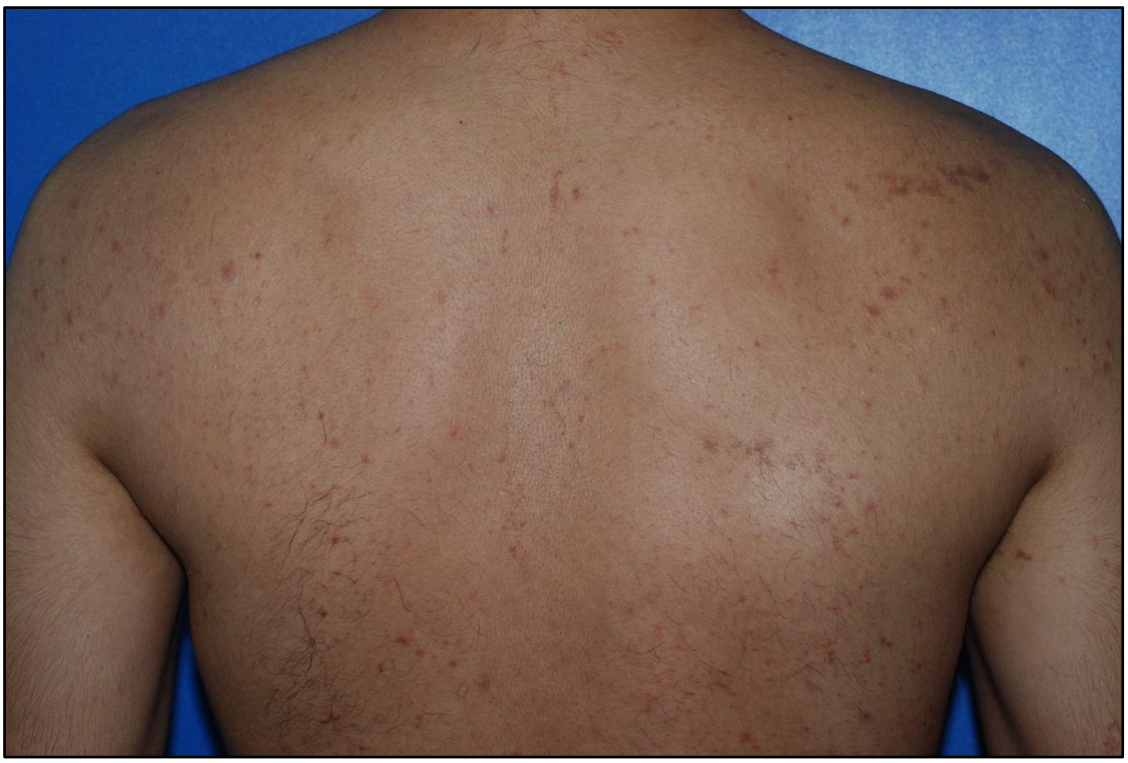
Liken planus deride kaşıntılı, viyolase, poligonal papüller ile karakterize; deri dışında mukoza, tırnak ve saçlı deri tutulumu yapabilen inflamatuvar bir hastalıktır. Lezyonların yerleşim yerine, morfolojisine ve dağılımına göre hastalık sınıflandırılmaktadır (1). Bu sınıflandırma içinde lineer liken planus (LLP) ender görülen bir varyant olup LLP'nin lineer, blaschkoid veya zosteriform paternde yerleşim gösteren olguları literatürde bildirilmiştir. Biz burada Blaschko çizgilerine yerleşmiş LLP olgusu sunmaktayız.

Olgu

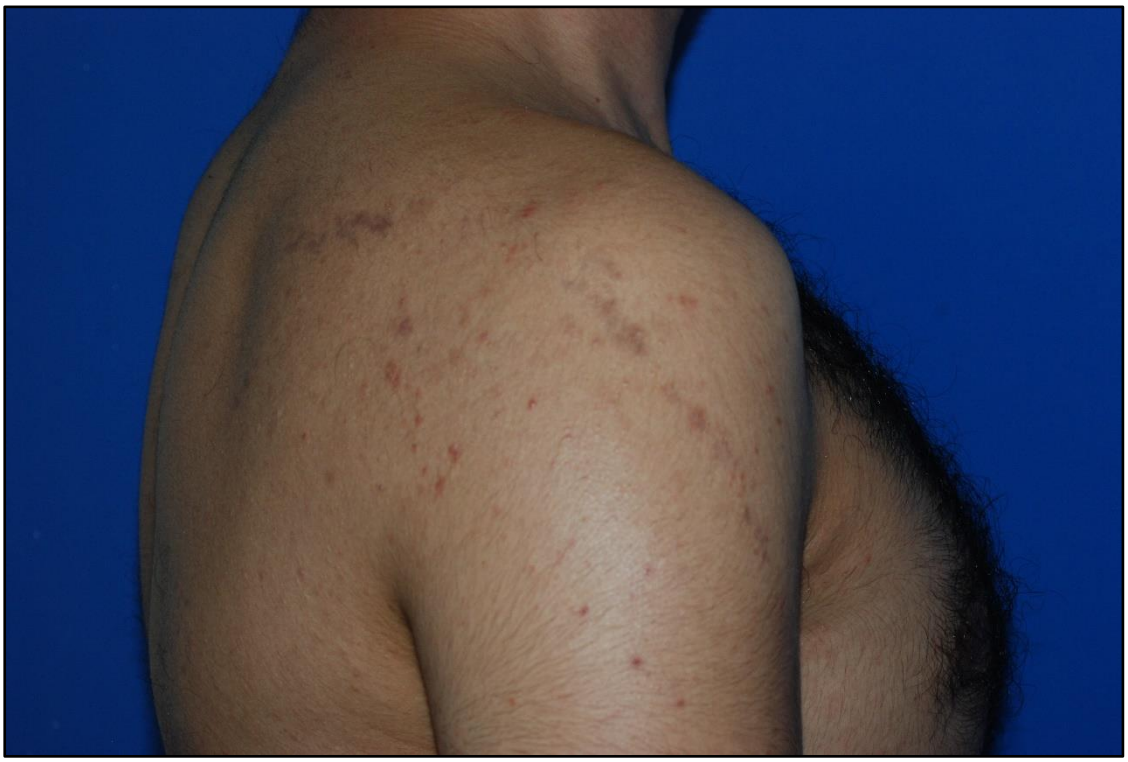
25 yaşında erkek hasta 2 ay önce sağ koldan başlayıp son bir aydır sırt, omuz, bel ve sağ bacakta mor-kahverengi renkte, hafif kaşıntılı döküntülerle polikliniğimize başvurdu. Hastanın yapılan dermatolojik muayenesinde sağ kol fleksör yüzde lineer dağılım gösteren ve sırtta akneiform lezyonların arasında sağ omuz üzerinden sağ skapula bölgesine lineer uzanan, sırtın sağ tarafı orta bölgede S şeklinde, aynı taraf lomber bölge ve bacak arka yüzde Blaschko çizgilerine uygun yerleşen livid renkte makulopapüler lezyonlar saptandı (Resim 1, 2, 3). Hastanın tırnak, mukoza ve saçlı deri muayenesi normaldi. İlaç kullanım hikayesi olmayan hastanın özgeçmişinde özellik yoktu. Rutin laboratuvar tetkikleri normaldi.

