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Kan Ürünleri Tedarik Zinciri

Blood Products Supply Chain

Gizem Gül Koç Ali Kokangül

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ABSTRACT

In daily life, blood products are transfused as part of medical treatments or surgical operations. This shows that stock management is very important, in case of need, if the desired blood product or products are not in the stock, the patient may be lost. On the other hand, collecting blood is an action that requires constant effort; in countries where donation is voluntary, many factors such as comfort, risks, convenience and accessibility can affect the donation decision. However, due to the pandemic process in recent years, blood donations have decreased in Turkey as well as in the world. When immigration from foreign countries is added to this, blood supply chain and stock management has become more important than ever in order to procure blood, separate it into its products, store it and deliver it to patients on time. The blood supply chain consists of giving blood and blood products from the donor to the recipient, that is, the person in need of blood, testing the blood product especially for infectious diseases before giving it to the patient, processing it to separate it into its products, and finally the relevant hospital, health center, intensive care units and distribution to services. However, whatever the circumstances, sufficient blood must be collected to meet the blood demand. In supply chain terminology, a good infrastructure is needed to match supply and demand, and to collect, process and distribute blood and its products. Although different configurations of the blood supply chain are implemented in hospitals in different countries of the world, the aim is the same, that is, to meet the demand for blood products with minimum cost and minimum waste. Scientists have dealt with the issue from different perspectives and carried out different studies in order to improve each process from the donation stage to the transfer stage to the patient. The most important of these studies are the simulation of the process and the researches on the supply chain.

ÖZET

Günlük hayatta gerek tıbbi tedaviler veya cerrahi ameliyatların bir parçası olarak kan ürünleri nakli yapılmaktadır. Bu durum stok yönetiminin çok önemli olduğunu gösterir, zira ihtiyaç durumunda stokta istenen kan ürünü veya ürünleri yoksa hasta kaybedilebilir. Öte yandan kan toplamak sürekli bir çaba gerektiren bir eylemdir; bağışın gönüllü olduğu ülkelerde konfor, riskler, kolaylık ve erişilebilirlik gibi birçok faktör bağış kararını etkileyebilir. Ancak son yıllarda pandemi süreci nedeni ile dünyada olduğu gibi Türkiye'de de kan bağışları azalmıştır. Buna dış ülkelerden göçler de eklenince kanı tedarik etmek, kanı ürünlerine ayrıştırmak, depolamak ve hastalara zamanında ulaştırmak adına kan tedarik zinciri ve stok yönetimi her zamankinden daha da önemli hale gelmiştir. Kan tedarik zinciri, kan ve kan ürünlerinin donörden yani kan bağışında bulunan kişiden alıcıya yani kan ihtiyacı olan kişiye verilmesi, kan ürününü hastaya verilmeden önce özellikle bulaşıcı hastalıklar yönünden test edilmesi, ürünlerine ayrıştırmak için işlenmesi ve nihayetinde de ilgili hastane, sağlık merkezi, yoğun bakım üniteleri ve servislere dağıtılması süreçlerini içerir. Ancak koşullar ne olursa olsun kan talebini karşılamak için yeterli miktarda kan toplanması gerekir. Tedarik zinciri terminolojisinde arz ile talebin eşleştirilmesi, kan ve ürünlerinin toplanması, işlenmesi ve dağıtılması için iyi bir altyapıya ihtiyaç vardır. Kan tedarik zincirinin farklı konfigürasyonları, dünyanın farklı ülkelerindeki hastanelerde uygulanmakla birlikte amaç aynıdır yani kan ürünleri talebini minimum maliyet ve minimum israfla karşılamaktır. Bilim insanları farklı bakış açılarıyla konuyu ele almış bağış aşamasından hastaya nakil aşamasına kadar geçen süredeki her bir süreci iyileştirme adına değişik çalışmalar yürütmüşlerdir. Bu çalışmalardan en önemlileri sürecin simüle edilmesi ve tedarik zincirine yönelik yapılan araştırmalardır.

Keywords:
Blood
Blood products
Donor
Supply chain

Anahtar Kelimeler:
Kan
Kan ürünleri
Donör
Tedarik zinciri

GİRİŞ

Kan ve kan ürünlerinin yönetimi insan ırkını özel olarak ilgilendiren bir sorundur. Kan ürünlerini elde etme aşamasında teknolojik gelişmeler olsa da donör kanına ve kandan üretilmiş ürünlere her zaman ihtiyaç olacağı kaçınılmaz bir gerçektir (1).

Kan sıradan bir doku örneği değildir. Bu derlemede kanın elde edilmesinden hastaya nakledilmesine kadar geçen süreç olarak ifade ettiğimiz kan tedarik zinciri, bu süreci etkileyen faktörler, bu problemler için getirilen çözüm önerileri gözden geçirilmiş, pandemi sürecinden geçtiğimiz şu günlerde konunun önemine dikkat çekilmek istenmiştir.

KAN BAĞIŞINI ETKİLEYEN FAKTÖRLER; DOĞAL AFETLER, PANDEMİ VE GÖÇLER

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yüzlerce insanın kan nakline ihtiyacı olmaktadır. Donör kan bağışı oldukça düzensizdir (1). Burada deprem, sel gibi doğal afetler, savaş ve pandemiler gibi olağanüstü durumların etkisi büyüktür. Bireyler, afetlerden sırasında kan bağışında bulunmaya isteklidir (2). Bununla birlikte, COVID-19 gibi bir pandemi diğer krizlerden çok farklıdır. Birincisi, doğal afetler ve savaş durumu gibi krizlerin aksine pandeminin herhangi bir birey için doğrudan bir sağlık tehdidi oluşturma potansiyeli olmasıdır. Bir kriz durumunda bireyler, etkilenen mağdurlara kıyasla kendilerini ayrıcalıklı hissedip yardım etme çabası içinde olsalar da söz konusu krizden kendileri etkilendiklerinde başkalarına yardım etme konusundaki kişisel yükümlülük duyguları azalabilir. İkincisi, COVID-19 son derece bulaşıcı olup hükümetler, şirketler ve bireyler için benzeri görülmemiş sorunlara yol açan kişinin kendisinin ve çevresinin sağlığına yönelik bir tehdittir. Hastalığın bulaşma riski algısı ve giderek zorlaşan koşullar (yani kısıtlamaların hafifletilmesi ve sıkılaştırılması) donör davranışını olumsuz yönde etkilemiştir. Mart 2020'de Almanya'da pandemiyi kontrol altına almak adına tüm nüfusa yönelik önlemlerin alınmasını takip eden ilk haftalarda daha az kan bağışı randevularının olması dikkat çekicidir. Bu durum pandemi nedeni ile çoğu hastane veya servislerin pandemi servisine dönüştürülmesi, rutin ameliyatlar ve tıbbi tedavilerin ertelenmesi dolayısı ile pandeminin başlangıç döneminde kan ihtiyacının azalması ile açıklanabilir (3). Ancak takip eden haftalarda, dünya genelinde tüm kan merkezleri bağışçı sayısında önemli azalmalar olduğunu ve stokların alarm verdiğini bildirmiştir (2). Bunda elektif ameliyatların yeniden yapılmaya başlanmasının rolü büyüktür. Nitekim dünya çapında yaklaşık 28,4 milyon planlı ameliyatların (%72,3) COVID-19 nedeniyle ertelendiği bildirilmiştir (4). Bu tablo uzun vadede daha yüksek bir kan talebini doğurmuştur. Pandemi ile ilgili diğer bir problem uzun yıllar sürecek olması, gönüllü kan bağışının pandemiden sonra bile ciddi şekilde etkilenebileceği bu durumun kan bankaları ve toplum için ciddi sonuçlar yaratabileceğidir. Tam da burada etkin kan bağışı/donör yönetimi çok önemlidir, çünkü özellikle bir bağışın üzerinden ne kadar çok zaman geçerse, bağışçının yeniden bağış yapma olasılığı o kadar azalmaktadır (5). Pandemi kadar önemli bir diğer sorun dış göçlerdir. Zira göçmen vatandaşlardan kan bağışı alınmadığı gibi ihtiyaçları durumunda Kızılay stokunda bulunan kan/kan ürünleri kullanılmaktadır. Bütün bu nedenler kanı tedarik etmek, kanı ürünlerine ayrıştırmak, depolamak ve hastalara zamanında ulaştırmak adına kan tedarik zinciri ve stok yönetimini her zamankinden daha da önemli hale getirmiştir. Zira ihtiyaç durumunda stokta istenen kan ürün veya ürünleri yoksa hasta kaybedilebilir. Bu olasılık, kan tedarik zinciri için karar vermenin oldukça önemli ve zor bir süreç olduğunu göstermektedir.

KAN TEDARİK ZİNCİRİ

Dünya Sağlık Örgütü (DSÖ) kan bağışçılarını gönüllü bağışçılar, takas ve paralı bağışçılar olmak üzere üç başlık altında toplamıştır. Kan ve kan ürünlerinin, toplanması, bir takım testlere tabii tutulması, ürünlerine ayrılması, depolanması, dağıtımı ve hastaya nakil süreçlerinin geneline kan tedarik zinciri denir. Her ne kadar kan bağışının büyük bir oranı gönüllü bağış ve takasa dayansa da bağış noktalarına ulaşım, kanın ürünlerine ayrıştırılması işlemi, depolama ve dağıtım hizmetleri beraberinde maliyeti de getirmektedir.

Genel olarak, verimli bir kan tedarik zinciri talebi karşılamalı ve aynı zamanda israfı ve maliyetleri en aza indirmelidir. Bağışçı gönüllüğü, bağış noktasına ulaşım (mesafe/maliyet), kan merkezindeki personelin bağışçıya yaklaşımı, kan alınmasından ürün çıktısına kadar geçen sürenin yönetimi, kan ürünlerini sınırlı raf ömrü, yetersiz stok gibi pek çok bileşen tedarik zincirinde aksaklıklara yol açar. Sistemin uygunluğu, özellikleri ve karmaşıklığı göz önüne alındığında, tüm aşamalarında karar verme sürecini desteklemek için sağlam metodolojiler geliştirmek gerektiği, insan hayatı tehlikede olduğunda, kan tedarik zincirinin gerçek dünyadaki önemi aşikardır.

KAN TEDARİK ZİNCİRİ PROBLEMLER VE ÇÖZÜM ÖNERİLERİ

Katsaliaki ve Brailsford'a göre, ürünler ve alt ürünler dahil olmak üzere kandan yüzden fazla farklı ürün elde edilebilir ki eritrositler ve trombosit suspansiyonu, plazma, ve kriyopresipitat bunların en önemlileri olarak kabul edilir (6). Kan ve kan ürünlerinin kendine has özellikleri vardır. Kan grupları, uyumlulukları ve kan ürünlerinin farklı raf ömürleri gibi faktörler karar verme sürecini karmaşık hale getirmektedir. Trombosit ve eritrosit suspansiyonu, taze donmuş plazma plazma ve kriyopresipitatın farklı raf ömürleri vardır. Trombositler sadece 5 günlük raf ömrü ile en kritik bileşendir, bunu 42 gün ile eritrosit ve son olarak bir yıl ile plazma ve kriyopresipitat takip eder. Bu, bir kan ürününün raf ömrü sona ermeden önce transfüze edilmemişse imha edilmesi gerektiği anlamına gelir.

Sağlıklı, süreğen ve ucuz kan temini ile ilgili ürünün bozulabilirliği göz önüne alınarak "bozulabilir envanter" yönetimi ile ilgili kapsamlı bir literatür vardır. Kan tedarik zinciri, 1960 yılından bu yana araştırmacıların ilgi odağı olmuş, konuya ilgi 1970-1980'li yıllarda giderek artmıştır. Özellikle bozulabilir olması gerçeğinden hareketle, etkili yöntemlerin geliştirilmesine çalışılmıştır (7).

Veinott, durağan talep varsayımı altında bir periyodik gözden geçirme politikası geliştirmiştir. Sonuçlar, bozulabilir envanter için optimal sipariş politikalarının, bozulmayan duruma yakından karşılık geldiğini göstermektedir. Optimal sipariş miktarları, Q* ekonomik sipariş miktarı (EOQ), talep oranı ve ömür formülü (EOQ = Q* = $\sqrt{2}$ AD/2) ile hesaplanır (8). Rasgele arz ve rasgele talep karşısında kan teminini aksaksız bir şekilde sürdürebilmek için yeterli düzeyde kan stoğuna sahip olmak gerekir.

Jennings'e göre kan merkezlerinde envanter kontrolünde ortaya çıkan problemler birkaç nedenden dolayı son derece karmaşıktır. Bunun nedenleri;

1. Arz ve talebin rastgele olması,
2. Yapılan çalışmalarda belirli bir hasta için talep edilen, cross-match (hastanın ve kan verecek kişinin kanlarının uyumlu olup olmadığını belirleyen süreç) yapılan ve hastanın kullanımı için rezerve edilen kanların yaklaşık %50'sinin sonuçta o hasta için gerekli olmadığının belirlenmiş olması,
3. Kanın bozulabilir bir ürün ve mevcut yasal ömrünün en fazla 21 gün ile sınırlı olması,
4. Her kan merkezinin tipik olarak bir dizi başka kan

merkezi ile etkileşime ve iletişime girmesidir (9).

Pierskalla ve Roach, çabuk bozulan envanter problemini çözme adına sistemin verimliliğini maksimize etmek, karşılanmayan kan/kan ürün miktarını ve kullanılamayan çok eski tarihli kan/kan ürünlerinin miktarının azaltmak olmak üzere üç amaç fonksiyonu belirlemiştir. Bu amaç fonksiyonları için First in First Out (ilk giren ilk çıkar yöntemi - FIFO) yönteminin optimal olduğunu göstermeye çalışmışlardır. Bunu kanıtlamak için bir dinamik programlama formülasyonu kullanmışlardır. FIFO yöntemine göre kanlar sıraya alınır. Bu sıra, kan/kan ürünlerinin temin edilme tarihine göre belirlenir. Önce stoğa giren kan listenin başında yer alırken daha sonra stoğa giren kanlar listede arka sıralara yerleştirilir. Bu şekilde sıralama yapıldıktan sonra kan/kan ürünlerinin kullanımı listeye göre gerçekleştirilir. Böylece kan/kan ürünlerinin imha edilmesinin önüne geçilmiş olur. Nitekim çalışmalarının sonunda FIFO yönteminin tüm amaç fonksiyonları için en iyi uygulamalardan biri olduğunu kanıtlamışlardır (10). Brodheim ve ark., Markov zincir yaklaşımı kullanarak kan/kan ürünlerinin ortalama raf ömrü ve ortalama imha süreleriyle ilişkili bir envanter modeli geliştirmiştir (11). Pierskalla ve ark., kan bankacılığı tedarik zincirini stratejik yönden ele almışlar ve

1. Kan bankacılığı hangi lokasyonlarda yapılmalı,
2. Kan bağışı alma ve kan nakli (transfüzyon hizmetleri), hangi kan merkezlerine verilmeli,
3. Bir bölgede kaç tane kan merkezi olmalı,
4. Kan merkezleri nerede olmalı ve
5. Talep ve arz nasıl koordine edilmeli gibi sorulara cevap bulmaya çalışmışlardır (12).

Bu sorular dışında kan alma, birden fazla kan ürünü elde etme, envanter seviyelerini belirleme ve kontrol etme, kanın hastanelere tahsisi, birden fazla bölgeye kan ve kan ürünleri verme gibi konularda optimal kararlar alma ile ilgili birçok taktiksel operasyonel yöntemler hakkında bilgiler aktarmışlardır (12).

Kendall ve Lee, Bölgesel Kan Merkezleri'nde kan/kan ürünlerinin bozulmasını dolayısı ile imha edilmesini azaltmak, transfüze edilen kanların kalitesini artırmak, aynı zamanda kan merkezindeki maliyetleri ve stokta ürün bulundurmamaktan kaynaklanan maliyetleri kabul edilebilir seviyede tutabilmek için hedef programlama yöntemini kullanmıştır. Stok seviyeleri, ulaşılabilir taze kan, kanın bozulması, üretim tarihi ve kan toplama maliyetini programlamanın hedef kısıtları olarak belirlemişlerdir. Çalışma sonucunda, fazla kan/kan ürünü stoklamanın önüne geçilmiş, yeterli sayıda taze kan talepleri karşılanmış ve sonuçta ihtiyaç duyulan donör miktarı azaltılmıştır (13).

Prastacos ve Brodheim, Programlanmış Kan Dağıtım Sistemi (PBDS) adı verilen prototip bilgisayar tabanlı bir yazılım programı geliştirmişlerdir. Bu program ile

1. Bölgede ihtiyaç duyulan minimum ulaşılabilir kan/kan ürünü miktarı,
2. Kan ürünlerinin yeterli olmadığı durumlarda yapılması gereken B planı,
3. Bu hedefe ulaşmak için gerekli etkin kan dağıtım politikası,
4. Alternatif hedeflere ulaşmak için bölgesel arz düzeyi gibi soruların cevabını bulmaya çalışmışlardır (14).

Omosigho, bozulabilir ürünlerin kullanım olasılığını hesaplamak için genel bir formül öne sürmüştür. Bir ürünün sabit ömürlü bozulabilir envanter sisteminde kullanılma olasılığı için bir tahmin edici önermiş ve bu tahmin ediciyi sistemin önemli çalışma özelliklerini belirlemek için kullanmışlardır. Sabit bozulabilir envanter sisteminde, en önemli performans ölçütleri olan arzı karşılayamama ve bozulmayı matematiksel ifadelerle ortaya koymuşlardır. Çalışma sonucunda FIFO yönteminin pratikte oldukça işe yarar bir uygulama olduğunu bildirmişlerdir (15).

Rytila ve Spens, kan tedarik zincirini daha etkili yönetebilmek için eksik kan ürünü miktarı ve içeriği, donörden kan temin etme süresi, eski tarihli ürünleri azaltma gibi değişik faktörleri dikkate alan farklı senaryoları simülasyon programı ile çalışmışlar, sonuçta farklı kan gruplarındaki bozulmaları azaltmayı ve stok maliyetini minimize etmeyi başarmışlardır (16). Erickson, bir hastane Kan Merkezi'nde, kan tedarikinin sürdürülebilirliğini sağlamak adına kapsamlı bir acil eylem planı geliştirmiştir. Çalışmasında değişik acil durum senaryoları oluşturup, problemlerin çözümüne dayalı bilgisayar tabanlı bir felaket tahmin modeli tasarlamıştır (17). Ghandforoush ve Sen, mobil kan merkezlerinde trombosit üretimi ve bu ürünün kan merkezlerine etkin dağıtılmasında karar destek sistemini kullanmışlardır. Bu yöntem ile talep ve tedariğin çok hızlı karşılanmasını sağlamış, fazla stoğun önüne geçerek maliyeti minimalize etmişlerdir (18). Zhou ve ark., yaptıkları simülasyon çalışmalarında küçük hastanelerin gün aşırı, yoğun hastanelerin günlük kan sipariş vermesi gerektiğini göstermişlerdir (19).

Stanger ve ark., en iyi uygulama ilkelerini belirlemek için hastane transfüzyon laboratuvarlarındaki eritrosit envanter yönetimine odaklanmış ve kullanım süresi dolmasından kaynaklanan kayıpları minimalize edecek önerilerde bulunmuşlardır. Çalışmaya dahil edilen hastanelerde transfüzyon laboratuvarı yöneticileri ile düşük israf ve iyi envanter yönetimi uygulamalarının etkenlerini belirlemeye çalışmışlardır. En iyi envanter yönetiminin karmaşık envanter modelleri ve algoritmalarının kullanılması olduğu, yetenekli, hizmet içi düzenli eğitim alan, deneyimli transfüzyon laboratuvarı personeli varlığının, elektronik çapraz eşleşme (cross-match), envanterin şeffaflığı ve basit yönetim prosedürlerinin performansı iyileştirdiğini göstermiştir (20). Li ve Liao, bir kan tedarik zincirindeki optimal parametreleri tahmin etmek için sinir ağları ve genetik algoritmalarla birleştirilmiş Taguchi yöntemini kullanarak bir model geliştirmiştir. Bu yöntem, metodoloji, optimal minimum ve maksimum envanterlerin yanı sıra donörlerin kan merkezlerine ulaşım yüzdesinin oranının bulunmasını sağlamaktadır (21). Duan ve Liao, rutin dışındaki kan taleplerini karşılayamama yüzdesini en aza indirmeyi amaçlayan bir optimizasyon modelinde belirsizliği dahil ederek bozulabilir ürünlerin tedarik zinciri envanter yönetimi için bir simülasyon optimizasyon modeli önermişlerdir (22).

Elston ve Pickrel, bir hastane Kan Merkezi'nde kan sipariş ve kullanım politikalarını belirlemek için simülasyon çalışması yapmışlar, çalışmalarında daha önce söylenenlerin aksine en uygun stok seviyelerinin

son kullanma tarihi en eski olan kan veya ürününün ilk önce kullanılmasıyla gerçekleşmediğini ve bu uygulamanın en iyi politika olmadığını ileri sürmüşlerdir. Kan merkezinden talep edilen kan veya kan ürününün son kullanım tarihinin dikkate alınmadığı durumlarda bozulmaların en az olacağını belirtmişlerdir. Bunun aksine talep edilen kanın son kullanım tarihleri dikkate alınarak yeni hazırlanan ürünlerin öncelikli olarak kullanıldığı durumlarda bozulmaların biraz daha fazla olabileceğini ortaya koymuşlardır (23). Tam kan envanteri problemini sınıflandıran ilk çalışma Jennings tarafından yapılmıştır. Jennings, hastane Kan Merkezi'nin performansını değerlendirmek için simülasyon modeli kullanmıştır. Envanterin geçmiş bilgilerini ve eksikleri gösteren takas eğrilerini keşfeden ilk araştırmacıdır. Jennings, kan tedarik zincirinin nasıl işlediğinin temellerini açıklamıştır ve performansın 3 temel ölçütünün ürünün olmaması, israf, nakliye ve maliyeti olduğunu ileri sürmüştür (9).

Cohen ve Pierskalla, muhtemel yeterli kan temin edememe yüzdesine ait problemleri göz önünde tutarak yeterli eritrosit teminini sağlamak için basit bir karar modeli önermişlerdir. Regresyon teknikleri ile simülasyon yöntemlerini birlikte kullanarak, günlük talep, ortalama aktarım, cross-match oranı ve cross-match serbest bırakma süresine bağlı olan bir hedef stok yöntemi geliştirmişlerdir. Modelleme tekniklerini, mevcut envanterde minimum toplam maliyetle maksimum düzeyde yararlanmayı sağlayacak birkaç kritik noktada, karar vermeye izin verecek şekilde genişletmişlerdir (24). Brennan ve ark. bir Kan Merkezi'nde üç farklı senaryo üzerinden simülasyon modeli oluşturmuş, donörlerin kuyrukta bekleme oranlarını ve birimler arası transfer sürelerini minimalize etmeyi hedeflemişlerdir. İki, üç birimdeki süreçleri birleştirerek, donör kabul, kuyrukta bekleme ve kanın ilgili yere transfer sürelerini azaltmışlardır (25). Fontaine ve ark., bir Kan Merkezi'nde transfüze edilen ışınlanmamış eritrosit veri setini analiz ederek stoktaki torbalanmış eritrositlerin ortalama yaşını belirlemişlerdir. Raf ömürleri farklı olan kanlar için geliştirdikleri simülasyon modelinde altı senaryo tanımlamışlardır. Daha kısıtlayıcı raf ömür kuralları uyguladıklarında eritrositlerin hazır bulunma oranlarında artış, bozulma oranlarında ise düşüş olduğunu saptamışlardır (26).

Kan/kan ürünün temin etme onu etkin kullanma adına hükümetler, klinisyenler, biyologlar, mühendisler ortak çalışmalara imza atıp etkin stok yönetimi, maliyeti ve imhayı minimalize etme adına ortak çalışmalar yürütmektedir. Bu çalışmalar tabi ki çok kıymetlidir. Bir diğer önemli nokta kayıtlı donörleri davet etme ve onları kan vermeye özendirmedir. Wevers ve ark. yaptıkları çalışmada davet edilen bağışçıların %55'inin bağış için geri döndüğünü, %45'inin ise geri dönmediğini ortaya koymuştur. Geri dönmeye karar veren ve geri dönmeyen bağışçıların özellikleri araştırıldığında yaş almış erkek bağışçıların geri dönme olasılıklarının daha yüksek olduğu görülmüştür. Benzer demografik özellikleri taşıyan kadınlarda da bu oran yüksek olmakla birlikte erkek cinsiyete göre düşük olduğu belirlenmiştir. Kan merkezine kan bağışı yapmayacaklarını bildiren bağışçıların öne sürdükleri en önemli nedenin yeterli zamanlarının olmamasıdır. Ayrıca baş ağrısı varlığı gibi kan bağışına engel teşkil etmeyen genel fiziksel problemler nedeniyle bağışı ertelemeyi tercih ettikleri de dikkati çekicidir. Bu durum donörlerin kan transfüzyonunun aciliyet gereken bir durum olduğunun farkında olmadıklarını göstermektedir.

SONUÇ

Kan tedarik zinciri bağışçıdan ürünün hastaya transfüzyonun kadar geçen bir halkalar silsilesidir. Bu basamaklardan herhangi birindeki aksama donör ve hasta için hayati komplikasyonlara neden olabilir. .Bu sürecin sağlıklı yürümesi adına her kan merkezinde tedarik zincirine yönelik matematiksel modellemeler yapılmalıdır. Zira her kan merkezinin kendi içinde farklı kan ürünü ihtiyacı, bölgesel ve yönetimsel özellikleri olabilir.

Çıkar Çatışması: Yazarlar bu çalışmada herhangi bir çıkara dayalı ilişki olmadığını beyan etmişlerdir.
Etik: Etik izin gerekmemektedir.
Finansal Destek: Yazarlar bu çalışmada finansal destek almadıklarını beyan etmişlerdir.
Son onay: Tüm yazarlar tarafından onaylanmıştır.
Bu makale "Kan Ürünleri Tedarik Zinciri Optimizasyonu" başlıklı doktora tezinin genel bilgilerinden derlenmiştir.

KAYNAKLAR

1. Belien J, Force H. Supply chain management of blood products: A literature review. European Journal of Operational Research. 2012; 217(1):1-16.
2. Veseli B, Sandner S, Studte S, Clement M. The impact of COVID-19 on blood donations. Plose One PLoS One. 2022;17(3):e0265171.
3. Haw J, Holloway K, Masser B, Merz EM, Thorpe R. Blood donation and the global COVID-19 pandemic: Areas for social science research. Vox Sang. 2021;116(4): 363–365.
4. COVID Surg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: Global predictive modelling to inform surgical recovery plans. Br J Surg. 2020;107(11): 1440–1449.
5. Thomas SA, Feng S, Krishnan TV. To retain? To upgrade? The effects of direct mail on regular donation behavior. Int J Res Mark. 2015;32(1): 48–63.
6. Katsaliaki K, Brailsford SC. Using Simulation to Improve the Blood Supply Chain. Operational Research for Emergency Planning in Healthcare. 2007(1): 353-372.
7. Nahmias S. Perishable Inventory Theory: A Review. Operations Research. 1982;30(4): 680–708.
8. Veinott AF. Optimal Policy for a Multi-Product, Dynamic, Nonstationary Inventory Problem. Management Science. 1965; 12(3): 151-315.
9. Jennings JB. Blood Bank Inventory Control. Management Science. 1973;19(6): 593-715.
10. Pierskalla WP, Roach CD. Optimal Issuing Policies for Perishable Inventory. Management Science. 1972;18(11): 603–614.
11. Brodheim E, Cyrus D, Gregory P. On the Evaluation of a Class of Inventory Policies for Perishable Products Such as Blood. Management Science. 1975; 21(11):1320–1325.
12. Pierskalla WP, Sassetti R, Cohen M, Deuermeyer B, Marritt R, Consolo J, et al. Regionalization of Blood Banking Services. In Executive Summary, edited by The Kendall KE, Lee SM. formulating Blood Rotation Policies with Multiple Objectives. Management Science. 1980; 26(11): 1145–1157.

13. Prastacos GP, Brodheim E. "PBDS: A Decision Support System for Regional Blood Management. Management Science. 1980;26(5): 451–463.
14. Omosigho SE. Determination of Outdate and Shortage Quantities in the Inventory Problem with Fixed Lifetime. International Journal of Computer Mathematics. 2002;79(11): 1169–1177.
15. Rytilä JS, Spens KM. Using Simulation to Increase Efficiency in Blood Supply Chains. Management Research News. 2006; 29(12); 801–819.
16. Erickson ML, Champion MH, Klein R, Ross RL, Neal ZM, Snyder EL. Management of Blood Shortages in a Tertiary Care Academic Medical Center: The Yale-new Haven Hospital Frozen Blood Reserve. Transfusion. 2008; 48(10): 2252–2263.
17. Ghandforoush P. Sen TK. A DSS to Manage Platelet Production Supply Chain for Regional Blood Centers. Decision Support Systems. 2010; 50(1): 32–42.
18. Zhou D, Lawrence CL, William P. Inventory Management of Platelets in Hospitals: Optimal Inventory Policy for Perishable Products with Regular and Optional Expedited Replenishments. Manufacturing & Service Operations Management. 2011;13 (4): 420–438.
19. Stanger SHW, Yates N, Wilding R, Cotton S. Blood Inventory Management: Hospital Best Practice. Transfusion Medicine Reviews. 2012; 26(2): 153–163.
20. Li YC, Liao HC. The Optimal Parameter Design for a Blood Supply Chain System by the Taguchi Method. International Journal of Innovative Computing Information and Control. 2012; 8(11): 7697–12.
21. Duan, Q, Liao TW. A New Age-based Replenishment Policy for Supply Chain Inventory Optimization of Highly Perishable Products. International Journal of Production Economics. 2013; 145(2): 658–671.
22. Elston RC, Pickrel JC. A Statistical Approach to Ordering and Usage Policies for a Hospital Blood Bank. Transfusion. 1963; 3(1): 41–47.
23. Cohen MA, Pierskalla WP. Target Inventory Levels for a Hospital Blood Bank or a Decentralized Regional Blood Banking System. Transfusion. 1979;19(4): 444-454.
24. Brennan JE, Golden BL, Rappoport JK. Go with the Flow: Improving Red Cross Bloodmobiles Using Simulation Analysis. Interfaces. 1992; 22(5):1-13.
25. Fontaine MJ, Yenho TC, Feryal E, Goodnough LT. Age of Blood as a Limitation for Transfusion: Potential Impact on Blood Inventory and Availability. Transfusion. 2010;50(10): 2233–2239.
26. Wevers A, Wigboldus DHJ, Kort WLAM, van Baaren R, Veldhuizen IJT. Characteristics of donors who do or do not return to give blood and barriers to their return. Blood Transfus. 2014; 12(Suppl 1): 37–43.

REVIEW

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Coxiella burnetii Enfeksiyonlarının Kardiyovasküler Tutulumları

Cardiovascular Manifestations of *Coxiella burnetii* Infections

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ABSTRACT
Q fever is a widespread zoonosis that is brought on by the intracellular pathogen Coxiella burnetii. Aortic aneurysm, endocarditis, vascular-graft infection, and chronic Q fever infections are usually linked to cardiovascular complications of C. burnetii infections. In this study, it was aimed to review the cardiovascular complications of Q fever.

ÖZET
Q ateşi, hücre içi patojen olan Coxiella burnetii'nin neden olduğu yaygın bir zoonozdur. Q ateşine bağlı olarak endokardit, aort anevrizması, vasküler greft enfeksiyonu, miyokardit gibi birçok kardiyovasküler komplikasyonlar olduğu bildirilmiştir. Bu çalışmada Q ateşinin kardiyovasküler komplikasyonlarının gözden geçirilmesi amaçlanmıştır.

Keywords:
Aortic aneurysm,
Coxiella burnetii,
Endocarditis,
Q fever,
Vascular-graft infection

Anahtar Kelimeler:
Aort anevrizması,
Coxiella burnetii,
Endokardit,
Q ateşi,
Vasküler-greft enfeksiyonu

GİRİŞ

Q ateşi, hayvancılık endüstrisi üzerinde önemli bir ekonomik etkisi olan yaygın bir zoonotik hastalıktır. Hücre içi, Gram negatif bakteri olan *Coxiella burnetii* bu hastalığın etkenidir (1). İlk olarak Avustralya'da 1937 yılında, mezbaha çalışanları arasında ateşli bir hastalık salgını ortaya çıkmış ve bu hastalık E.H. Derrick tarafından Q ateşi olarak tanımlanmıştır (1,2). Hemen hemen aynı zamanda, Montana'daki araştırmacılar, kenelerde kobay ateşine yol açan yeni bir organizma tespit etmişlerdir. Araştırmacılar, daha sonra Q ateşine ve kobay ateşine neden olan mikroorganizmanın aynı olduğunu keşfetmişlerdir. İkinci Dünya Savaşı sırasında, Avrupa'da askerler arasında Q ateşi salgınları görülmüştür. Ancak, enfeksiyonun ana rezervuarının ve bulaş yolunun ne olduğu savaştan sonra dahi anlaşılamamıştır (2). Q ateşinin prevelansı günümüzde dahi net bilinmemekle birlikte tüm dünyada endemik olduğu bildirilmiştir (1-4). Q ateşinin birincil rezervuarları sığır, koyun ve keçi gibi evcilleştirilmiş geviş getiren hayvanlardır. Enfekte çiftlik hayvanları (sıklıkla koyun, keçi veya sığırlardan) tarafından solunan enfekte aerosolun tipik olarak insanlara bulaşta etkili olduğu düşünülmektedir (1,3). Yakın zamanda yayınlanan bir çalışmada, *C. burnetii*'nin şiddetli rüzgarlarda 18 kilometreye kadar bulaşabildiği ve en yüksek enfeksiyon riski kaynağın beş kilometre yakınında meydana geldiği bildirmiştir (5). *C. burnetii*'nin aerosoller yoluyla akciğere ulaştığı ve bu yolla pnömoniye neden olabildiği tahmin edilmektedir (3). Çoğu durumda, *C. burnetii*'ye mesleki maruziyet, çobanlarda, veterinerlerde, hayvan bakıcılarında, mezbaha veya süt işçilerinde ve laboratuvar personelinde vardır. Mesleki olarak Q ateşi riski taşıyan kişiler arasında Q ateşi salgınları bildirilmiştir (1,4). Kenelerin de bu etkeni taşıdığı bildirilmiştir (6).