Hastadan alınan punch biyopsi sonucunda hafif lameller hiperkeratoz, bir alanda dermoepidermal bileşkede bant tarzında lenfohistiyositik infiltrasyon, bazal vakuoler dejenerasyon, apoptotik keratinositler; dermiste ve yüzeyel dermiste hemosiderin yüklü histiositler görüldü (Resim 4).

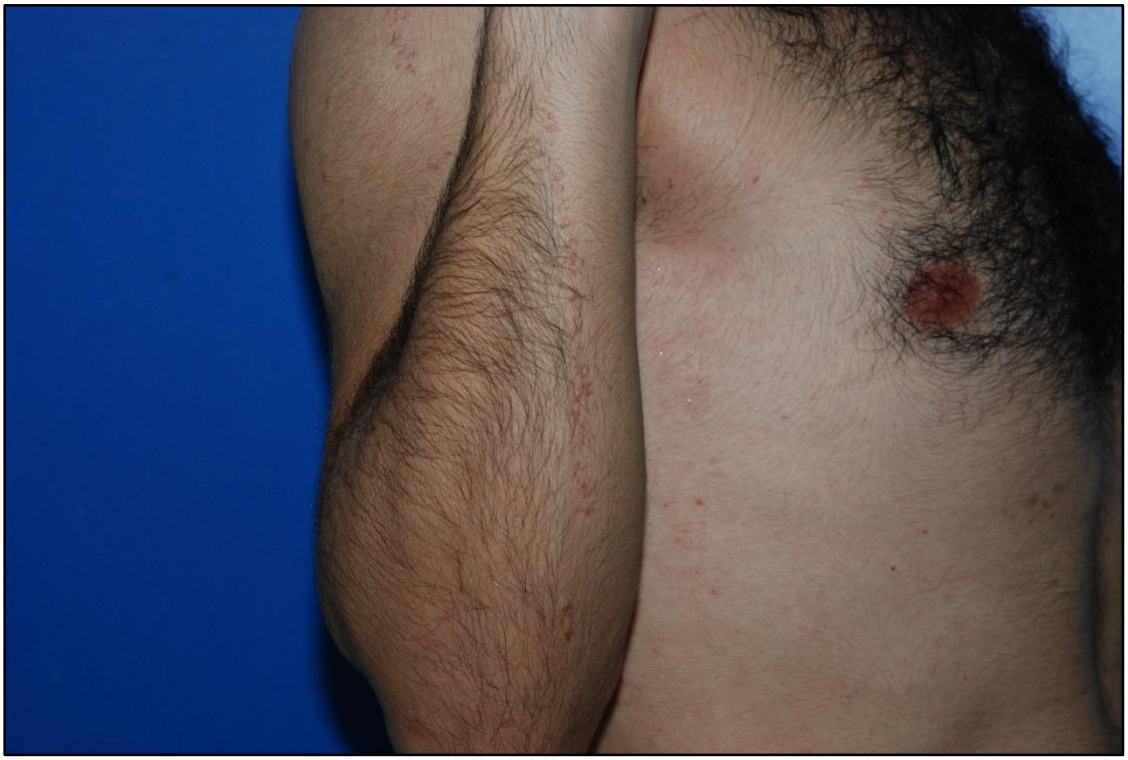
Klinik ve histopatolojik bulgularla Blaschko çizgilerine yerleşen LLP tanısı konuldu. Hastaya tek doz intramusküler triamsinolon asetonid uygulandı; kaşıntıları için levosetirizin içeren oral antihistaminik verildi. Bir ay sonraki kontrolünde lezyonların belirginliğinde azalma, bir kısmının kahverengi pigmentasyon bırakarak iyileştiği görüldü. Tedavinin devamında klobetazol propiyonat içeren merhem verildi.



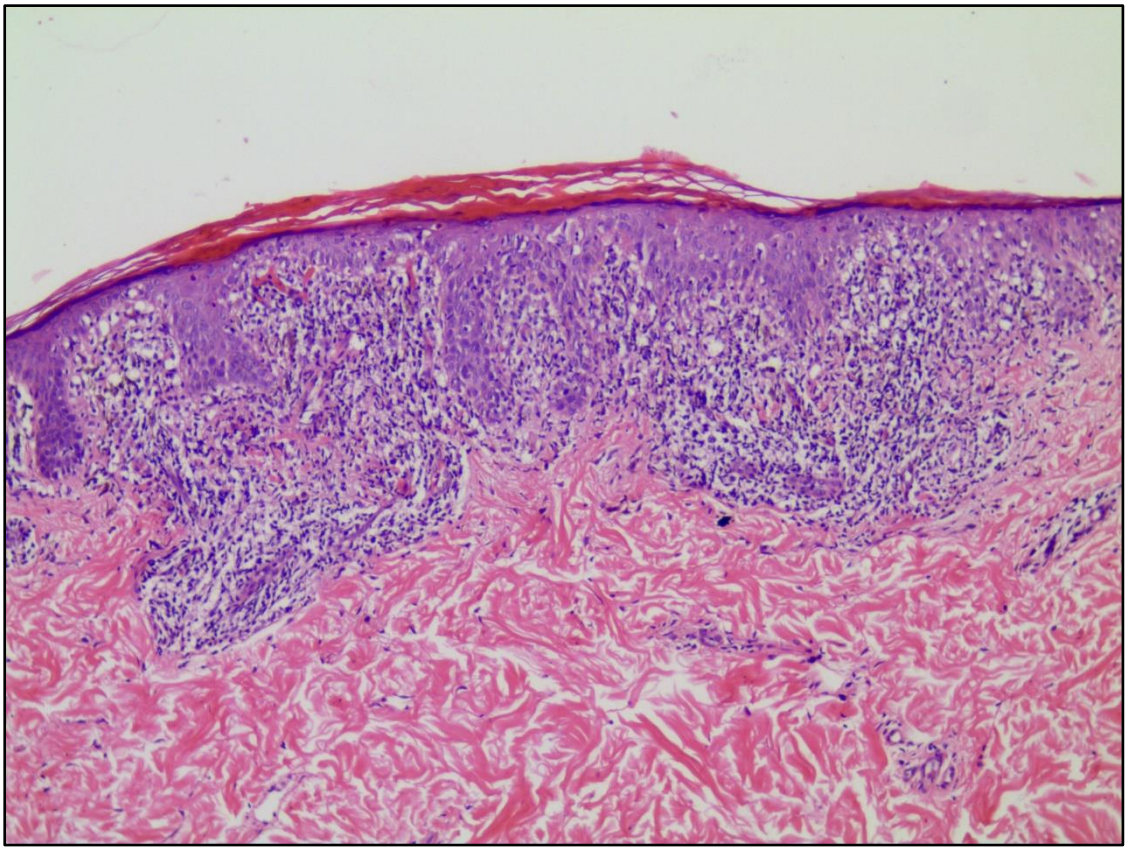
Resim 1. Sırtta akneiform lezyonların arasında sağ omuz üzerinden sağ skapula bölgesine lineer uzanan, sırtın sağ tarafı orta bölgede S şeklinde devam eden lividi mamkülopapüler lezyonlar.