C. burnetii ökaryotik hücrelerde çoğaldığı için tehlikeli bir patojen olarak kabul edilir (4). Q ateşinin patofizyolojisi hakkında çok fazla tartışma vardır. Bazı yazarlar, hastalığın akut ve kronik formlarından belirli suşların sorumlu olduğu teorisini ortaya koyarken (7), diğerleri konakçı özelliklerine veya inokulum miktarına daha fazla vurgu yapmıştır (8-10). Ayrıca, *C. burnettii* suşları arasındaki genetik farklılıkların virülanslarını ve konakçı adaptasyonunu etkileyebileceği bildirilmiştir (8,9).

İnsan enfeksiyonları asemptomatik, akut (hepatit, pnömoni ve grip benzeri semptomlarla birlikte), kronik (en sık endokardit ile) veya atipik (menenjit, ensefalit, gibi) olarak ortaya çıkabilir ve hamilelerde plasenta enfeksiyonuna yol açabilir (11). Akut Q ateşi olan hastalar, çoğu durumda klinik tanı ve ampirik tedaviye izin veren tipik bir klinik sunuma sahiptir. Akut Q ateşi olan hastanede yatan hastalar da iyi prognoza sahiptir (12). Q ateşi pnömonisi olan bireylerin %75 kadarı şiddetli bir baş

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ağrısına sahip olduğunu bildirmiştir (13). Etkenin büyük ölçüde akciğerden yayılmasının sonucu olarak, akut ve kronik Q ateşi formları oluşmaktadır. Akut enfeksiyon daha yaygındır ve teşhis edilen vakaların %70'ini oluşturur. Akut enfeksiyonda en yaygın belirtiler hepatit (%40), pnömoni ile beraber hepatit (%20), tek başına pnömoni (%17) veya yalnızca ateştir (%17) (4,6,11). Meningoensefalit (%1), menenjit (%1), miyokardit (%0.7), perikardit, osteomiyelit ve üveit/optik nörit ise çok nadir bildirilmiş sunumlarıdır (8,13). Kronik Q ateşindeki klinik ise akut Q ateşine benzer, ancak tekrarlayan veya inatçı bir yapıya sahip olan yaygın şikayetler baş ağrısı, ateş, titreme, gece terlemesi ve kas ağrısıdır (3,4,6). Kilo kaybı olabilir (7).

Sıklıkla bildirilmiş yaygın laboratuvar anomalileri anemi, trombositopeni, karaciğer fonksiyon testlerinde yükseklik ve hipergamaglobulinemidir. Lökositoz veya lökopeni mevcut olabilir (12,13). Fizik muayenede, hastaların yaklaşık %40'ında hepatosplenomegali ve çomak parmak (%20) saptandığı bildirilmiştir (14).

Semptomların belli belirsiz olması ve tanısal farkındalığın az olması gibi nedenlerle Q ateşi olguları yeterince saptanmamıştır (14). Ancak ölümcül olabilen ve sıklıkla endokardit olarak ortaya çıkan kronik Q ateşi gelişimi, primer enfeksiyonların %1-5'inde görülür, endokardit dışı diğer kardiyak sunumlar da görülebilir (1). Bu mikroorganizma akut veya kronik belirtiler gösterebilir, en tipik kronik belirtisi endokarditttir (12,13,15).

Bu çalışmada Q ateşinin kardiyovasküler komplikasyonlarının gözden geçirilmesi ve bu hastalık hakkında farkındalık yaratılması amaçlanmıştır.

***Coxiella burnetii* enfeksiyonlarının kardiyovasküler tutulumları**

Q ateşi sıklıkla, esas olarak enfeksiyonun kronik evrelerinin bir semptomu olarak ortaya çıkan kardiyovasküler tutuluma sahiptir. En sık görülen kardiyovasküler belirtiler endokardit, aort anevrizmaları ve vasküler greft enfeksiyonlarını içerir. Akut Q ateşi vakalarında nadiren miyokardit veya perikardit gibi diğer kardiyovasküler tutulumlar bildirilmiştir (4,8,13).

Yaşlı popülasyonda veya bağışıklığı baskılanmış olanlarda daha yaygın olan kronik enfeksiyon, endokardit anlamına gelir; ancak anevrizma ve vasküler greft enfeksiyonları daha nadir görülür (8,13).

2011'de yayınlanan bir derleme çalışması (16), Q-ateşi ile ilişkili vasküler komplikasyonları olan Pubmed'de yayınlanan 58 vakayı (49 erkek) incelemiştir. Bu çalışma sonuçlarına göre, hastaların yaşları 32-64 (30-83 yaş) arasında değişmekteydi. 26 hastada vasküler greft enfeksiyonu, 32 hasta enfekte aort anevrizması saptanmıştı. Ateş (n=40) ve ağrı (n=43) en sık görülen semptomlardı. Nadir olarak da anevrizma rüptürü (n=9), aorto-enterik fistül (n=4) ve alt ekstremite embolizasyonu (n=4) saptanmıştı. Bu hastaların ortalama 23 ay (dağılım 1-54 ay) süreyle antibiyotik tedavisi aldığı bildirilmişti (16).

A. Q ateşi ile ilişkili endokardit

Endokardit, kronik Q ateşinin ana belirtisidir, bunu vasküler enfeksiyonlar, kemik enfeksiyonları ve kronik hepatit izler. Birçok farklı ülkeden hem erişkinlerde hem de çocuklarda Q ateşi ile ilişkili endokardit vakaları bildirilmiştir (17-26). Q ateşi endokarditi, öncelikle 40 yaşın üzerindeki erkeklerde, bağışıklığı baskılanmış kişilerde, hamilelerde ve altta yatan kalp kapak hasarı olanlarda görülür (13,27,28). Valvülopatili hastalarda altta yatan kalp hastalığı doğuştan, romatizmal, dejeneratif veya sifilitik olabilir (13,27). *C. burnetii*'ye sekonder subakut veya kronik endokardit vakalarının çoğunun, akut Q ateşini takip eden iki ay ile iki yıl arasında geliştiği bildirilmekle beraber dokuz yıl sonrasında gelişen olgular da bildirilmiştir. Bununla birlikte, bu hastaların sadece %20-40'ında akut enfeksiyon anammezini vermektedir (29).

Sanayileşmiş ülkelerdeki kan kültürü negatif enfektif endokardit vakalarının %50'sine *C. burnetii*'nin neden olduğu düşünülmesine rağmen, *C. burnetii*'nin insidansı henüz tam olarak belirlenmemiştir. Q ateşi endokarditinin klinik öyküsü genellikle subakut ve kalıcıdır; hastalık yıllarca belirgin semptomlar olmadan ve ekokardiyografide vejetasyon görülmeden var olabilir, bakteriyel enfeksiyon kalp kapaklarını yavaş yavaş aşındırır (24). Ayrıca *C. burnetii*'ye bağlı endokarditte protez kalp kapakları veya altta yatan bir kapak bozukluğu her zaman mevcuttur (vakaların %88'i) (27).

Q ateşi ile ilişkili endokarditin tanısı nonspesifik klinik prezentasyon, Duke kriterlerinin duyarlılığının bu hastalarda düşük olması ve ekokardiyografide (EKO) vejetasyonların sıklıkla görülmemesi nedeniyle zordur (28). Kalp yetmezliği belirtileri ve embolik olaylar görülebilir. Ekokardiyografide en sık mitral veya aort kapakları etkilenir. Bununla birlikte, endokarditin olağan etiyolojilerinin aksine, Q ateşinin vejetasyonları küçüktür veya EKO ile saptanamayabilir (14,29). Ayrıca, perivalvüler genişleme ve apse oluşumu, bugüne kadar bildirilen sadece birkaç vaka ile oldukça sıra dışıdır (30,31). Uygun bakıma rağmen, Q ateşi endokarditi için ölüm oranları %24'e kadar çıkabilir (14,27). Endokarditin kardiyak olmayan belirtileri sıklıkla vardır. Bu bulgular splenomegali, çomak parmak ve purpurik döküntülerdir. Döküntü genellikle ekstremitelerde, mukozalarda ve konjonktivada meydana gelir. Bu purpurik lezyonlardan biyopsi yapılırsa immün kompleks vasküliti saptanır (32). PubMed veri tabanında "Q ateşi endokarditi" terimi üzerine yapılan bir inceleme çalışması, 1950 ile 2019 yılları arasında 185 vaka tanımladığı bildirilmiştir. Dahil edilen vakaların tanısı, kalp kapak materyallerinde *C. burnetii* için pozitif polimeraz zincir reaksiyonu (PCR) sonucu varlığı veya pozitif serolojik sonuçlarla konmuştur. 141 hastanın sadece %11'inin normal kalp kapaklarına sahip olduğu, (%56) kalp ameliyatı öyküsü varlığı ve hastaların çoğunda (%72) seyahat veya hayvan teması öyküsü olduğu bildirilmiştir. Genel ölüm oranı %17 olup, doğal ve yapay kapakların endokarditi için ölüm oranları sırasıyla %3 ve %12 olarak saptanmıştır. Ayrıca hidroksiklorokin ve doksisiklin kombinasyon tedavisi alan hastaların hiçbirinde mortalite gelişmediği bildirilmiştir (33).

Fransa'da akut Q ateşi tanısı konan 302 hastanın retrospektif olarak değerlendirildiği bir çalışmada, endokardit gelişen 102 hastada endokardit gelişmeyenlere kıyasla önceden var olan kapak hastalığı çok daha yaygın (% 93 ve %3) olarak saptanmıştır (34). Bu

çalışmada, önceden kapak hastalığı olan hastalarda akut Q ateşi sonrası tahmini endokardit riski yüzde 39 olarak bildirilmiştir. Ancak, Danimarka'da yapılan gözlemsel bir çalışmada, risk daha düşük çıkmıştır (35). Hatta bu kronik enfeksiyonun seyri sırasında endokardite eşlik eden diğer sistem tutulumları olan olgular da bildirilmiştir (35). Allan-Blitz ve arkadaşları (36), *C. burnetii* endokarditi ve menenjiti olan bir vaka bildirmiştir. Enfeksiyon, *C. burnetii* için yüksek serolojik titreler saptanarak teşhis edilmiş ve rezeke edilmiş kapak dokusundan izole edilen *C. burnetii* 16S rRNA sekanslaması ve beyin omurilik sıvısının PCR testi ile doğrulanmıştır.

Nadir olmakla birlikte, Q ateşi endokarditinin bir komplikasyonu olarak pulmoner ve plevral bulgular görülebilir. Embolik inme dışında nörolojik belirtiler ise nadirdir (37).

Ayrıca bu hastalarda romatoid faktör, antismooth kas antikorları (düşük titrelerde), antifosfolipid antikorları, antimitokondriyal antikorlar ve Coombs testi pozitiflikleri de bildirilmiştir (38). Yüksek seviyelerde antikardiyolipin antikorları, akut Q ateşinden endokardite hızlı ilerleme ile ilişkilendirilmiştir (39).

B. Q ateşi ile ilişkili miyokardit

Q ateşi ile ilişkili sadece birkaç nadir miyokardit vakası bildirilmiştir (39-47). Angelakis ve ark. (40) tarafından yayınlanan bir derleme çalışmasında 143 pediyatrik Coxiella enfeksiyonu olan olgunun ikisinde miyokardit, birinde vasküler enfeksiyon ve birinde endokardit varlığı bildirilmiştir. Başka bir çalışmada ise vakaların yalnızca %1'inden azında görülen miyokardit olduğu bildirilmiştir (41). Ancak, *C. burnetii*'nin güçlü bir miyokardiyal tropizme sahip olduğu gösterilmiştir (48).

Q ateşi miyokardit olgularında elektrokardiyografi (EKG), transtorasik ekokardiyografi (TTE) ve transözafagial ekokardiyografi (TEE) testi ön değerlendirmelerde sıklıkla kullanılmaktadır. Q ateşi ilişkili miyokardit semptomların başlamasından birkaç hafta sonra düzelen EKG'deki ST yükselmeleri (genellikle yaygın ST yükselmeleri) ile ilişkilendirilmiştir (42,43).

Fournier ve ark. (45) 1985 ve 1999 yılları arasında akut Q ateşi olan 1276 hastanın 8'inde miyokardit saptandığını bildirmiştir. Bunların ikisinde prekordiyal ağrı ve birinde kalp yetmezliği vardı. Dilate kardiyomiyopati 7 hastada tespit edildi ve bunlardan biri kalp nakli olan bir hasta olup, yedi hastanın ikisi tedavi görmelerine rağmen mortal seyretmişti. Ayrıca bir hastaya kalp yetmezliği nedeniyle kalp nakli planlanmıştı.

Q ateşi miyokarditinin spesifik olmayan semptomları sıklıkla gecikmiş veya atlanmış tanıya neden olarak mortalite ve morbiditeyi arttırır. Anjina benzeri göğüs ağrısı yaşayan ve Q ateşi risk faktörleri taşıyan hastaların *C. burnetii* enfeksiyonu açısından değerlendirilmesi gerekir. Kardiyomiyopatinin diğer daha yaygın nedenlerini dışladıktan sonra, *C. burnetii* tanısı serolojik testlerle doğrulanmalıdır. Kardiyak manyetik rezonans görüntüleme, teşhis doğruluğunu artırmak için yararlı bir tekniktir (47,48).

C. Q ateşi ile ilişkili vasküler tutulumlar

Q ateşi vasküler enfeksiyonu, Q ateşi endokarditi kadar iyi bilinen bir hastalıktır. Yüksek mortalite ve majör komplikasyonlarla ilişkilidir (15,49,50). Bu komplikasyon genellikle vaka raporları ve küçük vaka serilerinde tanımlanmıştır.

Hollanda'da yapılmış çok merkezli çalışmada (51) muhtemel kronik Q ateşi olan 284 hastanın 122'sine (%42) vasküler kronik Q ateşi teşhisi konduğu bildirilmiştir. Bu çalışmada bildirilen hastaların çoğunda anevrizma veya damar grefti öyküsü vardı. 122 hastanın neredeyse yarısının, akut veya geç komplikasyonlar (yeni progresif veya rüptüre anevrizmalar, aortoduodenal fistül, enfekte vasküler protez) için ameliyat gerektiren komplikasyonlar gösterdiği ve 122 hasta arasındaki genel mortalite, fistül de dahil olmak üzere anevrizma ile ilişkili komplikasyonlara bağlı olarak yaklaşık %25 olarak bildirilmiştir (51). Q ateşi ile ilişkili endokardit vakalarının sadece %3'ünde alt ekstremitede embolik olaylar olduğu bildirilmiştir (52). Faucon ve ark. (26) *C. burnetii* endokarditine bağlı akut ekstremite iskemi olgusu bildirmişlerdir. Bu olgu, atriyal flutter zemininde tekrarlayan akut sol ekstremite iskemisi nedeniyle hastaneye yatırılan ve *C. burnetii* endokarditi tanısı alan 68 yaşında bir erkek hastadır. Kobayashi ve ark. (53) ise tekrarlayan ateşle başvuran ve *C. burnetii*'ye bağlı vasküler greft enfeksiyonu tanısı konan, hayvanlarla doğrudan teması olmayan 61 yaşında bir erkek hastayı literatüre kazandırmıştır. Stokes ve ark. (54) ise mikotik anevrizma ve eşlik eden vertebral osteomiyelit olgusunu bildirmiştir. Bu olgu perirenal abdominal aort grefti olan C 67 yaşında bir olgu idi. Bu olgu enfekte abdominal greft nedeniyle opere edilmiş olup, Q ateşi tanısı kronik Q ateşi ile uyumlu seroloji (faz I serolojik IgG titresi 1:2048 ve faz II IgG titresi 1:1024) ve enfekte vasküler doku üzerinde yapılan *C. burnetii* için pozitif PCR varlığı ile konmuştu. Dvorak ve Bizzini (55) ise Streptococcus anginosus and *C. burnetii*'nin etken olduğu aorto-duodenal fistül ile komplike olan bir vasküler greft ko-enfeksiyon olgusunu bildirmiştir. Bendermacher ve ark. (56) torakoabdominal aort anevrizması gelişen bir *C. burnetii* olgusu bildirmiştir.