Resim 2. Sağ skapuladan sağ kola lineer devam eden lividi makülopapüler lezyonlar



Resim 3. Sağ ön kol ekstansör yüzde ve sağ kol deltoid bölgede lineer yerleşimli lividi makülopapüler lezyonlar



Resim 4. Hiperkeratoz ile dermoepidermal bileşkede bant benzeri lenfohistiyositik inflamasyon ve retelerde testere dişi görünümü (Hematoksilen-Eozin x100).

Tartışma

Liken Planus (LP) deri, deri ekleri ve mukozaları tutabilen, karakteristik klinik ve histopatolojik bulguları olan, kronik seyirli, inflamatuar bir dermatozdur. Toplumda görülme sıklığı %0,2-1 arasındadır. LP klasik olarak üzeri düz, mor renkli, poligonal, kaşıntılı papüller ile karakterizedir. Hastalık her yaşta görülmekle birlikte daha çok 30-60 yaşları arasında görülme sıklığı artmaktadır. Etiyolojisi ve patogenezi tam olarak bilinmeyen hastalıkta, viral enfeksiyonlar, otoimmün hastalıklar, ilaçlar, stres, travma gibi faktörlerin CD8+ T hücre aracılı otoimmün reaksiyon aracılığıyla bazal keratinosit apopitozuna yol açtığı düşünülmektedir. Lezyonların şekline, lokalizasyonuna ve morfolojilerine göre LP sınıflaması yapılır. Lineer LP bu sınıflama içinde nadir görülen varyantlardan birisidir. LLP tüm liken planuslu hastalaın %1'den azını oluşturmaktadır (1,2).

LLP için Blaschkoid LP ve Blaschkolineer LP gibi isimler de kullanılmıştır (2,3). Blaschko çizgileri ilk olarak Alfred Blaschko tarafından tanımlanmış olup sinir, damar ya da lenfatik yapıyı izlemeyen bu çizgilerin embriyonik hücrelerin gelişim ve göç yörüngesini yansıttığı düşünülmektedir. Bu çizgiler, omurganın üst bölgesinde V şeklini, karında S şeklini ve göğüsten üst kola doğru ters U şeklini izler. X'e bağlı, konjenital ve kazanılmış cilt hastalıkları Blaschko çizgilerine uygun yerleşim gösterebilmektedir. Blaschkoid LP'nin, postzigotik mozaizm sonucunda heterozigozite kaybından kaynaklandığı düşünülmektedir. Hasta hayatının herhangi bir döneminde LP etiyolojisindeki tetikleyici faktörlere maruz kaldığında lezyonların yalnızca mozaizm olan blaschko çizgilerinde lineer olarak tutulumuyla LLP oluştuğu varsayılmaktadır (4-6).

LLP'nin klinik seyrinde genellikle saçlı deri, tırnak ve mukoza tutulumu olmadığından klasik LP'den farklılık göstermektedir. Literatür incelendiğinde Blaschko çizgileri boyunca unilateral dağılım gösteren LP vakalarında sıklıkla gövde ve ekstremite tutulumu olduğu görülmüştür (7). Bunun yanında yüz yerleşimi olan olgu serileri de yayınlanmıştır (8). Hastamızda sağ kolda, sırtın sağ tarafında, aynı taraf lomber bölge ve bacakta blasko çizgilerine uygun lezyonları vardı. Bunun yanında hastamızda saçlı deri, mukoza ve tırnak tutulumu bulunmamaktaydı.

Ayırıcı tanıda liken striatus, liken nitidus, inflamatuar lineer verruköz epidermal nevüs, lineer porokeratoz, lineer psoriasis, lineer Darier hastalığı düşünülmelidir (1,2). Klinik ayrım mümkün olmadığında histopatolojik inceleme yapılmalıdır. LP'nin klasik histopatolojisinde, üst dermiste yoğun mononükleer hücre infiltrasyonu, hiperkeratoz, hipergranüloz, testere dişi görünümüne yol açan düzensiz akantoz, bazal hücre vakualizasyonu gibi epidermal bulgular, dermoepidermal bileşkede dejenere keratonisitler görülmektedir (1). Hastamızın histopatolojik incelemesi sonucunda LP tanısı doğrulanmıştır.

LLP genellikle iyi seyirlidir ve kendini sınırlar. Lezyonların yaygınlığı ve yerleşim yeri tedavi seçeneği için belirleyici olmaktadır. Hastalığın seyrinde tedavi ile birlikte iyileşme yanında lezyonların bir kısmı pigmentasyon bırakarak iyileşebilir. Tedavide topikal kortikosteroidler ve kalsinörin inhibitörleri; sistemik tedavide oral veya intramüsküler kortikosteroid, siklosporin, metotreksat, dapson, asitretin, antimalaryaller (klorokin ve hidroksiklorokin) ve fototerapi kullanılabilir (1,2). Hastamıza oral antihistaminikle birlikte triamsinolon asetonid intramusküler olarak uygulanmış olup bir ay sonraki kontrolünde lezyonların belirginliğinde azalma, bir kısmının kahverengi pigmentasyon bırakarak iyileştiği görülmüştür. Tedavinin devamında hastaya topikal klobetazol propiyonat verilmiştir.

Sonuç olarak Blaschko çizgilerine yerleşen LLP ile ilgili sınırlı sayıda vaka sunulmuş olup bu olgumuzun litaratüre katkı sunacağı düşüncesindeyiz.

Bilgilendirilmiş Onam: Bireyden yazılı ve sözlü onam alınmıştır.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Yazar Katkıları: Fikir/Konsept: T.S., F.N.Ş., E.H.İ.; Tasarım: T.S., F.N.Ş., E.H.İ.; Materyal: F.N.Ş., E.H.İ.; Veri toplama/işleme: T.S., F.N.Ş., E.H.İ.; Literatür tarama: T.S., F.N.Ş.; Taslak oluşturma/makale yazımı: T.S., F.N.Ş.; Eleştirel inceleme: T.S., F.N.Ş., E.H.İ. Yazarlar bu yazının tüm içeriğinin sorumluluğunu kabul etmiş ve yayınlanmak için gönderilmesini onaylamıştır.

Kaynaklar

1. Aksoy B. Liken planus ve likenoid dermatozlar. In: Gürel MS, Aksu AEK, Durdu M, Erdemir VAT, Karadağ AS, editors. Temel Dermatoloji. 1st ed. İstanbul: İstanbul Tıp Kitapevleri; 2023. p. 376-94.
2. Weston G, Payette M. Update on lichen planus and its clinical variants. Int J Womens Dermatol. 2015;1(3): 140-9.
3. Criscito MC, Brinster NK, Skopicki DL, Seidenberg R, Cohen JM. Blaschkoid lichen planus: Throwing "curve" in the nomenclature of linear lichen planus. JAAD Case Rep. 2020;6(3):237-9.
4. Gupta S, Gupta S, Thomas M, Mahendra A. Unilateral lichen planus along the lines of Blaschko: A rare clinical presentation. Acta Med Indones. 2012;44(2):163-4.
5. Yayla D, Çakmak SK, Oğuz ID, Gönül M, Özhamam E, Çolak A, Gül Ü. Two cases of unilateral lichen planus following the lines of blaschko. Ann Dermatol. 2014;26(5):636-8.
6. Moss C. Mosaicism and linear lesions. In: Bolognia JL, Jorizzo JL, Schaffer JV, editors. Dermatology. 3rd ed. China: Elsevier Limited; 2012. p. 943-62.
7. Dayal S, Sahu P, Verma P, Amrani A, Khare, R. Unilateral blaschkoian lichen planus: A series of cases with review of literature. J Clin Diagn Res. 2017;11(5), WR01-05.
8. Merio L, Tounkara T-M, Battesti G, Cordoliani F, Arsouza A, Bagot M, Battistella M, Petit A. Blaschko-linear lichen planus of the face: A retrospective study of 6 cases and a literature review. Ann Dermatol Venereol. 2022;149(2):112-8.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):146-150, doi:10.47493/abantmedj.1324250

An Extremely Rare Cause of Acute Symptomatic Seizure in Toddlers: Apricot Seed Ingestion

Çocuklarda Akut Semptomatik Nöbetin Oldukça Nadir Bir Nedeni: Kayısı Çekirdeği Yutulması

İpek DOKUREL ÇETİN [1*], Cansen ÇENELİ [2]

[1] Balıkesir University Medical Faculty Hospital, Department of Pediatrics, Division of Pediatric Neurology, Balıkesir, Türkiye

[2] Balıkesir University Medical Faculty Hospital, Department of Pediatrics, Balıkesir, Türkiye

Geliş Tarihi (*Received*): 07.07.2023 **Kabul Tarihi (*Accepted*):** 15.08.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Abstract

One of the most frequent causes of seizures in children is an acute symptomatic seizure. To forecast risk of recurrence of seizure, it's crucial to identify the trigger element at the root of the problem. Cyanide inhibits cell oxygen utilization and cellular respiration through inactivation of mitochondrial cytochrome oxidase. Cyanide is one of the most lethal toxins ever discovered for the human body. Early treatment enables the avoidance of harmful outcomes, including death. This case report represents case of a 2-year-old girl presented with an acute symptomatic seizure after eating a few apricot kernels and her quick recovery with antidote after cyanide poisoning was suspected. The patient was discharged without experiencing any long-term effects of cyanide poisoning.

Keywords: Cyanide, Children, Acute Symptomatic Seizure

&

Öz

Çocuklukta nöbetlerin en sık nedenlerinden biri akut semptomatik nöbettir. Nöbetin tekrarlama riskini tahmin etmek için sorunun kökündeki tetikleyici unsuru belirlemek çok önemlidir. Siyanür, mitokondriyal sitokrom oksidazın inaktivasyonu yoluyla hücre oksijen kullanımını ve hücresel solunumu inhibe eder. Siyanür, insan vücudu için şimdiye kadar keşfedilen en öldürücü toksinlerden biridir. Erken tedavi, ölüm dahil zararlı sonuçların önlenmesini sağlar. Bu vaka sunumu, birkaç kayısı çekirdeği yedikten sonra akut semptomatik nöbet ile başvuran ve siyanür zehirlenmesinden şüphelenildikten sonra panzehirle hızla iyileşen 2 yaşındaki bir kız çocuğunu sunmaktadır. Hasta siyanür zehirlenmesinin uzun süreli etkisi görülmeden taburcu edilmiştir.

Anahtar Kelimeler: Siyanür, Çocuk, Akut Semptomatik Nöbet

Atıf/Cite as: Dokurel İ. , Çeneli C. An extremely rare cause of acute symptomatic seizure in toddlers: Apricot seed ingestion. Abant Med J. 2023; 12(2): 8-9. doi:10.47493/abantmedj.1324250

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*] **Sorumlu Yazar (Corresponding Author):** İpek Dokurel Çetin, **e-mail**: dripekdokurel@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

Introduction

The immature brain of children is more prone to epileptogenesis and propagation of seizures. Acute symptomatic seizures were provoked by any acute condition such as a toxic or metabolic disturbance, fever, head trauma, or acute stroke, are differed from epileptic seizures. The American Academy of Neurology has advised having laboratory screening tests based on certain clinical conditions in evaluating a child's first seizure (1). However, due to its rarity, cyanide poisoning in pediatric seizures is challenging for clinicians in terms of diagnosing, verifying, and treating it early.

Cyanide is particularly hazardous to the central nervous, respiratory, and cardiovascular systems. Cyanide poisoning is uncommon in children, but it is potentially fatal. In general, inhaling smoke from a fire, consuming pesticides, polishing metal, and consuming cyanogenic foods are all potential sources of cyanide exposure (2-4). Several plants, including apricot, peach, plum, and cherry contain cyanide glycosides (5,6). Amygdalin was the first cyanogenic glycoside isolated from plants. Amygdalin was originally found in bitter almonds [Prunus dulcis Mill. var. amara (DC.) H. Moore] (7) Amygdalin is found in many Rosaceae seeds and is mostly derived from bitter apricots, semen prunus, almonds, and peach kernel (8).

The amygdalin is hydrolyzed and converted to hydrogen cyanide in the stomach (9). Cyanide binds to ferric iron in the cytochrome oxidase a-a3 complex and inhibits aerobic metabolism. The rate of lactate is increased, due to Krebs cycle disruption, resulting in metabolic acidosis. As a result, cyanide significantly reduces the level of ATP and increases the level of lactate in the brain (10).Patients with delayed diagnosis and treatment have higher mortality and morbidity rates (11). Antidotes such as sodium thiosulfate, sodium nitrite, amyl nitrite, and hydroxocobalamin can be utilized. Though, hydroxocobalamin stands out in its efficacy and safety profile (12,13).