Teşhis edilen vakaların sayısındaki bu artış, muhtemelen insidansındaki artıştan ziyade hastalığın daha iyi tanınmasından kaynaklanmaktadır (16). Ancak bu konuda halen literatür bilgisi sınırlıdır. Örneğin bu komplikasyonun primer tutulum veya hastalık seyrinde gelişen bir tutulum olduğu konusu tartışmalıdır (56,57).

***Coxiella burnetii* enfeksiyonlarının kardiyovasküler tutulumlarında mikrobiyolojik tanı**

Q ateşi endokarditi ve vasküler enfeksiyonun mikrobiyolojik tanısı esas olarak serolojiye dayanır. Bu nedenle, klinik olarak şüphelenilen Q ateşi endokarditi olan faz I immünoglobulin G (IgG) antikorunun belirli bir cut off titresi, seroloji akut bir enfeksiyonu geçmişteki bir enfeksiyondan ayırt edemese de kolayca tanı koyar (58). Bununla birlikte, doğru bir teşhis için faz I IgG antikor titresinin uygun cut off değeri tartışmalıdır. Yüksek faz I IgG antikor titresi, kardiyovasküler riski olan asemptomatik hastalarda bulunurken, düşük titreli belgelenmiş endokarditi olan hastalar vardır (59,60).

Faz I IgG antikoru için tekrarlanan testler, bağışıklığı baskılanmış konakçılar, masif transfüzyonu olanlar veya akut Q ateşi endokarditi olanlar dışında Q ateşi endokarditi tanısı için oldukça duyarlıdır. Bu nedenle, Q ateşi enfeksiyonu, özellikle akut Q ateşi endokarditi olduğundan şüphelenilen kişilerde, faz I IgG antikor

titresi<800 olsa bile, bu tür birkaç vakanın raporları göz önüne alındığında, tekrarlanan testler yapılmadan dışlanamaz. (16,39,52,61).

Serolojik test sonuçları, numunelerin bir referans laboratuvarına gönderilmesi sırasında da gecikebilir. Kanda, kalp kapakçıklarında veya diğer cerrahi doku biyopsi örneklerinde *C. burnetii* DNA'sını saptamak için PCR yönteminin geliştirilmesi bu sorunların azaltılmasına yardımcı olmuştur. PCR'nin avantajları arasında erken teşhis, sonuçlar için kısa geri dönüş süresi ve yüksek özgüllük yer alır (34,57). Bununla birlikte, *C. burnetii* DNA'sı, Q ateşi endokarditi tanısı için sınırlı duyarlılıktadır çünkü enfeksiyonun yalnızca erken evrelerinde saptanabilir (4). Bu sınırlamaya rağmen, pozitif *C. burnetii* PCR tanıyı daha kesin hale getirir. Bu nedenle, Q ateşi endokarditi veya vasküler enfeksiyon için %100 öngörü değeri olan tek bir test yoktur. Son zamanlarda PCR ve serolojik test sonuçlarını içeren yeni kriterler önerilmiştir (4,59,60).

TEDAVİ

Q ateşi endokarditi tedavisinde uzun süreli (en az 18 ay) hidroksiklorokin ve doksisiklin kombinasyon tedavisi önerilmektedir (7,37). Doksisiklin oral olarak günde iki kez 100 mg, hidroksiklorokin günde üç kez oral olarak 600 mg veya 200 mg olarak verilir. Doksisiklini tolere edemeyen hastalar (örn. mide bulantısı) minosiklin alabilir (37).

Hücre içi bir patojen olan *C. burnetii*, etkili hücre içi konsantrasyonlara ulaşan antibiyotiklerle en iyi şekilde tedavi edilir. Doksisiklin, kinolonlar, klaritromisin, eritromisin ve trimetoprim/sülfametoksazolün tümü akut Q ateşi için etkiliyken, günde 200 mg doksisiklin daha üstün olarak ortaya çıkmıştır. Beta-laktamlar ve azitromisin ise etkili değildir (13,37).

Q ateşi endokarditi için, kombinasyon tedavisi monoterapiden daha üstündür ve hastaların çoğunluğu, özellikle perivalvüler genişleme mevcutsa, kalp cerrahisi gerektirir (13).

Antimalaryal ilaç olan hidroksiklorokin, *C burnetii*'nin bulunduğu fagolizozomun pH'ını yükseltme kabiliyeti nedeniyle bir tetrasiklin ile kombinasyon halinde önerilmektedir (7,62,63).

Maor ve ark. (64) çalışmalarında, cerrahi tedavinin hem Q ateşi endokarditi hem de vasküler greft enfeksiyonu için iyi sonuçlar verdiğini bildirmiştir. Cerrahi prosedürün zamanlaması ile hastaların sonuçları arasında bir ilişki ise bulunmamıştır (64).

Gebe kadınlar trimetoprim-sülfametoksazol (günde iki kez 160 mg trimetoprim ve 800 mg sülfametoksazol) ile tedavi edilmelidir. Trimetoprim/sülfametoksazol, antifolat etkilerine ikincil olarak artmış konjenital anormallikler (öncelikle idrar yolu ve kardiyovasküler anormallikler) riski ile ilişkili olduğundan, bu tür kadınlara folik asit verilmelidir veya protez kapağı olanlarda genellikle 24 ay tedavi önerilmektedir. Faz I antijenlerine karşı IgG antikorlarının titresi en az dört kat azalırsa tedavi durdurulabilir (37).

En az 18 aylık tedavi önerisi, uzun süreli antibiyotik tedavisine rağmen dokuda canlı *C. burnetii* varlığına dayanmaktadır (57,65). Örnek olarak, Q aateşi endokarditi olan 28 hasta üzerinde yapılan bir çalışmada, kalp kapakçıklarında (immünohistokimyasal analiz, kültür ve PCR kullanılarak) *C. burnetii* saptanması, yalnızca bireyler en az bir yıl antibiyotik tedavisi aldıktan sonra önemli ölçüde azalmış olarak bildirilmiştir (65).

Q ateşi endokarditinde hasarlı bir kapağı değiştirmek için cerrahi genellikle hemodinamik bozulma için endikedir. Mümkünse, yeni kapağın enfeksiyon riskini en aza indirmek için kapak değişiminden önce en az üç haftalık antimikrobiyal tedavi verilmelidir (13,29).

Postoperatif olarak, yeni protez kapağı olan hastalar 24 ay süreyle tedavi edilmelidir, yabancı madde içermeyen onarılmış enfekte kapağı olanlar ise ameliyat tarihinden itibaren 18 ay boyunca doğal kapak endokarditi olarak tedavi edilebilir (37).

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KAYNAKLAR

1. Škultéty L. Q fever and prevention. Epidemiol Mikrobiol Imunol. 2020;69(2):87-94.
2. Hirschmann JV. The Discovery of Q Fever and Its Cause. Am J Med Sci. 2019;358(1):3-10. doi: 10.1016/j.amjms.2019.04.006.
3. España PP, Uranga A, Cillóniz C, Torres A. Q Fever (Coxiella Burnetii). Semin Respir Crit Care Med. 2020;41(4):509-521. doi: 10.1055/s-0040-1710594.
4. Eldin C, Mélenotte C, Mediannikov O, Ghigo E, Million M, Edouard S, et al. From Q Fever to Coxiella burnetii Infection: a Paradigm Change. Clin Microbiol Rev. 2017;30(1):115-190. doi: 10.1128/CMR.00045-16.
5. Clark NJ, Soares Magalhães RJ. Airborne geographical dispersal of Q fever from livestock holdings to human communities: a systematic review and critical appraisal of evidence. BMC Infect Dis. 2018;18(1):218. doi: 10.1186/s12879-018-3135-4.
6. Ekici A, Gürbüz, E, Halidi AG, Ünlü AH, Aydemir S. Kene Isırığı Şikâyetiyle Hastaneye Başvuran Hastalardan Çıkarılan Kenelerde Coxiella burnetii ve Ehrlichia canis'in Moleküler Yöntemlerle Araştırılması. Commagene Journal of Biology. 2021; 5 (2): 199-203.
7. Samuel JE, Frazier ME, Mallavia LP. Correlation of plasmid type and disease caused by Coxiella burnetii. Infect Immun. 1985;49(3):775-779. doi: 10.1128/iai.49.3.775-779.1985.
8. Stein A, Raoult D. Q fever endocarditis. Eur Heart J. 1995;16 Suppl B:19-23. doi: 10.1093/eurheartj/16.suppl_b.19.
9. Raoult D, Brouqui P, Marchou B, Gastaut JA. Acute and chronic Q fever in patients with cancer. Clin Infect Dis. 1992;14(1):127-130. doi: 10.1093/clinids/14.1.127.
10. Kanfer E, Farrag N, Price C, MacDonald D, Coleman J, Barrett AJ. Q fever following bone marrow transplantation. Bone Marrow Transplant. 1988;3(2):165-166.
11. Melenotte C, Protopopescu C, Million M, Edouard S, Carrieri MP, Eldin C, et al. Clinical Features and Complications of Coxiella burnetii Infections From the French National Reference Center for Q Fever. JAMA Netw Open. 2018;1(4):e181580. doi: 10.1001/jamanetworkopen.2018.1580.

12. Ergas D, Keysari A, Edelstein V, Sthoeger ZM. Acute Q fever in Israel: clinical and laboratory study of 100 hospitalized patients. Isr Med Assoc J. 2006;8(5):337-341.
13. Hartzell JD, Marrie TJ, Raoult D. Coxiella burnetii (Q Fever). In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Amsterdam: Elsevier; 2020. p. 2360–2367.
14. Brouqui P, Dupont HT, Drancourt M, Berland Y, Etienne J, Leport C, et al. Chronic Q fever. Ninety-two cases from France, including 27 cases without endocarditis. Arch Intern Med. 1993;153(5):642-648. doi: 10.1001/archinte.153.5.642.
15. McCaughey C, Murray LJ, McKenna JP, Coyle PV, O'Neill HJ, Wyatt DE, et al. Lack of association between serological evidence of past Coxiella burnetii infection and incident ischaemic heart disease: nested case-control study. BMC Infect Dis. 2005;5:61. doi: 10.1186/1471-2334-5-61.
16. Wegdam-Blans MC, Vainas T, van Sambeek MR, Cuypers PW, Tjhie HT, van Straten AH, et al. Vascular complications of Q-fever infections. Eur J Vasc Endovasc Surg. 2011;42(3):384-392. doi: 10.1016/j.ejvs.2011.04.013
17. Armstrong MR, McCarthy KL, Horvath RL. A contemporary 16-year review of Coxiella burnetii infective endocarditis in a tertiary cardiac center in Queensland, Australia. Infect Dis (Lond). 2018;50(7):531-538. doi: 10.1080/23744235.2018.1445279.
18. Karageorgou I, Kogerakis N, Labropoulou S, Hatzianastasiou S, Mentis A, Stavridis G, et al. Q Fever Endocarditis and a New Genotype of Coxiella burnetii, Greece. Emerg Infect Dis. 2020;26(10):2527-2529. doi: 10.3201/eid2610.191616.
19. Wery F, Delaere B, Schraverus P, Higny J. Q fever endocarditis. Acta Cardiol. 2021;76(6):668-669. doi: 10.1080/00015385.2020.1762028.
20. Briggs BJ, Raoult D, Hijazi ZM, Edouard S, Angelakis E, Logan LK. Coxiella burnetii Endocarditis in a Child Caused by a New Genotype. Pediatr Infect Dis J. 2016;35(2):213-214. doi: 10.1097/INF.0000000000000970.
21. Yahav D, Kuznitz I, Reisfeld S, Eliakim-Raz N, Bishara J. Polymicrobial Q Fever and enterococcal aortic prosthetic valve endocarditis with aortic root abscess. Vector Borne Zoonotic Dis. 2015;15(5):326-328. doi: 10.1089/vbz.2015.1777.
22. Garg P, Chan S, Peeceeyen S, Youssef G, Graves SR, Sullivan R. Culture-negative polymicrobial chronic Q fever prosthetic valve infective endocarditis utilizing 16S ribosomal RNA polymerase chain reaction on explanted valvular tissue. Int J Infect Dis. 2022;121:138-140. doi: 10.1016/j.ijid.2022.05.011.
23. Jalal Z, Duperril M, Séguéla PE, Melenotte C, Chabaneix J, Raoult D, Thambo JB. First Case of Q Fever Endocarditis Involving the Melody® Transcatheter Pulmonary Valve in an Afebrile Child. Pediatr Cardiol. 2018;39(1):195-197. doi: 10.1007/s00246-017-1723-5.
24. Sonsöz MR, Agüloğlu Bali E, Aydoğan M, Mercanoğlu F, Şimşek Yavuz S. Q fever endocarditis: is it always subacute or chronic? Turk Kardiyol Dern Ars. 2020;48(1):72-76. doi: 10.5543/tkda.2019.59153.
25. al-Hajjar S, Hussain Qadri SM, al-Sabban E, Jäger C. Coxiella burnetii endocarditis in a child. Pediatr Infect Dis J. 1997;16(9):911-913. doi: 10.1097/00006454-199709000-00020.
26. Faucon AL, Mainardi JL, Zamfir O, Gorka H, Bruneval P, Pruna A. Coxiella burnetii endocarditis on bioprosthetic aortic valve, with peripheral arterial embolism. Cardiovasc Pathol. 2018;34:38-39. doi: 10.1016/j.carpath.2018.02.001.
27. Griffin AT, Espinosa M, Nakamatsu R. Q fever endocarditis: an unusual presentation. Am J Med Sci. 2012;344(6):480-484. doi: 10.1097/MAJ.0b013e3182684979.
28. Houpikian P, Habib G, Mesana T, Raoult D. Changing clinical presentation of Q fever endocarditis. Clin Infect Dis. 2002;34(5):E28-31. doi: 10.1086/338873.
29. Buijs SB, Bleeker-Rovers CP, van Roeden SE, Kampschreur LM, Hoepelman AIM, Wever PC, et al. Still New Chronic Q Fever Cases Diagnosed 8 Years After a Large Q Fever Outbreak. Clin Infect Dis. 2021;73(8):1476-1483. doi: 10.1093/cid/ciab476.
30. Ilany J, Dresner J, Shemesh O, Rudensky B, Abraham AS. An unusual case of Q fever endocarditis. Cardiology. 1993;83(4):285-288. doi: 10.1159/000175982.
31. Fort S, Fraser AG, Fox KA. Extensive aortic valve ring abscess formation: a rare complication of Q fever endocarditis. Postgrad Med J. 1989;65(764):384-386. doi: 10.1136/pgmj.65.764.384.
32. Maurin M, Raoult D. Q fever. Clin Microbiol Rev. 1999;12(4):518-553. doi: 10.1128/CMR.12.4.518
33. Jaltotage B, Ali U, Dorai-Raj A, Rankin J, Sanfilippo F, Dwivedi G. Q Fever Endocarditis: A Review of Local and all Reported Cases in the Literature. Heart Lung Circ. 2021;30(10):1509-1515. doi: 10.1016/j.hlc.2021.04.022.
34. Fenollar F, Fournier PE, Raoult D. Molecular detection of Coxiella burnetii in the sera of patients with Q fever endocarditis or vascular infection. J Clin Microbiol. 2004;42(11):4919–4924.
35. de Lange MMA, Gijsen LEV, Wielders CCH, van der Hoek W, Scheepmaker A, Schneeberger PM. Should Acute Q-Fever Patients be Screened for Valvulopathy to Prevent Endocarditis? Clin Infect Dis. 2018;67(3):360-366. doi: 10.1093/cid/ciy128.
36. Allan-Blitz LT, Sakona A, Wallace WD, Klausner JD. Coxiella burnetii Endocarditis and Meningitis, California, USA, 2017. Emerg Infect Dis. 2018;24(8):1555–1557. doi: 10.3201/eid2408.180249.
37. Uptodate. Q fever endocarditis. Erişim tarihi: 10 Kasım 2022. Erişim: https://www.uptodate.com/contents/q-fever-endocarditis
38. Levy P, Raoult D, Razongles JJ. Q-fever and autoimmunity. Eur J Epidemiol. 1989;5(4):447-453. doi: 10.1007/BF00140139.
39. Million M, Walter G, Bardin N, Camoin L, Giorgi R, Bongrand P, et al. Immunoglobulin G anticardiolipin antibodies and progression to Q fever endocarditis. Clin Infect Dis. 2013;57(1):57-64. doi: 10.1093/cid/cit191.
40. Angelakis E, Johani S, Ahsan A, Memish Z, Raoult D. Q fever endocarditis and new Coxiella burnetii genotype, Saudi Arabia. Emerg Infect Dis. 2014;20(4):726-728. doi: 10.3201/eid2004.131603.
41. Carrascosa M, Velasaco F, Izquierdo R, Salcines-Caviedes JR, Gómez Amigo V, Canga-Villegas A. Acute Q fever myocarditis: thinking about a life-threatening but potentially curable condition. Int J Cardiol. 2012;158:e17–e19.
42. Angelini A, Calzolari V, Calabrese F, Boffa GM, Maddalena F, Chioin R, Thiene G. Myocarditis mimicking acute myocardial infarction: role of endomyocardial biopsy in the differential diagnosis. Heart. 2000;84(3):245-250. doi: 10.1136/heart.84.3.245.
43. Vogiatzis I, Dimoglou G, Sachpekidis V. Q fever myocarditis. Hippokratia. 2008;12(1):46-49.
44. Pfammatter JP, Paul T, Flik J, Drescher J, Kallfelz HC. Q-Fieber-assoziierte Myokarditis bei einem 14jährigen Jungen [Q-fever associated myocarditis in a 14-year-old boy]. Z Kardiol. 1995;84(11):947-950.
45. Fournier PE, Etienne J, Harle JR, Habib G, Raoult D. Myocarditis, a rare but severe manifestation of Q fever: report of 8 cases and review of the literature. Clin Infect Dis. 2001;32(10):1440-1447. doi: 10.1086/320159.
46. Hammami R, Bahloul A, Charfeddine S, Feki W, Ayed NB, Abid L, et al. Q fever presenting as myocarditis. IDCases. 2021;23:e01056. doi: 10.1016/j.idcr.2021.e01056.
47. Jacobson A, Sutthiwan P. Myocarditis: A rare manifestation of acute Q fever infection. J Cardiol Cases. 2019;20(2):45-48. doi: 10.1016/j.jccase.2019.03.012.
48. Dupuis G, Péter O, Pedroni D, Petite J. Aspects cliniques observés lors d'une épidémie de 415 cas de fièvre Q [Clinical aspects observed during an epidemic of 415 cases of Q fever]. Schweiz Med Wochenschr. 1985;115(24):814-818.
49. Karhof S, van Roeden SE, Oosterheert JJ, Bleeker-Rovers CP, Renders NHM, de Borst GJ, et al. Primary and secondary arterial fistulas during chronic Q fever. J Vasc Surg. 2018;68(6):1906-1913.e1. doi: 10.1016/j.jvs.2018.01.044.
50. Buijs SB, Stuart SK, Oosterheert JJ, Karhof S, Hoepelman AIM, Renders NHM, et al. Long-term serological follow-up after primary Coxiella burnetii infection in patients with vascular risk factors for chronic Q fever. Eur J Clin Microbiol Infect Dis. 2021;40(7):1569-1572. doi: 10.1007/s10096-021-04179-5.
51. Broos PP, Hagenaars JC, Kampschreur LM, Wever PC, Bleeker-Rovers CP, Koning OH, et al. Vascular complications and surgical interventions