In this article, we aimed to present a rare case of acute symptomatic seizure due to cyanide intoxication with apricot kernel ingestion, is successfully treated with hydroxoycobalamin.

Case Report

A previously healthy 2-year-old girl was admitted to the pediatric emergency department (PED) for loss of consciousness. In the PED, she had generalized tonic clonic contraction of the extremities, staring and pallor lasting for 5 minutes. After the seizure, the initial evaluation revealed post-ictal confusion, tachycardia (174 beats/min) (Figure 1), prolonged capillary refill time (>3s) tachypnea(36/min), and hypotension(66/47mmHg) with low GCS (9/15). Intravenous fluid and dopamine(5mcg/kg/min) infusion were initiated. Her complete blood count, biochemical and coagulation analyzes were within normal limits. Tympanic temperature was 36.7°C, acute phase reactants were negative, and empirical intravenous acyclovir (40mg/kg/day) and ceftriaxone (100mg/kg/day) were administered with high suspicion of encephalitis.

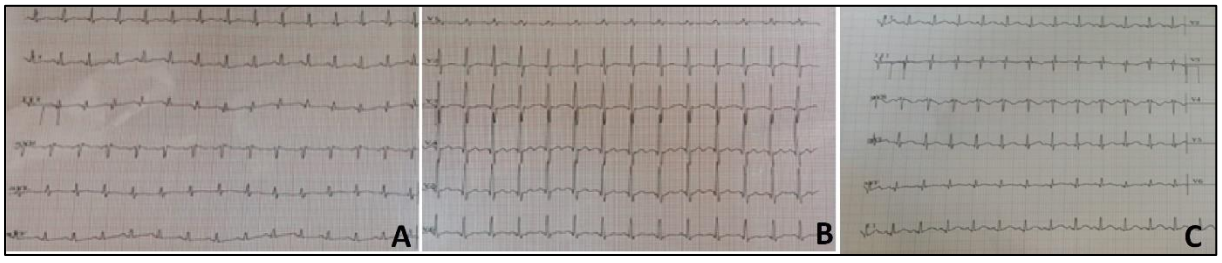


Figure 1. The electrocardiogram of 2-year-old girl with sinus tachycardia performed after acute symptomatic seizure due to cyanide ingestion. A, B are before the treatment with hydroxycobalamin. C is after the treatment with hydroxycobalamin.

As metabolic disorders such as hypoglycemia may produce loss of consciousness accompanied by seizures, the blood glucose (124mg/dL) and ammonia (54µmol/L) levels were normal. High anion-gap metabolic acidosis and high lactate levels were detected in blood gas analysis and sodium bicarbonate replacement therapy was initiated (Table 1). The patient's mother said she ate 10–15 apricot kernels for 45 min before she was collapsed. In the PED, gastric lavage was performed with activated charcoal. Hydroxycobalamin (70 mg/kg/dose) was given by intravenous infusion over one hour as antidote. She was consulted by pediatric cardiologist for sinus tachycardia and mildly elonged QTc(440ms) (Figure 1). Informed consent form is taken from the family.

Discussion

An acute symptomatic seizure is defined as a clinical seizure occurring at the time of a systemic insult or in close temporal association with a documented brain insult by the International League Against Epilepsy. Approximately 25,000 to 40,000 children per year in the United States have a first unprovoked seizure. However, most children do not go on to develop epilepsy later in life. In our case, cyanide poisoning due to apricot kernel consumption provoked an acute symptomatic seizure, and this was successfully managed with hydroxocobalamin.

The main action of cyanide is for the production of essential cellular energy sources of oxygen in the form of ATP. It inhibits oxidative phosphorylation, a process in which it is used. Ingestion of cyanide by inhalation symptoms begin within minutes, and in a few minutes with oral ingestion. Early symptoms are headache, dizziness, confusion, and mydriasis. These symptoms result from brain tissue hypoxia and coma may develop with convulsions afterwards. Early respiratory and cardiovascular findings are tachypnea and tachycardia, followed by apnea, hypotension, and cardiac arrhythmias (14).

Since this clinical picture, which can be fatal, is rare, it can be difficult to recognize by clinicians. Therefore, to consider the oral poisoning by cyanide is important for early diagnosis and treatment. Ünal et al. reported that the symptoms of a 3.5-year-old boy started 45 minutes after he ate the apricot kernels. This period after poisoning is a long period of time that leads to the development of serious symptoms if left untreated. After the patient came to the hospital, 2 cardiac arrests developed and he was resuscitated. After 24 hours, a cyanide antidote kit was found and treatment with an antidote was started. In the brain MRI of the patient, hemorrhagic damage was detected in the bilateral lentiform nuclei. After 12 days of hospitalization, the patient was discharged with neurological sequelae (tetraparesis and rigidity), and tetraparesis continues after 8 months of follow-up (6). In the article of Peddy et al., a 17-year-old male patient with potassium cyanide toxicity, who presented with seizures, apnea and cardiovascular collapse, was reported. In this case, there was a similar clinical picture due to potassium cyanide intake, cardiac arrhythmias, cerebral infarction were observed and resulted in brain death (2). In these two cases, a cyanide antidote kit containing sodium nitrite and sodium thiosulfate was applied as antidote treatment. In the study of Bıcılıoğlu et al., 4 cases aged 2, 2.5, 3 and 3.5 years due to apricot kernel ingestion were presented. Three of these cases were in severe poisoning state. In one, the symptoms developed 30 minutes after the apricot kernel ingestion, and in the other two, 2 hours later. These three cases of severe poisoning were administered hydroxycobalamin at a dose of 70mg/kg after 6 hours,8 hours and 12 hours. All three cases were discharged without any sequelae (15). Our patient was also a case of severe cyanide poisoning and recovered without sequelae for early diagnosis and early hydroxoycobalamin treatment.

Most of the studies on cyanide poisoning in the literature consist of animal experiments. These experiments show that the amount of cyanide administered to observe signs of poisoning in rats or mice represents a relatively large volume compared to that given for the same effect to occur in a human. Rice et al. observed rats for overt signs of toxicity immediately following poisoning across a broad range of doses (4– 128 mg/kg) (16). Sodium nitroprusside (SNP) which is an inorganic cyanogen, is a potent vasodilator commonly used as an anti-hypertensive agent in postoperative cardiac surgical patients. Despite, cyanide toxicity can occur with SNP therapy. Any concentration of sodium nitroprusside exceeding 3.5 mg/kg/min,

based on the Federal Drug Administration, may be fatal to humans. There are certain risk factors that have been associated with the development of harmful levels of cyanide and negative effects in children. Nevertheless, there is a lack of proof regarding the indications and symptoms of toxicity associated with SNP infusions in pediatric patients. (17). Based on the current literature, it appears that there is limited evidence supporting a connection between elevated cyanide levels and symptoms of cyanide poisoning. Although randomized controlled studies with multiple cases of cyanide poisoning due to ingestion of apricot kernels are not available in the literature due to the rarity of their observation, considering the small number of case reports, early diagnosis and early hydroxycobalamin treatment seem to be effective for good results.