after world's largest Q fever outbreak. J Vasc Surg. 2015;62(5):1273-1280. doi: 10.1016/j.jvs.2015.06.217.
52. Million M, Thuny F, Richet H, Raoult D. Long-term outcome of Q fever endocarditis: a 26-year personal survey. Lancet Infect Dis. 2010;10(8):527-535. doi: 10.1016/S1473-3099(10)70135-3.
53. Kobayashi T, Casado Castillo F, Barker JH, Herwaldt L. Coxiella burnetii vascular graft infection. IDCases. 2021;25:e01230. doi: 10.1016/j.idcr.2021.e01230.
54. Stokes W, Janvier J, Vaughan S. Chronic Q Fever in Alberta: A Case of Coxiella burnetii Mycotic Aneurysm and Concomitant Vertebral Osteomyelitis. Can J Infect Dis Med Microbiol. 2016;2016:7456157. doi: 10.1155/2016/7456157.
55. Dvorak S, Bizzini A. Streptococcus anginosus and Coxiella burnetii vascular graft co-infection. IDCases. 2020;19:e00697. doi: 10.1016/j.idcr.2020.e00697.
56. Bendermacher BL, Peppelenbosch AG, Daemen JW, Oude Lashof AM, Jacobs MJ. Q fever (Coxiella burnetii) causing an infected thoracoabdominal aortic aneurysm. J Vasc Surg. 2011;53(5):1402-1404. doi: 10.1016/j.jvs.2010.11.102.
57. Botelho-Nevers E, Fournier PE, Richet H, Fenollar F, Lepidi H, Foucault C, et al. Coxiella burnetii infection of aortic aneurysms or vascular grafts: report of 30 new cases and evaluation of outcome. Eur J Clin Microbiol Infect Dis. 2007;26(9):635-640. doi: 10.1007/s10096-007-0357-6.
58. Li JS, Sexton DJ, Mick N, et al.. Proposed modifications to the duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000;30(4):633–638.
59. Raoult D. Chronic Q fever: expert opinion versus literature analysis and consensus. J Infect. 2012;65(2):102–108.
60. Wegdam-Blans MC, Kampschreur LM, Delsing CE, et al. Chronic Q fever: review of the literature and a proposal of new diagnostic criteria. J Infect. 2012;64(3):247–259.
61. Grisoli D, Million M, Edouard S, Thuny F, Lepidi H, Collart F, et al. Latent Q fever endocarditis in patients undergoing routine valve surgery. J Heart Valve Dis. 2014;23(6):735–743.
62. Levy PY, Drancourt M, Etienne J, Auvergnat JC, Beytout J, Sainty JM, et al. Comparison of different antibiotic regimens for therapy of 32 cases of Q fever endocarditis. Antimicrob Agents Chemother. 1991;35(3):533-537. doi: 10.1128/AAC.35.3.533.
63. Deyell MW, Chiu B, Ross DB, Alvarez N. Q fever endocarditis: a case report and review of the literature. Can J Cardiol. 2006;22(9):781-785. doi: 10.1016/s0828-282x(06)70295-1.
64. Maor Y, Sternik L, Orlov B, Rahav G, Keller N, Raanani E, Kogan A. Coxiella burnetii Endocarditis and Aortic Vascular Graft Infection: An Underrecognized Disease. Ann Thorac Surg. 2016;101(1):141-145. doi: 10.1016/j.athoracsur.2015.06.075.
65. Fournier PE, Marrie TJ, Raoult D. Diagnosis of Q fever. J Clin Microbiol. 1998;36(7):1823-1834. doi: 10.1128/JCM.36.7.1823-1834.1998.

ORIGINAL ARTICLE

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Fibrinogen/Albumin Ratio in Patients with Pulmonary Embolism

Pulmoner Emboli Olan Hastalarda Fibrinojen/Albümin Oranı

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ABSTRACT

Objective: *Pulmonary embolism is associated with a high mortality rate when it is not diagnosed emergently. Our aim was to investigate the relationship between the fibrinogen/albumin ratio and pulmonary embolism.*

Material and Method: *Patients who were suspected to have pulmonary embolism and who underwent routine blood testing to initiate the diagnostic process were included in this prospective study. Their fibrinogen and albumin values were evaluated.*

Results: *A total of 130 patients were included in the study. Pulmonary embolism was detected in 71 (54%) of the patients. Of those, 7 (9.9%) were subsegmental, 50 (70.4%) were segmental, and 14 (19.7%) were massive pulmonary. The fibrinogen/albumin ratio of the subjects in the control group was 99.1 (75.2–167.9), whereas the fibrinogen/albumin ratio in the pulmonary embolism group was 151 (125.1–220.5), significantly higher than the control value (P < 0.001). When ROC analysis was performed in the pulmonary embolism group, the fibrinogen/albumin ratio was found to be a significant predictive factor (AUC: 0.724; 95% CI = 0.635–0.814; P < 0.001). When the fibrinogen/albumin ratio was 119.3, the sensitivity was 77.5%, and specificity was 61.0%.*

Conclusion: *Fibrinogen levels and fibrinogen/albumin ratio were significantly higher in patients with pulmonary embolism.*

ÖZET

Amaç: *Pulmoner emboli teşhis edilemediğinde yüksek ölüm oranı ile ilişkilidir. Amacımız fibrinojen/albümin oranı ile pulmoner emboli arasındaki ilişkiyi araştırmaktı.*

Gereç ve Yöntem: *PE olduğundan şüphelenilen ve rutin kan testi yapılan hastalar bu prospektif çalışmaya dahil edilmiştir. Fibrinojenleri ve albümin değerleri değerlendirildi.*

Bulgular: *Çalışmaya toplam 130 hasta dahil edildi. PE, hastaların 71'inde (%54) tespit edildi. Bunlardan 7'si (%9,9) subsegmental, 50'si (%70,4) segmental ve 14'ü (%19,7) masif idi. Kontrol grubundaki deneklerin FAR(Fibrinojen albumin oranı) 'si 99.1 (75.2–167.9) iken, PE grubundaki FAR 151 (125.1–220.5) olup, kontrol grubundan anlamlı derecede yüksekti (P < 0,001). PE grubunda ROC analizi yapıldığında FAR önemli bir öngörücü faktör oldu (AUC: 0.724; %95 GA = 0.635-0.814; P < 0.001). FAR, duyarlılık %77.5 ve özgüllük %61.0 idi.*

Sonuç: *PE'li hastalarda fibrinojen düzeyleri ve FAR anlamlı olarak daha yüksekti.*

Keywords:
Pulmonary embolism, Fibrinogen/albumin ratio, Mean platelet volume

Anahtar Kelimeler:
Pulmoner emboli, Fibrinojen/albümin oranı, Ortalama trombosit hacmi

INTRODUCTION

Pulmonary embolism (PE) is a general problem of deep vein thrombosis (1). Generally, part of the thrombus from the leg clogs the main pulmonary arteries or smaller pulmonary arteries (2). PE is associated with a high mortality rate when it is not diagnosed emergently. Treatment should be started immediately upon diagnosis. Differential diagnosis includes myocardial infarction, pneumonia, pericardial effusion, and aortic dissection (3,4).

Fibrinogen is a plasma protein synthesized in the liver that converts into fibrin during coagulation. It increases in infections, tissue damage, pregnancy, collagen tissue diseases, and many cancers. Fibrinogen levels are decreased in cases of haemolytic diseases, severe blood loss, phosphorus poisoning, disseminated intravascular coagulation, blood transfusion, and burns. The main function of fibrinogen is to provide coagulation (5). Albumin, another protein synthesized in the liver, has a half-life of 21 days. It maintains osmotic pressure with its colloid structure. Serum albumin levels decrease in cases of liver diseases (cirrhosis), kidney diseases (renal excretion), malnutrition, burns, and infections (especially sepsis). It is a negative acute phase reactant (6).

This study was aimed to figure out the differences in fibrinogen, albumin, and the fibrinogen/albumin ratio (FAR) values between patients with and without PE, to identify a potential diagnostic marker to assist emergency physicians with diagnosis and decrease unnecessary pulmonary computed tomography angiography.

MATERIAL AND METHODS

The study was approved by Ethical Board (Meeting

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Table 1: Demographic characteristics of the groups and laboratory results

Characteristic	Control Group	Patient Group	P-value
Age	65.1 ± 11.6	68.2 ± 15.3	0.144
Sex (female)	32 (54.2%)	28 (39.4%)	0.093
Shortness of breath	24 (%40.7)	43 (%60.6)	
Syncope	4 (%6.8)	1 (%1.4)	
Leg swelling	4 (6.8%)	5 (7%)	
Chest pain	12 (20.3%)	2 (2.8%)	
Haemoptysis	4 (6.8%)	0	
Other complaint	11 (18.6%)	20 (28%)	
Malignancy (yes)	21 (35.6%)	20 (28.2%)	
Glucose	121.0 (105.0-136.0)	133.0 (100.0-180.0)	0.099
BUN	23.4 (16.0-29.4)	20.0 (14.5-32.7)	0.305
Creatinine	0.9 ± 0.4	0.9 ± 0.3	0.568
ALT	22.0 (12.0-30.0)	19.0 (12.0-29.0)	0.733
AST	20.0 (15.0-35.0)	22.0 (15.0-35.0)	0.582
LDH	264.0 (223.0-388.0)	270.0 (221.0-328.0)	0.893
Haemoglobin	11.3 ± 2.4	11.3 ± 2.5	0.984
Leukocytes	9.8 (6.7-13.8)	11.6 (8.2-15.4)	0.423
Neutrophils	7.1 (4.5-10.8)	9.0 (5.3-12.6)	0.283
Lymphocytes	1.5 (1.1-2.2)	1.4 (0.7-1.8)	0.283
RDW	16.9 ± 4.7	16.3 ± 2.9	0.389
MPV	9.6 ± 1.2	10.3 ± 1.8	0.021
Platelets	256.0 (183:0-313.0)	249.0 (190.5-343.0)	0.894
CRP	38.0 (18.3-121.0)	63.3 (30.6-134.0)	0.177
D-dimer	2633.3 ± 1441.3	3462.4 ± 1385.6	0.001
Albumin	3.2 ± 0.7	3.1 ± 0.6	0.302
Fibrinogen	379.5 ± 187. 6	520.6 ± 191.1	<0.001
Fibrinogen/albumin ratio	99.1 (75.2-167.9)	151 (125.1-220.5)	<0.001
Neutrophil/lymphocyte ratio	4.7 (2.9-8.0)	5.6 (3.6-12.7)	0.061

ALT: *Alanine aminotransferase;* ***AST:*** *Aspartate aminotransferase;* ***LDH:*** *Lactose dehydrogenase;* ***CRP:*** *C-reactive protein;* ***RDW:*** *Erythrocyte distribution width in blood;* ***MPV:*** *Mean platelet volume in blood.*

Decision No. 2018/1434). This prospective study was conducted with patients who were admitted to our university hospital emergency department with the suspicion of PE between July 1, 2018 and February 1, 2019. Patients with suspected pulmonary embolism who were consulted with chest diseases and had computed tomography pulmonary angiography (CTPA) were included in the study. One hundred thirty patients demographic data were collected. The age, gender, biochemistry, arterial blood gas, haemogram test results, and coagulation results of the patients were recorded. Patients who were under the age of 18 were excluded from the study.

Biochemical Markers

Coagulation tubes were centrifuged at 4000 rpm for 5 min. Fibrinogen was measured using a Siemens BCS XP haemostasis system (Siemens Healthcare Diagnostics, Los Angeles, CA, USA). Albumin was measured spectrophotometrically using an Abbott Architect Plus spectrophotometer (Abbott Park, IL, USA). Haemogram was analyzed using automatic blood counter (Beckman-Coulter Co, Miami, Florida).

Statistics

Categorical variables were defined as the mean ± standard deviation or frequency and percentage. Student's t-test was used to compare normally distributed variables. Normal distribution was evaluated with the Kolmogorov-Smirnov test ($P < 0.05$). Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic sensitivity and specificity of the FAR. Groups with non-normal distribution were evaluated using the Mann-Whitney U test. A P-value < 0.05 was considered significant.

RESULTS

The data of a total of 130 patients who were suitable for the working conditions were examined. The patients who evaluated within the scope of the study, 71 were included in the study group (PE), and 59 were placed in the control group (no PE). The mean ages of the PE group and the control group were 68.2 ± 15.3 years and 65.1 ± 11.6 years, respectively. Considering the ages, it was determined that

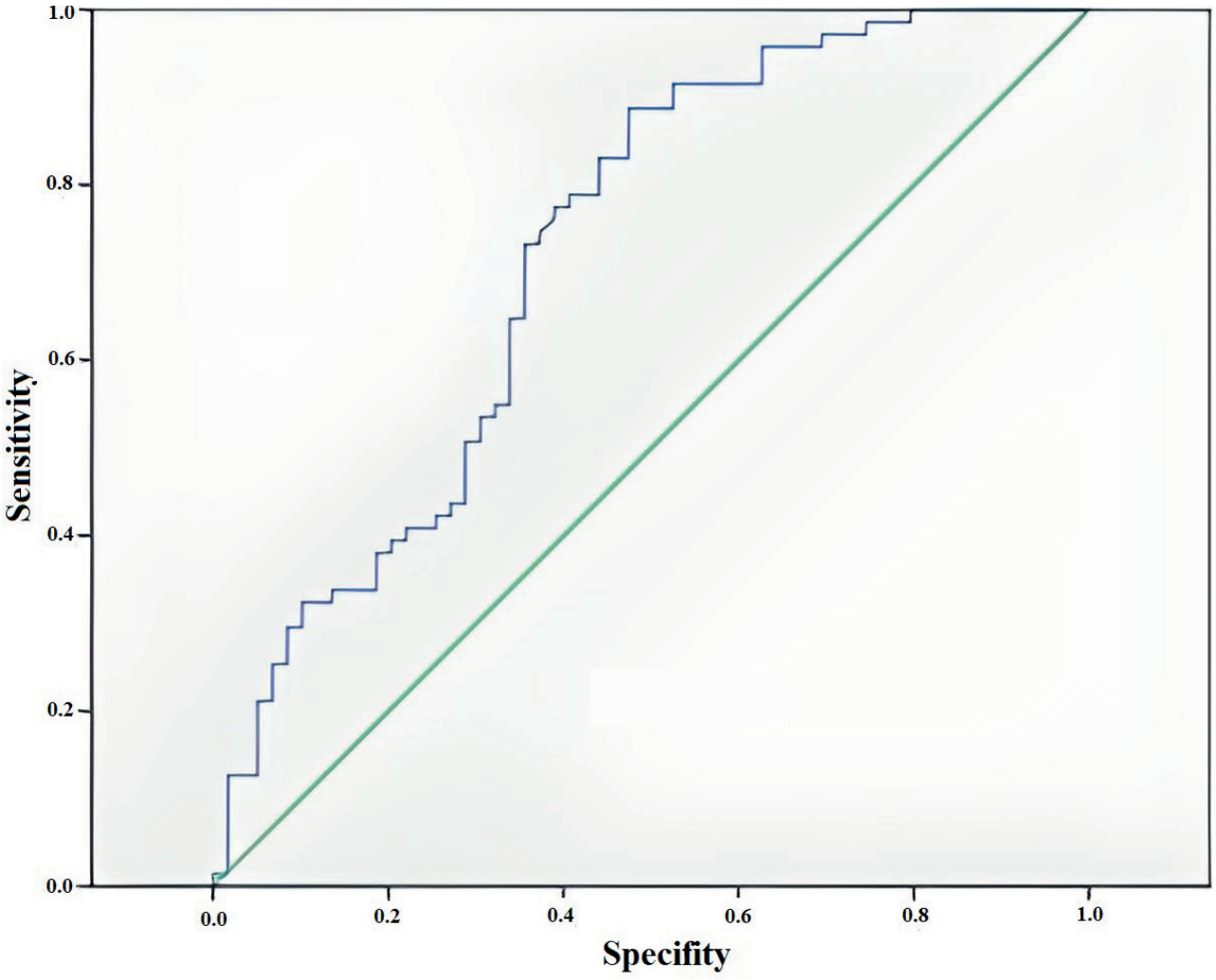

Figure 1: Fibrinogen/albumin ratio (FAR) in receiver operating characteristic (ROC) analysis in the pulmonary embolism (PE) patient group.

there was no statistical difference between the two groups (P = 0.144). PE was detected in 71 (54%) of the patients. Of those, 7 (9.9%) were subsegmental, 50 (70.4%) were segmental, and 14 (19.7%) were massive pulmonary. The neutrophil/lymphocyte ratio, D-dimer level, and mean platelet volume (MPV) of the PE patients were 5.6 (3.6–12.7), 3962.4 ± 1385.6 ng/mL FEU, and 10.3 ± 1.8 fL, respectively. In the control group, these values were 4.7 (2.9–8.0), 2633.3 ± 1441.3 ng/mL FEU, and 9.6 ± 1.2 fL, respectively. Demographic characteristics and laboratory results of the groups are given in Table 1.

The albumin values of the subjects in the control group were 3.2 ± 0.7 g/dL, and the albumin values of the patients in the PE group were 3.1 ± 0.6 g/dL. In the statistical evaluation between the groups, no significant difference was found in terms of albumin levels (P = 0.302). Fibrinogen levels were significantly higher in the PE group (520.6 ± 191 mg/dL) than in the control group (379.5 ± 187.6 mg/dL; P < 0.001). The FAR of the subjects in the control group was 99.1 (75.2–167.9), whereas the FAR in the PE group was 151 (125.1–220.5), significantly higher than the control value (P < 0.001). When ROC analysis was performed in the PE group, the FAR was found to be a significant predictive factor (AUC: 0.724; 95% CI = 0.635–0.814; P < 0.001). When the FAR was 119.3, the sensitivity was 77.5%, and specificity was 61.0% (Figure 1).

Twenty-seven patients (38%) were followed-up in the service and Forty-four patients (62%) were placed in the intensive care unit (ICU). Nine patients died in the first 3 days of treatment, 11 patients died within 7 days, and 14 patients died within 30 days. Six patients were referred to a different hospital because there was no intensive care unit, and their outcomes are unknown. Mortality rate with known outcomes in the PE group was 21%.

DISCUSSION

It should be noted that this study is the first to evaluate FAR in patients with PE. The most important step in the diagnosis of PE is emergent diagnosis. The gold standard for diagnosis is CTPA. CTPA is expensive, exposes the patient to radiation, and can also cause complications due to the use of contrast agents. The PERC rule (7), Wells and Geneva score (8,9), and D-dimer test are used to prevent unnecessary pulmonary CT angiography. Although the negative predictive value of the D-dimer test is high, there is unfortunately no test that can diagnose PE (10). Therefore, new laboratory tests and new biomarkers are needed.

Increased levels of fibrinogen increase coagulation, and reductions in albumin also increase platelet aggregation and facilitate thrombus formation. In a study by Karahan

et al., fibrinogen levels and FAR were evaluated in 68 patients with ST-elevation myocardial infarction (STEMI). Significantly higher fibrinogen and FAR were detected in STEMI patients (11).

In a study by Demir et al, the FAR was significantly higher in the patient group whose Syntax Score was moderate-high compared to the group with low Syntax Score (12).

In a study Kuyumcu et al., the FAR levels were significantly lower in normal ascending aortic diameter group compared with ascending aortic aneurysm group ($p<0.001$) (13).

Qiaodong et al. evaluated the FAR in 151 hepatocellular carcinoma patients. Patients underwent liver resection and were followed to evaluate survival. Patients with a high FAR had poorer survival and a higher recurrence rate (14). In a study conducted by Sun et al., the FAR was compared between 455 control patients and 455 patients newly diagnosed with colorectal cancer. The FAR was significantly higher in patients with colorectal cancer (15). In a study by Wei-Ming et al., 160 patients with rheumatoid arthritis and 159 control patients were enrolled. The FAR was compared between groups, and was found to be significantly higher in rheumatoid arthritis patients (16).

In terms of fibrinogen levels, when patients with and without PE were evaluated, a significant difference ($P < 0.001$) and a significant difference in FAR ($P < 0.001$) were found. No statistical correlation was found between the size of PE and FAR.

CONCLUSION

The FAR can be helpful in the diagnosis of PE. Based on the FAR value, physicians may recommend treatment for PE or referral to an ICU.

Limitations: The study had limitations: These were limited time and conducting single center.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: This study was approved by the Adnan Menderes University Ethics Committee (Meeting Decision No. 2018/1434).

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REFERENCES

1. Dirican N, Duman A, Sağlam G, Arslan A, Ozturk O, Atalay S, et al. The diagnostic significance of signal peptide-complement C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein-1 levels in pulmonary embolism. Ann Thorac Med. 2016;11(4):277-282.
2. Essien EO, Rali P, Mathai SC. Pulmonary Embolism. Med Clin North Am. 2019;103(3):549-564.
3. Laporte S, Mismetti P, Décousus H, Uresandi F, Otero R, Lobo JL, et al. Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: Findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. Circulation. 2008;117:1711– 16.
4. Aujesky D, Jiménez D, Mor MK, Geng M, Fine MJ, Ibrahim SA. Weekend versus weekday admission and mortality after acute pulmonary embolism. Circulation. 2009;119(7):962-8.
5. Bithel TC. Blood coagulation. In: Lee GR, Bithell TC et al. Wintrobes Clinical Hematology, 9th ed. Philadelphia Lea Febiger. 1993;1:568-70.
6. Infusino I, Panteghini M. Serum albumin: accuracy and clinical use. Clin Chim Acta. 2013;419:15-8.
7. Kline JA, Courtney DM, Kabrhel C, Moore CL, Smithline HA, Plewa MC, et al. Prospective multicenter evaluation of the pulmonary embolism rule out criteria. J Thromb Haemost. 2008;6:772.
8. Le Gal G, Righini M, Roy PM, Sanchez O, Aujesky D, Bounameaux H, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med. 2006;144(3):165–71.
9. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: Increasing the model's utility with the SimpliRED D-dimer. Thromb Haemost. 2000;83 (3):416–20.
10. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism: The task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC) endorsed by the European Respiratory Society (ERS). Eur Heart J. 2014;35(43):3033-73.
11. Karahan O, Acet H, Ertaş F, Tezcan O, Çalişkan A, Demir M, et al. The relationship between fibrinogen to albumin ratio and severity of coronary artery disease in patients with STEMI. Am J Emerg Med. 2016;34(6):1037-42.
12. Demir M, Özbek M, Aktan A, Ertaş F. Fibrinogen to Albumin Ratio Predicts Burden of Coronary Artery Disease in Patients with NSTEMI. Dicle Med J. 2021;48(4):688-695.
13. Kuyumcu MS, Aydın O. Fibrinogen-to-albumin ratio may be a predictor for ascending aortic aneurysm. Rev Assoc Med Bras. 2021;67(6):868-872.
14. Xu Q, Yan Y, Gu S, Mao K, Zhang J, Huang P, et al. A Novel Inflammation-Based Prognostic Score: The Fibrinogen/Albumin Ratio Predicts Prognoses of Patients after Curative Resection for Hepatocellular Carcinoma. J Immunol Res. 2018;2018:e4925498.
15. Sun F, Tan YA, Gao QF, Li SQ, Zhang J, Chen QG, et al. Circulating fibrinogen to pre-albumin ratio is a promising biomarker for diagnosis of colorectal cancer. J Clin Lab Anal. 2019;33(1):e22635.
16. Yang WM, Zhang WH, Ying HQ, Xu YM, Zhang J, Min QH. Two new inflammatory markers associated with disease activity score-28 in patients with rheumatoid arthritis: Albumin to fibrinogen ratio and C-reactive protein to albumin ratio. International Immunopharmacology. 2018, 293-298.

ORIGINAL ARTICLE

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Evaluation of Species Distribution and Antibiotic Susceptibility of Blood Culture Isolates of Patients Followed in the Intensive Care Unit Before and During the COVID-19 Pandemic: Retrospective, Single-Center Analysis

COVID-19 Pandemisi Öncesi ve Döneminde Yoğun Bakım Ünitesinde Takip Edilen Hastaların Kan Kültürü İzolatlarının Tür Dağılımı ve Antibiyotik Duyarlılıklarının Değerlendirilmesi: Retrospektif, Tek Merkez Analizi

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ABSTRACT

Objective: *This study aims to identify the microorganism species isolated from blood cultures of patients hospitalized in the ICU of a tertiary center before and during the COVID-19 pandemic and to investigate their antibiotic susceptibility.*

Material and Method: *Patients hospitalized in the ICU two years before and after the COVID-19 pandemic between March 15, 2019, and March 15, 2021, were divided into two groups, and their blood cultures were evaluated retrospectively. Isolated microorganisms and their antibiotic susceptibility were analyzed.*

Results: *A total of 1282 patients' blood cultures were analyzed, and demographic data were similar between groups. Blood culture growth was detected in 39.6% (n=202) of the patients in the pre-pandemic period and 41% (n=317) in the pandemic period. Gram-positive bacteria were isolated in 71.3%, gram-negative bacteria in 21.6%, and Candida spp. in 7.1% of the population. Klebsiella spp. was significantly higher, and Enterococcus spp. was significantly lower in blood cultures during the pandemic. In the COVID-19 period, although not significant, a decrease in antibiotic susceptibility was detected for Staphylococcus aureus, Klebsiella spp., E.coli, Enterobacter spp., and Pseudomonas spp. There was a statistically significant decrease in susceptibility to teicoplanin and linezolid in coagulase-negative staphylococci (CNS). During the pandemic, 57.6% (n=172) of the patients were positive for COVID-19. In COVID-19-positive patients, while Candida spp. was significantly higher, no decrease in antifungal susceptibility was detected.*

Conclusion: *The severe COVID-19 infection in immunocompromised patients may have led to a significant increase in secondary infections, contributing to the increase in Klebsiella strains isolated from patients in the pandemic period and the reduction in antimicrobial susceptibility. The decrease in cross-contamination in these patients, who were followed up in isolated rooms in our ICU, was influential in the significantly lower detection of Enterococcus strains. High-dose steroids in the treatment effectively increased the number of isolated Candida strains.*

Keywords:
Antibiotic sensitivity
COVID-19
Blood culture
Intensive care unit

ÖZET

Amaç: *Bu çalışmanın amacı, COVID-19 pandemisi öncesi ve döneminde tersiyer bir merkezin Yoğun bakım ünitesinde (YBÜ) yatan hastaların kan kültürlerinden izole edilen mikroorganizma türlerinin tanımlanması ve antibiyotik duyarlılıklarının araştırılmasıdır.*

Gereç ve Yöntem: *15 Mart 2019 ile 15 Mart 2021 arasındaki COVID-19 pandemisi öncesi ve sonrası 2 yıllık süreçte YBÜ'de yatan hastalar iki gruba ayrılarak kan kültürleri retrospektif olarak değerlendirildi. İzole edilen mikroorganizmalar ve antibiyotik duyarlılıkları analiz edildi.*

Bulgular: *Toplamda 1282 hastanın kan kültürü analiz edildi, demografik veriler gruplar arasında benzerdi. Pre-pandemik dönemdeki hastaların %39.6'sında (n=202) ve pandemik dönemdekilerin %41'inde (n=317) üreme saptandı. Tüm popülasyonun %71.3'ünde gram pozitif bakteriler, %21.6'sında gram negatif bakteriler ve %7.1'inde Candida spp. izole edildi. Pandemi dönemindeki kan kültürlerinde Klebsiella spp. anlamlı olarak yüksek, Enterococcus spp. ise anlamlı olarak düşüktü. COVID-19 döneminde Staphylococcus aureus, Klebsiella spp., E.coli, Enterobacter spp. ve Pseudomonas spp. için antibiyotik duyarlılıklarında anlamlı olmasa da azalma tespit edildi. Koagülaz negatif stafilokoklarda (KNS) ise teikoplanin ve linezolid duyarlılığında istatistiksel olarak anlamlı azalma mevcuttu. Pandemi dönemindeki hastaların %57.6'sı (n=172) COVID-19 pozitifti. COVID-19 pozitif hastalarda ise Candida spp. oranları anlamlı olarak yüksek iken antifungal duyarlılıkta azalma saptanmadı.*

Sonuç: *COVID-19 enfeksiyonunun bağışıklık sistemi zayıflamış hastalarda ağır seyretmesi, sekonder enfeksiyonlarda anlamlı artışa yol açarak pandemi dönemindeki hastalardan izole edilen Klebsiella suşlarında artışta ve antimikrobiyal duyarlılıktaki azalmalarda etkili olmuş olabilir. YBÜ'mizde izole odalarda takip edilen bu hastalardaki çapraz bulaşın azalmasının Enterococcus suşlarının anlamlı olarak düşük saptanmasında, tedavide yüksek doz steroidlerin kullanılmasının ise izole edilen Candida suşlarının artmasında etkili olduğunu düşünüyoruz.*

Anahtar Kelimeler:
Antibiyotik duyarlılığı
COVID-19
Kan kültürü
Yoğun bakım ünitesi

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INTRODUCTION

Intensive Care Units (ICUs) are the hospital departments where nosocomial infections, antibiotic use, and resistant microorganisms are frequently seen due to invasive procedures and lengthy hospital stays. Over the years, the types of microorganisms that cause bacteremia and their antibiotic susceptibility may change. Intermittent determination of the distribution of causative organisms and their antibiotic susceptibility is essential, as it guides empirical treatment (1).

Despite optimization of the conditions of ICUs and advances in antimicrobial therapy, bloodstream infections are still a cause of high mortality and morbidity (2). Blood cultures are an essential diagnostic test frequently used in ICUs. Demonstrating microorganisms in the patient's bloodstream is vital for diagnosing and diagnosing sepsis (3). Extended length of stay in ICUs due to the COVID-19 pandemic and the use of various drugs in the treatment may change the distribution of microorganisms that may cause secondary infections and their antibiotic susceptibility.

This study aims to identify the microorganism species isolated from blood cultures of patients hospitalized in the ICU of a tertiary center before and during the COVID-19 pandemic and to investigate their antibiotic susceptibility.