In conclusion, clinicians should consider cyanide poisoning in patients who have presented an acute symptomatic seizure, a change in consciousness. Apricot seeds consumption should be interrogated. It should behold that hydroxocobalamin antidote medication administered quickly can save lives.

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Author Contributions: Idea/Concept: I.D.Ç., C.Ç.; Design: I.D.Ç., C.Ç.; Data Collection/Processing: I.D.Ç., C.Ç.; Analysis/Interpretation: I.D.Ç., C.Ç.; Literature Review: I.D.Ç., C.Ç.; Drafting/Writing: I.D.Ç., C.Ç.; Critical Review: I.D.Ç., C.Ç. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Nardone R, Brigo F, Trinka E. Acute Symptomatic Seizures Caused by Electrolyte Disturbances. J Clin Neurol. 2016;12(1):21-33.
2. Peddy SB, Rigby MR, Shaffner DH. Acute cyanide poisoning. Pediatr Crit Care Med. 2006;7(1):79-82.
3. Geller RJ, Barthold C, Saiers JA, Hall AH. Pediatric cyanide poisoning: causes, manifestations, management, and unmet needs. Pediatrics. 2006;118(5):2146-58.
4. Geslain G, Tilea B, Heraut F, Rubinsztajn R. Smoke inhalation injury in a 2-year-old domestic fire victim. Arch Pediatr. 2020;27(4):223-6.
5. Akıl M, Kaya A, Ustyol L, Aktar F, Akbayram S. Acute cyanide intoxication due to apricot seed ingestion. J Emerg Med. 2013;44(2):e285-6.
6. Unal O, Ozen O, Caksen H. Acute Cyanide Intoxication Related to Apricot Seed: The Findings of Cranial Magnetic Resonance Imaging. J Neurol Sci. 2016;33(1);171-6.
7. Yulvianti M, Zidorn C. Chemical Diversity of Plant Cyanogenic Glycosides: An Overview of Reported Natural Products. Molecules. 2021;26(3):719.
8. Zhang D, Ye J, Song Y, Wei Y, Jiang S, Chen Y, et al. Isomerization and Stabilization of Amygdalin from Peach Kernels. Molecules. 2023;28(11):4550.
9. Cigolini D, Ricci G, Zannoni M, Codogni R, De Luca M, Perfetti P, et al. Hydroxocobalamin treatment of acute cyanide poisoning from apricot kernels. BMJ Case Rep. 2011;2011:bcr0320113932.
10. Leavesley HB, Li L, Prabhakaran K, Borowitz JL, Isom GE. Interaction of cyanide and nitric oxide with cytochrome c oxidase: implications for acute cyanide toxicity. Toxicol Sci. 2008;101(1):101-11.
11. Chen F, Jiang L, Yang B. Visual loss caused by acute cyanide poisoning: a case report. Clin Toxicol (Phila). 2011;49(2):121-3.
12. Cmorej P, Bruthans P, Halamka J, Voriskova I, Peran D. Life-Threatening Cyanide Intoxication after Ingestion of Amygdalin in Prehospital Care. Prehosp Emerg Care. 2022;26(3):455-8.
13. Schwarz ES. Inhalants. Crit Care Clin. 2021;37(3):687-702.
14. Graham J, Traylor J. Cyanide Toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. 2023 Feb 13. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507796/

15. Bıcılıoğlu Y, Yıldırım İ, Özkaya PY, Bal A. Pediatric cyanide poisoning after ingestion of apricotseeds. J Pediatr Emerg Intensive Care Med. 2020;7(2):85-8.
16. Rice NC, Rauscher NA, Langston JL, Myers TM. Behavioral toxicity of sodium cyanide following oral ingestion in rats: Dose-dependent onset, severity, survival, and recovery. Food Chem Toxicol. 2018;114:145–54.
17. Moffett BS, Price JF. Evaluation of sodium nitroprusside toxicity in pediatric cardiac surgical patients. Ann Pharmacother. 2008;42(11):1600–4.
18. Thomas C, Svehla L, Moffett BS. Sodium-nitroprusside-induced cyanide toxicity in pediatric patients. Expert Opin Drug Saf. 2009;8(5):599–602.

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):151-152, doi:10.47493/abantmedj.1293401

Multidisciplinary Approach in Planning Health Services

Sağlık Hizmetlerinin Planlanmasında Multidisipliner Yaklaşım

Abuzer ÖZKAN [1*], Kadir ÖZSİVRİ [1]

[1] Department of Emergency Medicine, University of Health Sciences Bağcılar Training and Research Hospital, Istanbul, Türkiye

Geliş Tarihi (*Received*): 06.05.2023 **Kabul Tarihi (*Accepted*):** 06.06.2023 **Yayın Tarihi (*Published*):** 01.08.2023

Dear Editor,

We read the article with great interest the article titled "Does St-Elevation Myocardial Infarction Wait for The Vacation to End?" published in the last issue of your journal in 2022 and prepared by Polat and Demir (1). We thank the authors and editorial board for this interesting and informative article. We congratulate them. However, we would like to talk about spatial analysis that will bring a different perspective to the subject. We would like to emphasize the importance of spatial analysis in health planning.

Accessibility is the ease of access for individuals to anything that provides a purposeful benefit, such as a service, product, or device. İt should also be considered how many users can access any useful situation or activity. The inadequacy and inaccuracies in the physical arrangement of settlements can significantly hinder individuals' access to services. This can occur in people with insufficient physical ability. In the selection of urban equipment (health, fire department, education, etc.), decision-makers should evaluate the accessibility of buildings and services correctly. (2).

As approaching the issue in terms of emergency health units, accessibility is undoubtedly of vital importance for both individual and social emergencies (natural / technological disasters, work / traffic accidents, etc.). Having emergency management stages; Spatial accessibility is a prerequisite for establishing an emergency response management that works in all phases of preparedness, mitigation, response, and recovery, and ensuring the effectiveness of all emergency response tools used (3).

Cardiovascular diseases are the group of diseases that cause the most deaths in developed countries. The situation is not expected to change in the coming years. Coronary artery disease is the most common of these diseases and is associated with high mortality and morbidity. Coronary artery disease is clinically manifested as silent ischemia, stable angina pectoris, acute coronary syndrome, heart failure and sudden death. It is vital that patients get to coronary angiography within hours and minutes (4). At this point, the importance of spatial planning of health centers, especially cardiology centers, emerges. Especially in today's information and communication age, it is not acceptable to not be able to access health services due to distances.

Geographic information systems (GIS) are a system that deals with the management, analysis and presentation of geographic information. Thanks to this system, with the development of the information

Atıf/Cite as: Özkan A. , Özsivri K. Multidisciplinary Approach in Planning Health Services. Abant Med J. 2023; 12(2): 9-10.