MATERIAL AND METHOD

For this retrospective cross-sectional study, approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (date:22.06.2022 number:152). The principles of the Declaration of Helsinki complied with the investigation. Microorganisms and antibiotic susceptibilities grew in the blood cultures of patients hospitalized at the University of Health Sciences Istanbul Kanuni Sultan Süleyman Training and Research Hospital ICU between March 15, 2019, and March 15, 2020, before the COVID-19 pandemic and between March 15, 2020, and March 15, 2021, were compared. All patients aged 18 years and older who stayed in the ICU for more than 24 hours without missing clinical and laboratory results were included in the study. This retrospective cross-sectional study did not determine the sample size; all patients between the relevant dates were included.

It was accepted as causative when the same microorganism was produced simultaneously in at least two blood cultures taken from the patients. If only one of the blood cultures showed growth, if the patient's clinic was compatible, or if the same microorganism was isolated in a different infection site, it was considered a factor. When *Bacillus* spp., *Corynebacterium* spp., *coagulase-negative staphylococcus* (CNS), *Micrococcus* spp., and *Propionibacterium acnes*, which belong to the skin flora, grew in only one of the blood cultures taken at the same time, it was considered as contamination (4). Repeated blood cultures from patients were not included in the study.

Blood cultures in BACTEC Plus aerobic media bottles sent to the laboratory were incubated in the BACTEC-FX automated blood culture (Becton Dickinson, USA) device. All plates were incubated for 18−24 hours at 37 °C. All strains were identified at the species level using the VITEK 2 (bioMerieux, France) method. Antimicrobial susceptibility tests of the identified strains were performed in Phoenix 100 (Becton Dickinson Co., Sparks, Maryland, USA) device according to the manufacturer's operating procedures, according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Statistical analysis

SPSS 29.0 (SPSS Inc., Chicago, USA) program was used to analyze the data. Descriptive data are expressed as the number of patients, percentage, mean, and standard deviation. The conformity of the variables to the normal distribution was evaluated analytically (Shapiro-Wilks test) and visually (histogram). The Mann-Whitney U test was used to analyze the quantitative variables that were not normally distributed among the groups. Chi-square tests were applied to examine whether the isolated microorganisms and their antibiotic susceptibility significantly changed in the pre-pandemic and pandemic periods. The statistical significance limit was accepted as $p<0.05$.

RESULTS

One thousand two hundred eighty-two patients' blood culture samples were analyzed in the ICU two years before and after the COVID-19 pandemic between March 15, 2019, and March 15, 2021. No significant difference was observed in demographic data before and during COVID-19. Of the blood culture samples included in the study, 39.7% (n=510) were sent during the pre-pandemic

Table 1: Demographic data of patients and classification of microorganisms isolated from blood cultures

Variable	Total (n=519)	Pre-pandemic period (n=202)	Pandemic period (n=317)	P-value
Age (years)	62.4 (19.3)	60.4 (20.4)	63.6 (18.4)	0.087*
Gender, n (%)				0.071**
Female	239 (46.1)	103 (51)	136 (42.9)	
Male	280 (53.9)	99 (49)	181 (57.1)	
Microorganism classification, n (%)				
Gram positive	370 (71.3)	147 (72.8)	223 (70.3)	0.552**
Gram negative	112 (21.6)	42 (20.8)	70 (22.1)	0.728**
Candida spp.	37 (7.1)	13 (6.4)	24 (7.6)	0.624**

Values are the number of patients (n), percentage, mean, and standard deviation.
**Mann-Whitney U test, **Pearson Chi-square test*

period and 60.3% (n=772) during the pandemic period. Growth was detected in the patient's blood cultures of 39.6% (n=202) in the pre-pandemic period and 41% (n=317) in the pandemic period. Contamination was detected in 11.9% (n=61) of blood cultures in the pre-pandemic period and 12.4% (n=96) of blood cultures in the pandemic period. In the whole population, gram-positive bacteria were isolated in 71.3% (n=370), gram-negative bacteria in 21.6% (n=112), and *Candida* spp. in 7.1% (n=37) of blood cultures (Table 1).

CNS was isolated from 62.4% (n=126) of the blood cultures in the pre-pandemic period, *Acinetobacter* spp. from 8.4% (n=17), and *Enterococcus* spp. from 8.4% (n=17). During the pandemic, CNS was isolated in 60.6% (n=192) of blood cultures, *Klebsiella* spp. in 10.8% (n=34), and *Candida* spp. in 7.9%. In blood cultures during the pandemic, *Klebsiella* spp. was significantly higher (p=0.006), and *Enterococcus* spp. was significantly lower (p=0.04). However, an insignificant increase in *Candida* spp. (6.4% vs. 7.6%) was observed during the pandemic period (p=0.536) (Table 2).

In the pandemic period, antibiotic susceptibility decreased in *E.coli*, *Enterobacter* spp, and *Pseudomonas* spp, although it was not significant (p>0.05) (Table 3).

During the pandemic, a decrease in the sensitivity of almost all antibiotics was observed in CNS and *Staphylococcus aureus*, although it was not significant. A significant decrease in sensitivity to erythromycin, clindamycin, levofloxacin, linezolid, and teicoplanin was observed in CNS during the pandemic period (p<0.05). There was no significant difference in antibiotic susceptibility in *Staphylococcus aureus* before and after the pandemic. However, *Staphylococcus aureus* was found to be methicillin-resistant at a rate of 26.3% (n=5). A significant decrease in ampicillin susceptibility was detected for *Enterococcus* spp. (p<0.05) (Table 4).

During the pandemic period, 57.6% of the patients followed in the ICU were positive for COVID-19 (n=172). Compared to COVID-19-positive patients with COVID-19-negative patients during and before the pandemic, isolated *Candida* spp. were significantly higher (p=0.022). There was no significant difference in

Table 2: Distribution of microorganisms isolated from blood cultures in the pre-pandemic and pandemic period

	Pre-pandemic period (n=202)	Pandemic period (n=317)	P-value
CNS	126 (62.4)	192 (60.6)	0.935*
Enterococcus spp.	17 (8.4)	13 (4.1)	0.04*
Staphylococcus aureus	4 (2)	15 (4.7)	0.104*
Klebsiella spp.	8 (4)	34 (10.7)	0.006*
Escherichia coli	11 (5.4)	15 (4.7)	0.716*
Acinetobacter spp.	17 (8.4)	14 (4.4)	0.061*
Pseudomonas spp.	2 (1)	5 (1.6)	-
Enterobacter spp.	3 (1.5)	2 (0.6)	-
Candida spp.	13 (6.4)	25 (7.9)	0.536*

Values are the number of patients (n) and percentage.
CNS: Coagulase-negative staphylococcus
**Pearson Chi-square test*

Table 3: Antibiotic susceptibility of gram-negative microorganisms isolated from blood cultures in the pre-pandemic and pandemic period

	***Klebsiella* spp.**		***E.coli***		***Acinetobacter* spp.**		***Pseudomonas* spp.**		***Enterobacter* spp.**	
	BP n=8	AP n=34	BP n=11	AP n=15	BP n=17	AP n=14	BP n=2	AP n=5	BP n=3	AP n=2
Amikacin	50	32.4	81.8	73.3	29.4	14.3	50	60	100	50
Gentamicin	50	52.9	81.8	66.7	23.5	14.3	100	60	66.7	50
İmipenem	25	20.6	90.9	60	11.8	7.1	100	20	100	50
Meropenem	25	20.6	72.7	46.7	11.8	14.3	100	40	100	50
Ciprofloxacin	12.5	17.6	54.5	46.7	17.6	14.3	100	60	66.7	50
PIP-TAZO	100	100	100	100	0	100	100	100	100	0
Cefepime	0	100	100	100	100	100	100	100	100	100
TMP-SMX	37.5	41.2	81.8	46.7	17.6	21.4	0	0	100	50
Ampicilin	12.5	8.8	36.4	33.3	0	0	0	0	0	0
Colistin	100	100	100	100	100	100	100	100	100	100

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic
PIP-TAZO: Piperacilin-tazobactam, TMP-SMX: Trimethoprim-sulfamethoxazole

Table 4: Antibiotic susceptibility of gram-positive microorganisms isolated from blood cultures in the pre-pandemic and pandemic period.

	CNS		***Staphylococcus aureus***		***Enterococcus* spp.**	
	BP n=25	AP n=40	BP n=4	AP n=15	BP n=17	AP n=13
Penicillin	0	5	0	0	-	-
Erythromycin	32*	7.5	75	53.3	-	-
Clindamycin	48**	17.5	100	60	-	-
Levofloxacin	32*	2.5	100	33.3	-	-
Linezolid	96*	75	100	53.3	76.5	84.6
Teicoplanin	92**	62.5	100	73.3	82.4	76.9
Vancomycin	88	87.5	100	86.7	88.2	76.9
Ampicillin	-	-	-	-	76.5**	38.5
Gentamicin	48	27.5	100	93.3	47.1	15.4
TMP-SMX	68	70	100	93.3	5.9	30.8

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic, CNS: Coagulase-negative staphylococcus,
TMP-SMX: Trimethoprim-sulfamethoxazole
**There is a significant difference p<0.05, Fisher's Exact test*
***There is a significant difference p<0.05, Pearson Chi-square test*

Table 5: Antifungal susceptibilities for Candida spp isolated from pre-pandemic and pandemic blood cultures

	***Candida* spp.**	
	BP n=13	AP n=24
Amphotericin B	84.6	92
Fluconazole	61.5	60.0
Caspofungin	69.2	88
Voriconazole	76.9	72
Micafungin	69.2	88.0
Flucytosine	69.2	68

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic

antifungal susceptibility for *Candida* spp. according to the periods (p>0.05) (Table 5).

DISCUSSION

Sepsis is an important problem with high morbidity and mortality. The treatment must determine antibiotic susceptibility by isolating the microorganism causing sepsis in the blood culture (5). It has been reported that 14% of COVID-19-positive patients have a severe clinical course, and 5% need ICU (6). Zhou et al. reported secondary bacterial infection in 50% of patients infected with SARS-CoV-2 and died (4).

Microorganisms grown in blood cultures vary over time and between hospitals and countries. An international cohort study reported that gram-negative bacteria were isolated more frequently (58.3%) in ICUs (7). In a multicenter study from Canada, the rates of gram-positive and negative bacteria isolated from patients in the ICU were reported as 58.6% and 21.2%, respectively (8). In studies from Turkey, the most commonly reproduced microorganisms in ICUs are *gram-positive cocci,* especially c*oagulase-negative staphylococci* (1,3,9). Sirin et al. (1) reported the rates of gram-positive and negative bacteria isolated as 44.9% and 40.3%, respectively, and Küçükateş et al. (9) reported 58.5% and 35.7%. Aytac et al. reported 60.7% gram-positive, 35% gram-negative, and 4.3% *Candida* spp. in the pre-pandemic period (3). Studies have reported methicillin resistance in CNS between 40% and 90.7% (3,10). Vancomycin and teicoplanin are the most preferred antibiotics for treating methicillin-resistant staphylococcal infections. However, strains with decreased susceptibility to glycopeptide group antibiotics have been reported recently (11). Aytac et al. stated that CNSs were 100% sensitive to vancomycin and teicoplanin before and during the pandemic (3). In our study, 71.3% gram-positive bacteria, 21.6% gram-negative bacteria, and 7.1% yeast were isolated in the population. Consistent with the literature, CNS was most frequently isolated in the pre-pandemic period (62.4%) and during the pandemic period (60.6%). There was no significant difference in CNS reproduction rates in the pre-pandemic and pandemic periods. While no change was observed in vancomycin sensitivity for CNS, a significant decrease was observed in teicoplanin and linezolid sensitivity. There may be a decrease in teicoplanin and linezolid sensitivity due to the high rate of secondary bacterial infections observed during the COVID-19 pandemic and the antibiotic therapy applied to CNS in our ICU. The microorganism differences reported between centers may be due to conditions such as the characteristics of the patients followed in ICUs, ICU bed capacity, different antibiotic treatment protocols applied, and whether the cause of bacteremia is community or hospital origin.

Contamination can be seen due to improper skin antisepsis during sample collection for blood culture. In only one of the blood cultures sent from the same patient simultaneously, CNS belonging to the skin flora, *Bacillus* species (other than *B.anthracis*), *Micrococcus* spp., *Corynebacterium* spp., *Propionibacterium* spp. reproduction is considered as contamination (3,12). Studies show that CNS strains are the most common contamination factor (13-14). As a good quality indicator, the contamination rate is required to be

below 3% (1). In studies from Turkey, contamination rates have been reported between 8.6% and 17.8% (1,15). In our study, 11.9% of contamination was observed in the pre-pandemic period and 12.4% in the pandemic period. There was no significant difference between the contamination rates before and after the pandemic. High contamination rates may be due to insufficient skin antisepsis, such as not paying attention to hand hygiene and not using gloves. Staphylococcus aureus and CNS usually constitute the majority of Gram-positive bacteria isolated from blood cultures. Karlowsky et al. CNS and Staphylococcus aureus rates 42% and 16.5%, respectively (16). In our study, CNS and *Staphylococcus aureus* was isolated at a rate of 62.4% and 2% in the pre-pandemic period and 60.6% and 4.7% during the pandemic period. According to global surveillance data, *Staphylococcus aureus* strains may differ in countries, hospitals, and even in different units (17). A surveillance study covering European countries reported that MRSA rates ranged from 5-100% and decreased in some countries over the years (18). In Staphylococcus aureus, methicillin resistance has been reported between 15.3% and 60.4% (9-12,19). Aytaç et al. reported methicillin resistance at a rate of 50% in the pre-pandemic period and 75% in the pandemic period (3). In our study, *Staphylococcus aureus* was found to be 50% (n=2) before and 20% (n=3) during the pandemic. Studies from Turkey have reported that no vancomycin resistance was found in methicillin-resistant and susceptible strains (20-21). Aytac et al. said that CNS was 100% sensitive to vancomycin and teicoplanin before and during the pandemic (3). In our study, *Staphylococcus aureus* was 100% sensitive to vancomycin in the pre-pandemic period, while 13.3% resistance was detected during the pandemic. *Enterococci* are among the leading causes of nosocomial infections. Sirin et al. (1) 13.6%, and Çetin et al. (22) reported that *enterococci* grew at 8%. In our study, *Enterococcus* spp. was significantly less isolated during the pandemic (8.4% vs. 4.1%). Due to the severe prognosis of COVID-19 patients followed in the ICU during the pandemic, the shorter duration of stay in the ICU and the less cross-contamination because they often stay in isolated rooms may cause a decrease in the number of enterococci. The most crucial problem in *enterococci* is the increasing resistance to glycopeptide antibiotics. Sirin et al. reported no glycopeptide resistance in *E. faecalis,* whereas 15.5% vancomycin and 13.8% teicoplanin resistance were in *E. faecium* (1). In our study, before the pandemic, vancomycin and teicoplanin resistance in *Enterococcus spp.* was 11.8% and 17.6%, respectively. During the pandemic period, it was found to increase to 23.1% in both vancomycin and teicoplanin. However, no significant difference was observed between the periods (Table 4). It is important to determine risk factors for vancomycin-resistant enterococcal colonization and infection, to screen patients at risk with rectal swab sampling, and to take isolation precautions.

E.coli, Klebsiella spp., *Pseudomonas* spp., and *Acinetobacter* spp. were reported to be the most frequently isolated gram-negative bacteria in patients followed up in the ICU (1,3,8,16,18). Our study's most frequently isolated gram-negative bacteria were *Klebsiella* spp., *Acinetobacter* spp., and *E.coli*, respectively. There was a significant increase in the reproduction rate of *Klebsiella* spp, during the pandemic period compared to the pre-pandemic period (3.9% vs. 10.8%, p=0.006) (Table 2). It is known that COVID-19 is more common and severe in immunocompromised patients. *Klebsiella spp*. may have been isolated more frequently during the pandemic since it can cause infections such as surgical wounds, pneumonia, bacteremia, and urinary and respiratory system infections, especially in individuals with weakened immune systems. It has been reported that bacteremia caused by *Pseudomonas aeruginosa* and *Acinetobacter* spp. is challenging to treat. Resistance development and mortality are high in ICUs where patients with weakened immunity are high (23). Sirin et al. reported that Acinetobacter spp. and *Pseudomonas aeruginosa* were isolated at a rate of 13.1% and 4.8%, respectively, from blood culture samples (1). In our study, *Acinetobacter* spp. was detected in 8.4% of the population before and 4.4% during the pandemic. *Pseudomonas* spp. was lower than the literature before the pandemic (1%) and during the pandemic (1.6%). In recent years, the increased carbapenemase production in these bacterial species has led to increasing resistance to carbapenem group antibiotics. In the literature, imipenem susceptibility has been reported between 51-82% in *Pseudomonas aeruginosa* and 14-61% in *Acinetobacter baumannii* (22,24). In our study, while the susceptibility to imipenem in *Acinetobacter* spp. and *Pseudomonas* spp. was 11.8% and 100% in the pre-pandemic period, it decreased to 7.1% and 20% during the pandemic period. However, the decrease in sensitivity during the pandemic period was insignificant (Table 3).