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Abuzer Özkan, **e-mail**: ebuzerozkan@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License

sector in every field of daily life, location-based projects are developed and possible solutions for most of the social and technical problems that arise can be made with spatial analysis (5). It is a fact accepted by those concerned that GIS emerged as a decision support system for many institutional entities. As of this content, GIS enables the provision of a quality service as well as its contribution to the efficient use and sustainability of all kinds of resources within the corporate structure. In addition, it is the most effective management support system today in achieving a minimum problematic corporate structure by maximizing the satisfaction of both the service recipient and the service provider (6).

As a result, spatial planning of health centers has a strategic importance, as in the case of acute coronary syndrome. Planning should be done with the joint work of many disciplines such as geography, geomatic engineering, health management, civil engineering, geology and interdisciplinary studies should be carried out.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Author Contributions: Idea/Concept: A.Ö., K.Ö.; Design: A.Ö., K.Ö.; Analysis/Interpretation: A.Ö., K.Ö.; Literature Review: A.Ö., K.Ö.; Drafting/Writing: A.Ö., K.Ö.; Critical Review A.Ö., K.Ö. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

References

1. Polat E, Demir MC. Does St-Elevation Myocardial Infarction Wait for The Vacation to End? Abant Med J. 2022;11(3):312-9.
2. Kemeç S, Kamacı Karahan E, Mert Y. Van Kenti Acil Sağlık Birimlerinin Mekansal Erişilebilirlik Durum Analizi. Yüzüncü Yıl Üniversitesi Fen Bilimleri Enstitüsü Dergisi. 2019;24(1): 22-32.
3. Şahbaz K, Özkan A. Geographical Information Systems and Health. J Exp Clin Med. 2022;39(1):311-2.
4. Özkan A, Sönmez E, Özdemir S, et al. The Diagnostic Value of SCUBE1 in Unstable Angina Pectoris Patients. Eurasian J Emerg Med. 2016;15:167-71.
5. Özdemir S, Şahbaz K. Acil Tıbbi Tedavi Sistemlerin Organizasyonu ve Coğrafi Bilgi Sistemleri. Phnx Med J. 2021;3(3):146.
6. Özdemir S, Şahbaz K. Spatial Analysis and Evaluation of Carbon Monoxide Poisoning Admitted to A Tertiary Hospital- A Pilot Study. Eurasian J Tox. 2020;2(2):35-9.

Derleme / Review

Abant Tıp Dergisi

Abant Medical Journal

Abant Med J 2023;12(2):153-156, doi:10.47493/abantmedj.1196931

Hasta ile İlk Karşılaşma: Yaptıklarım Yeterli mi?

First Encounter with The Patient: Is What I've Done Enough?

Orçun BARKAY [1*], Faruk KARAKEÇİLİ [1]

[1] Erzincan Binali Yıldırım Üniversitesi, Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Erzincan, Türkiye

Geliş Tarihi (*Received*): 31.10.2022 **Kabul Tarihi (*Accepted*):** 19.07.2023 **Yayın Tarihi (*Published*):** 31.08.2023

Öz

Edinsel immün yetmezlik sendromu (AIDS), günümüze kadar birçok yaşamı etkilemiştir. Sadece 2021 yılında yaklaşık 1,5 milyon [1,1-2 milyon] yeni tanı alan olgu ve 650.000 [510.000-860.000] insan immün yetmezlik virusu (HIV) ile ilişkili ölüm saptanmıştır. Kronik aktif bir enfeksiyon olarak tanımlanabilecek olan bu enfeksiyonun yönetiminde hasta ile ilk karşılaşmada yapılması gerekenler hayati önem arz ettiği için tekrar gözden geçirilmesi amaçlanmıştır.

HIV/AIDS rehberleri, kitaplar taranmış ve bu aşamada yapılması önerilenler derlenmiştir.

Hastalık, sadece kişinin fiziksel olarak sağlığını bozmakla kalmayıp ek olarak damgalanma korkusu, aile içi baskı, toplum baskısı gibi birçok psiko-sosyal probleme de neden olmaktadır. Hatta bu durumlar, çoğu zaman hastayı hastalığın seyrinden daha çok etkilemektedir. Tanı ve tedavi öncesinde her hastalıkta olduğu gibi anamnez ve fizik muayene çok önemlidir. Anamnez, diğer hastalıklardan farklı, özellikli olarak daha da derinleştirilerek alınmalıdır. Hastaların hastalığı hakkında her atılacak adımda detaylı olarak bilgilendirilmesi, hasta-hekim güven ilişkisi kurulması gereklidir. Tanı, tedavi ve takipte viral yük, CD4 pozitif T lenfosit sayısı gibi spesifik ve hemogram, biyokimyasal parametreler gibi non-spesifik testler istenmelidir. Gerekirse diğer branşlar ile iş birliği içinde hasta yönetilmelidir.

HIV/AIDS yönetiminin temelini hasta ile ilk görüşme oluşturmaktadır.

Anahtar Kelimeler: AIDS, HIV, Yönetim

&

Abstract

Acquired immunodeficiency syndrome (AIDS) has affected many lives until today. In 2021 alone, approximately 1.5 million [1.1-2 million] newly diagnosed cases and 650,000 [510,000-860,000] human immunodeficiency virus (HIV)-related deaths were detected. It is aimed to review this situation as it is vital that what should be done in the first encounter with the patient at the management of this infection which can be defined as a chronic active infection.

HIV/AIDS guidelines and books were reviewed and suggested to be done at this stage were compiled.

The disease not only impairs the physical health of the person, but also causes many psycho-social problems such as fear of stigma, family pressure, and social pressure. In fact, these conditions often affect the patient more than the course of the disease. Before diagnosis and treatment, anamnesis and physical examination are very important as in any disease. The anamnesis should be specifically taken further, unlike other diseases. It is necessary to inform patients about their disease in detail at every step taken, and to establish a patient-doctor trust relationship. Specific tests such as viral load, CD4 positive T lymphocyte count and non-specific tests such as complete blood count and biochemical parameters should be requested in diagnosis, treatment and follow-up. If necessary, the patient should be managed in cooperation with other specific branches.

The basis of HIV/AIDS management is the first interview with the patient.

Keywords: AIDS, HIV, Management

Atıf/Cite as: Barkay O. , Karakeçili F. Hasta ile ilk karşılaşma: Yaptıklarım yeterli mi?. Abant Med J. 2023; 12(2): 9-10.

Copyright © Published by Bolu Abant Izzet Baysal University, Since 2022 – Bolu

[*]**Sorumlu Yazar (Corresponding Author):** Orçun Barkay, **e-mail**: orcun.barkay@erzincan.edu.tr

This work is licensed under a Creative Commons Attribution 4.0 International License

Giriş

Klinik bir tablo olarak ilk kez 1981 yılında tanımlanan edinsel immün yetmezlik sendromu (AIDS) epidemisi, günümüze kadar yaklaşık 40,1 milyon [33,6-48,6 milyon] yaşamı etkilemiştir. 2021 yılında yaklaşık 1,5 milyon [1,1-2 milyon] yeni tanı alan olgu dikkati çekmektedir. Yine 2021 yılında 650.000 [510.000-860.000] kişi insan immün yetmezlik virusu (HIV) ile ilgili nedenlerden dolayı hayatını kaybetmiştir (1). İnsan immün yetmezlik virusu (HIV) enfeksiyonu, kabaca kronik aktif bir enfeksiyon olarak tanımlanabilir. Yıllar içinde hastalarda akut ve kronik değişimler gözlenebilir. Hasta ile ilk karşılaşmada atılması gereken her adım hastanın ve hastalığın yönetiminde hayati önem taşımaktadır. Kronik aktif bir enfeksiyon olarak tanımlanabilecek olan bu enfeksiyonun yönetiminde hasta ile ilk karşılaşmada yapılması gerekenler hayati önem arz ettiği için tekrar gözden geçirilmesi amaçlanmıştır.

Gereç ve Yöntemler

HIV/AIDS rehberleri, kitaplar taranmış ve bu aşamada yapılması önerilenler derlenmiştir.

Bulgular

Diğer kronik hastalıklardan farklı olarak bulaşıcı bir hastalık olması nedeniyle toplum sağlığı için önem arz etmektedir. Ancak asıl önemli nokta, hastalığın daha tanı aşamasında hastaların toplum içindeki konumlarını, mesleklerini ve dolayısıyla ekonomik durumlarını, aileleriyle ilişkilerini, psiko-sosyal durumlarını yani tamamıyla yaşam kalitelerini etkileyebilmesidir. Bu durum maalesef HIV enfeksiyonuna sahip bireylerin damgalanma korkusu yüzünden gelişmektedir. Hastaların çoğu hastalığın seyrinden daha çok bu durumdan etkilendiklerini ve bu durum ile uğraşmak zorunda kaldıklarını ifade etmektedir.

Her hastalıkta olduğu gibi HIV enfeksiyonunda da anamnez ve fizik muayene çok önemlidir. Ancak hastalardan alınacak olan anamnezin klasik anamnezden farklı yönleri mevcuttur. Özellikle damgalanma korkusu nedeniyle bu hastalara psiko-sosyal danışmanlık da sağlanmalıdır. Laboratuvar tetkikleri ve görüntüleme yöntemleri ise hastaların bazal durumlarının değerlendirilmesi ve eşlik edebilecek olan komorbiditeler, fırsatçı enfeksiyonlar gibi durumların saptanması için kullanılmaktadır (2,3).

Maddeler halinde ilk karşılaşmada yapılması gerekenler şu şekildedir:

Bilgilendirme (2,3):

- Hastanın, mevcut durumu ve hastalığı hakkında detaylı olarak bilgilendirilmesi (Anti-HIV pozitifliği sonrasında ve doğrulama testi sonrasında),
- D-86 formunun doldurulması,
- Eşin bilgilendirilmesi (öncelikle hastadan partnerini bilgilendirmesi istenir)

gereklidir.

Anamnez (2,3):

Klasik anamneze ek olarak:

- Mesleği, işi (sosyo-ekonomik ve sosyo-kültürel durum),
- Nerede, kiminle yaşadığı,
- Hayvan besleme öyküsü,
- Seyahat öyküsü,
- Olası bulaş yolu, zamanı,
- Cinsel yönelimi ve davranışları,
- Alışkanlıkları (sigara, alkol, madde vb. kullanımı),
- Ailesiyle ilişkili durumları,
- HIV ilişkili belirtileri,
- Tıbbi özgeçmişi,

- Durumu hakkında farkındalık düzeyi

sorgulanmalıdır.

Duruma göre tekrarlayan görüşmeler yapılmalıdır.

Fizik muayene:

Eksiksiz bir sistemik muayene yapılmalıdır.

- Ek olarak; göz dibi bakısı, özellikle lenfatik sistemin değerlendirilmesi, nörolojik muayene yapılmalı,
- HIV ilişkili hastalıkların bulguları özellikle aranmalı,
- Kardiyovasküler risk hesaplanmalıdır.

Laboratuvar ve görüntüleme tetkikleri (2-4):

İlk anti-HIV pozitif test sonucu, doğrulama testi sonucu hasta dosyasına eklenmelidir.

- CD4 T lenfosit düzeyi,
- Viral yük düzeyi,
- Hemogram, geniş biyokimya, TİT,
- Serolojik testler,
- Kemik mineral dansitometri,
- Elektrokardiyogram,
- Akciğer grafisi,
- PPD/IGRA,
- Genotipik direnç testi,
- HLA-B*5701,
- PAP-smear,
- Semptom ve bulgulara göre gerekli olan radyolojik görüntülemeler

yapılmalı ve dosyaya eklenmelidir.

Konsültasyonlar:

Hastanın klinik belirti ve bulgularına göre gerekli konsültasyonlar istenmelidir.

Sonuç

Hepsinden önemlisi hasta-hekim ilişkisi kurulmalı, hastanın güveni kazanılmalı; hastaya hastalığı ve durumu hakkında soru işaretleri bırakmadan tam bir bilgilendirme yapılmalı, bu süreçte yalnız kalmayacağı hissettirilmelidir. Son olarak; hasta tedaviye hazırlanmalı ve hastanın tedavi-takip sürecine maksimum uyumu sağlanmalıdır.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Yazar Katkıları: Fikir/kavram: O.B., F.K.; Tasarım/Dizayn: O.B., F.K.; Danışmanlık: O.B., F.K.; Veri toplama/işleme: O.B.; Analiz/Yorum: F.K.; Literatür Tarama: O.B.; Taslak/makale yazma: O.B., F.K.; Eleştirel İnceleme: O.B., F.K. Yazarlar bu yazının tüm içeriğinin sorumluluğunu kabul etmiş ve yayınlanmak için gönderilmesini onaylamıştır.

Kaynaklar

1. World Health Organization. HIV Key Facts [Internet]. (cited 2022 Oct 14). Avaliable from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids)

2. Gokengin D, Kurtaran B, Korten V, Tabak F, Ünal S. HIV/AIDS Tanı İzlem ve Tedavi El Kitabı. 2nd rev. ed. Türkiye: Türk HIV/AIDS Platformu; 2021.
3. European AIDS Clinical Society. EACS Guidelines version 11.0, October 2021. (cited 2022 Oct 14). Avaliable from: https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf
4. Simonetti FR, Dewar R, Maldarelli F. Diagnosis of Human Immunodeficiency Virus Infection. In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Philadelphia, USA: Elsevier, 2019. P. 138-39.

Abant Medical Journal