It has been emphasized that aminoglycosides, generally used with another antimicrobial, are the most effective antibiotics after colistin in *Acinetobacter* spp. and Pseudomonas aeruginosa (1). Turk Dagi et al. reported that gentamicin and amikacin resistance in *Acinetobacter baumannii* were 79% and 59%, respectively (25). In our study, gentamicin and amikacin resistances for *Acinetobacter* spp. were 76.5% and 71.6% before the pandemic. Consistent with the literature, aminoglycosides, except colistin, were the most sensitive antibiotics for *Acinetobacter* spp. However, although not significant, a decrease in sensitivities was observed during the pandemic (Table 3).

Different members of the *Enterobacteriaceae* family, especially *E. coli* and *K. pneumoniae*, can resist broad-spectrum beta-lactam antibiotics with their ability to produce extended-spectrum beta-lactamases (ESBL). Sirin et al. reported that *E. coli* and *Proteus* species were relatively more susceptible among ESBL-producing species, while *Klebsiella* species had higher antibiotic resistance rates (1). In our study, following the literature, the antibiotic susceptibility of *Klebsiella* spp. was lower than *E.coli*. Although insignificant during the pandemic, a sensitivity decrease was observed in both *Klebsiella* spp. and *E.coli* against beta-lactam group antibiotics. Although colistin has been reported to be the most effective antimicrobial against *A. baumannii* isolates, it has been

reported that colistin resistance has increased in recent years (26). Our study did not detect colistin resistance for *Klebsiella* spp. and *Acinetobacter* spp. both before and during the pandemic (Table 3).

It has been reported that the frequency of hospital-acquired candidemia has increased in recent years, and it is isolated between 6-10% in ICUs (1,3). In a study from Brazil, a ten-fold increase in the frequency of candidemia was reported in COVID-19 patients receiving high-dose steroids (27). Rapid diagnosis and treatment are important in invasive yeast infections since higher mortality has been reported in COVID-19 cases that do not receive treatment than those who receive antifungal treatment. In our study, *Candida* spp. was detected at a rate of 6.4% before and 7.6% during the pandemic period. During the pandemic period, 57.6% of our patients followed in the ICU were found to be positive for COVID-19. The rates of *Candida* spp. isolated from the blood cultures of COVID-19-positive patients were significantly higher than those of COVID-19-negative patients (p=0.022).

Limitations

The study's limitations are retrospective, single-center, and the patient sample is small.

CONCLUSION

In conclusion, we think that the severe course of COVID-19 infection in patients with weakened immune systems may have caused a significant increase in secondary infections, which may have contributed to the increase in Klebsiella strains isolated from patients in the pandemic period, as well as the decrease in susceptibility to gram-positive and negative microorganisms. The decrease in cross-contamination in these patients, who are frequently followed in isolated rooms in our ICU, may have played a role in the significantly lower detection of *Enterococcus* strains. The increase in candidemia in COVID-19-positive patients may be due to the prolonged hospital stay and high-dose steroid use in treatment, and more effective infection control programs and rational antibiotic use policies should be implemented in similar pandemic periods that may occur in the future.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: For this retrospective cross-sectional study, approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (date:22.06.2022 number:152)

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REFERENCES

1. Şirin MC, Ağuş N, Yılmaz N, Bayram A, Yılmaz-Hancı S, Şamlıoğlu P, et al. Microorganisms isolated from blood cultures of the patients in intensive care units and their antibiotic susceptibilities. Turk Hij Den Biyol Derg. 2017;74(4):269-278. DOI: 10.5505/TurkHijyen.2017.94899
2. Hoenigl M, Wagner J, Raggam RB, Prueller F, Prattes J, Eigl S, et al. Characteristics of hospital-acquired and community-onset blood stream infections, South-East Austria. PLoS One. 2014;9(8):e104702.
3. Aytaç Ö, Şenol FF, Şenol A, Öner P, Aşçı Toraman Z. A Comparison of the Species Distribution and Antibiotic Susceptibility Profiles of Blood Culture Isolates from Intensive Care Unit Patients Before and During COVID-19 Pandemic. Turk Mikrobiyol Cemiy Derg. 2022;52(1):39-47.
4. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-1062.
5. Florio W, Morici P, Ghelardi E, Barnini S, Lupetti A. Recent advances in the microbiological diagnosis of bloodstream infections. Crit Rev Microbiol. 2018;44(3):351-370.
6. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-151.
7. Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F, et al. Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med. 2012;38(12):1930-1945.
8. Zhanel GG, DeCorby M, Laing N, Weshnoweski B, Vashisht R, Tailor F, et al. Antimicrobial resistant pathogens in intensive care units in Canada: Results of the Canadian National Intensive Care Unit (CAN-ICU) Study, 2005-2006. Antimicrob Agents Chemother. 2008;52(4):1430-1437.
9. Küçükateş E, Gültekin N. Antimicrobial Susceptibility and Microorganisms Isolated from Blood Cultures of Hospitalized Patients in Intensive Care Units. Haseki Tip Bul. 2016;54(2):97-102.
10. Asaad AM, Ansar Qureshi M, Mujeeb Hasan S. Clinical significance of coagulase-negative staphylococci isolates from nosocomial bloodstream infections. Infect Dis (Lond). 2016;48(5):356-360.
11. Çalık Ş, Tosun S, Altın Ü, Arı A, Olut AI, Yüksel Ergin Ö. Is There Clinical Significance of Coagulase-Negative Staphylococci Isolated from Blood Cultures? Flora. 2017;22(1):34-41.
12. Kirn TJ, Weinstein MP. Update on blood cultures: how to obtain, process, report, and interpret. Clin Microbiol Infect. 2013;19(6):513-520.
13. Stohl S, Benenson S, Sviri S, Avidan A, Block C, Sprung CL, et al. Blood cultures at central line insertion in the intensive care unit: comparison with peripheral venipuncture. J Clin Microbiol. 2011;49(7):2398-2403.
14. Vicent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009;302(21):2323-2329.
15. Duman Y, Kuzucu Ç, Çuğlan S. Bacteria Isolated from Blood Cultures and Their Antimicrobial Susceptibility. Erciyes Medical Journal. 2011;33(3):189-196.
16. Karlowsky JA, Jones ME, Draghi DC, Thornsberry C, Sahm DF, Volturo GA. Prevalence and antimicrobial susceptibilities of bacteria isolated from blood cultures of hospitalized patients in the United States in 2002. Ann Clin Microbiol Antimicrob. 2004;3:7. DOI: 10.1186/1476-0711-3-7
17. Lakhundi S, Zhang K. Methicillin resistant Staphylococcus aureus: molecular characterization, evolution and epidemiology. Clin Microbiol Rev. 2018;31(4):e00020-18.
18. Köck R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, et al. Methicillin-resistant Staphylococcus aureus (MRSA): Burden of disease and control challenges in Europe. Euro Surveill. 2010;15(41):19688.
19. Kula Atik T, Uzun B. Evaluation of Resistance in Staphylococcus aureus Strains Isolated From Blood Cultures to Methicillin and Other Antimicrobial Agents. Klimik Derg. 2020;33(2):132-136.
20. Gülmez D, Gür D. Microorganisms Isolated from Blood Cultures in Hacettepe University İhsan Doğramacı Children's Hospital from 2000 to

2011: Evaluation of 12 Years. J Pediatr Inf. 2012;6(13):79-83.
21. Altunsoy A, Aypak C, Azap A, Ergönül O, Balık I. The impact of a nationwide antibiotic restriction program on antibiotic usage and resistance against nosocomial pathogens in Turkey. Int J Med Sci. 2011;8(4):339-344.
22. Çetin F, Mumcuoğlu F, Aksoy A, Gürkan Y, Aksu N. Microorganisms isolated from blood cultures and their antimicrobial susceptibilities. Turk Hij Den Biyol Derg. 2014;71(2):67-74.
23. Kılınç Ç, Güçkan R, Kahveci M, Kayhan Y, Pirhan Y, Özalp T. Distribution of Gram Negative Isolates in Blood Cultures and Their Antibiotic Resistance. Int J Basic Clin Med. 2015;3(3):125-130.
24. Uzun B, Gungor S, Yurtsever SG, Afsar İ, Demirci M. Evalution of Resistance to Various Antibiotics in Pseudomonas aeruginosa and Acinetobacter baumannii Strains Isolated from Blood Cultures of Intensive Care Patients. Ankem Derg. 2012;26(2):55-60. DOI:10.5222/ankem.2012.055
25. Türk Dağı H, Arslan U, Tuncer İ. Antibiotic Resistance of Acinetobacter baumannii Strains Isolated from Blood Cultures. ANKEM Derg. 2011;25(1):22-26.
26. Lee CR, Lee JH, Park M, Park KS, Bae IK, Kim YB, et al. Biology of Acinetobacter baumannii: Pathogenesis, antibiotic resistance mechanisms, and prospective treatment options. Front Cell Infect Microbiol. 2017;7:55.
27. Riche CVW, Cassol R, Pasqualotto AC. Is the frequency of candidemia increasing in COVID-19 patients receiving corticosteroids? J Fungi (Basel). 2020;6(4):286.

ORIGINAL ARTICLE

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Kapadokya Bölgesinde Karbonmonoksit Zehirlenmelerinin Analizi ve Meteorolojik Verilerle Karşılaştırılması

Analysis of Carbon Monoxide Poisoning in Cappadocia Region and Comparison with Meteorological Data

Mustafa Alpaslan

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ABSTRACT

Objective: *Analyzing patients diagnosed with CO poisoning in the emergency department, the aim is to evaluate the weather conditions seen on the admission dates of the patients and to provide up to date information to the literature.*

Material and Methods:*It was conducted retrospectively in a secondary care hospital, by screening the patients diagnosed with CO poisoning with the T-58 ICD code between 01.01.2021 and 31.12.2021. Comparisons were made with the weather data of 2021 from the meteorology institution.*

Results: *Within the scope of the study, 169 patients were evaluated with the diagnosis of CO poisoning. The mean age was 35.20±22.58 years. It was seen that the most applications were in the winter months and in the morning hours during the day. The mean carboxyhemoglobin (COHb) values of the patients were 24.29±8.81 and the mean blood lactate level was 2.82±1.98 mmol/L. It was concluded that there was a significant relationship between COHb level and lactate level. The average wind direction on the days when the cases were seen was 209.84°±94.3°, the average wind speed was 2.53±1.33 m/sec, and the average daily precipitation was 4.69±6.89 kg/m².*

Conclusion: *Carbon monoxide poisoning is most common during the winter months. According to the results of the study, there was a significant increase in the number of cases on the days of southwestern winds. In order to prevent poisoning, weather conditions should be monitored and necessary precautions should be taken.*

ÖZET

Amaç: *Acil serviste karbon monoksit (CO) zehirlenmesi teşhisi konulan hastaları analiz etmek, hastaların başvuru tarihlerinde görülen hava koşullarını değerlendirmek ve literatüre güncel bilgiler sunmaktır.*

Gereç ve Yöntem: *İkinci basamak bir hastanede retrospektif olarak 01.01.2021-31.12.2021 tarihleri arasında T-58 ICD kodu ile CO zehirlenmesi teşhisi konulan hastaların taranması ile yapılmıştır. Meteoroloji kurumundan alınan 2021 yılına ait hava durumu verileri ile karşılaştırmalar yapılmıştır.*

Bulgular: *Çalışma kapsamında 169 hasta CO zehirlenmesi teşhisi ile değerlendirildi. Yaş ortalaması 35,20±22,58 di. En çok başvurunun kış aylarında ve gün içerisinde sabah saatlerinde olduğu görüldü. Hastaların karboksihemoglobin (COHb) değerleri ortalama 24,29±8,81 ve kan laktat düzeyi ortalama 2,82±1,98 mmol/L olarak ölçüldü. Karboksihemoglobin düzeyi ile laktat düzeyi arasında anlamlı ilişki olduğu sonucuna varıldı. Vakaların görüldüğü günlerdeki rüzgâr yönü ortalaması 209,84°±94,3°, ortalama rüzgâr hızı 2,53±1,33 m/sn ve ortalama günlük yağış miktarı 4,69±6,89 kg/m² olmuştur.*

Sonuç: *Karbon monoksit zehirlenmesi en sık kış aylarında görülmektedir. Çalışma sonuçlarına göre lodos rüzgârları olduğu günlerde anlamlı derecede vaka sayısında artış olmuştur. Zehirlenmelerin önüne geçilmesi için hava koşullarının takibi yapılmalı ve gerekli uyarılar yapılarak tedbirler alınmalıdır.*

Keywords:
Carbon monoxide poisoning
Carboxyhemoglobin and lactate relationship
Windy weather

Anahtar Kelimeler:
Karbon monoksit zehirlenmesi
Karboksihemoglobin ve laktat ilişkisi
Rüzgârlı Hava

GİRİŞ

Karbon monoksit gazı, kokusu ve rengi olmayan zehirli bir gaz olup karbon içeren materyallerin yeterli derece yanmaması ile ortaya çıkar (1). Son derece zehirli olan bu gaz kişide uyarı ya da semptom vermeden dahi hızla ölüme yol açabilir. Karbon monoksit gazı en sık; soba bacasından sızma, şofbende oluşan gaz sızıntısı, otomobil egzozları ve yangınlarda görülür (1,2). Karbon monoksit gazı hemoglobine normal oksijenden 250 kat daha fazla bağlanarak çok daha hızlı şekilde dokulara ulaşarak kısa sürede ölümcül sonuçlar doğurabilir (1). Karbon monoksit gazı, kapalı ortamlarda daha çok görülür ve iyi bir havalandırma ile dahi ortamda birikmiş vaziyette bulunabilir (2). Semptom vermeden zehirlenmelere neden olabilir. Teşhis ve tedavi süreci ne kadar hızlı olursa aynı oranda morbidite ve mortalite azalmaktadır (2). Semptom görülen ve zehirlenme şüphesi olan hastalar en sık acil servise başvurmaktadır. Başvuruların büyük çoğunluğu soğuk ve/veya rüzgârlı havalarda olmaktadır (3). Karbon monoksit zehirlenmeleri, yaşanılan bölgenin hava şartları ve toplumun sosyoekonomik şartlarına göre bazı bölgelerde daha sık görülmektedir (4). Hastalar

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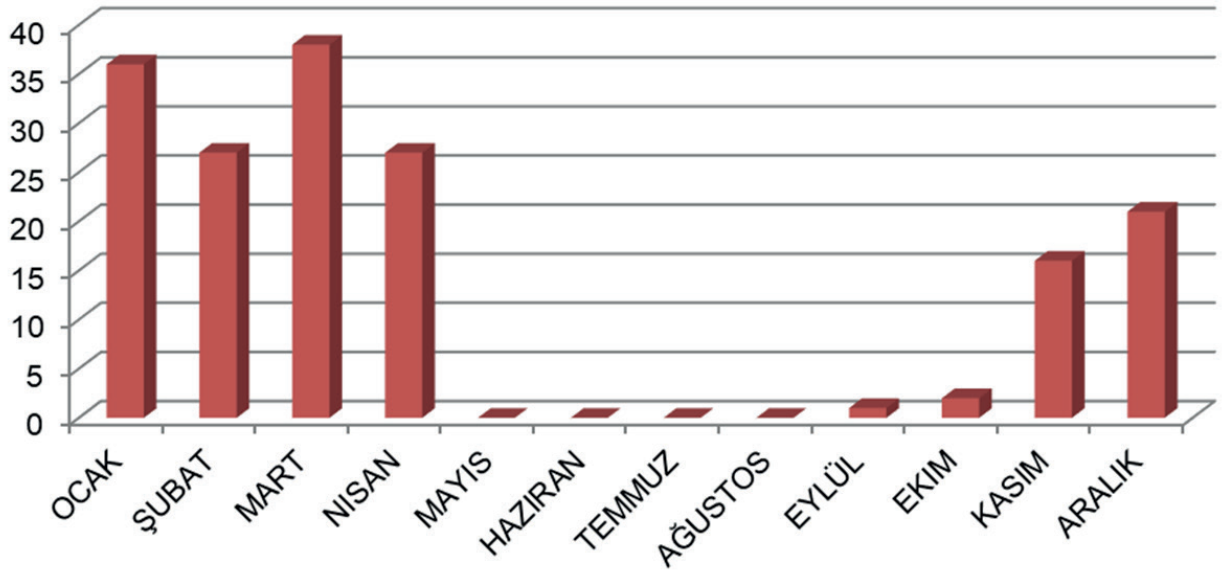
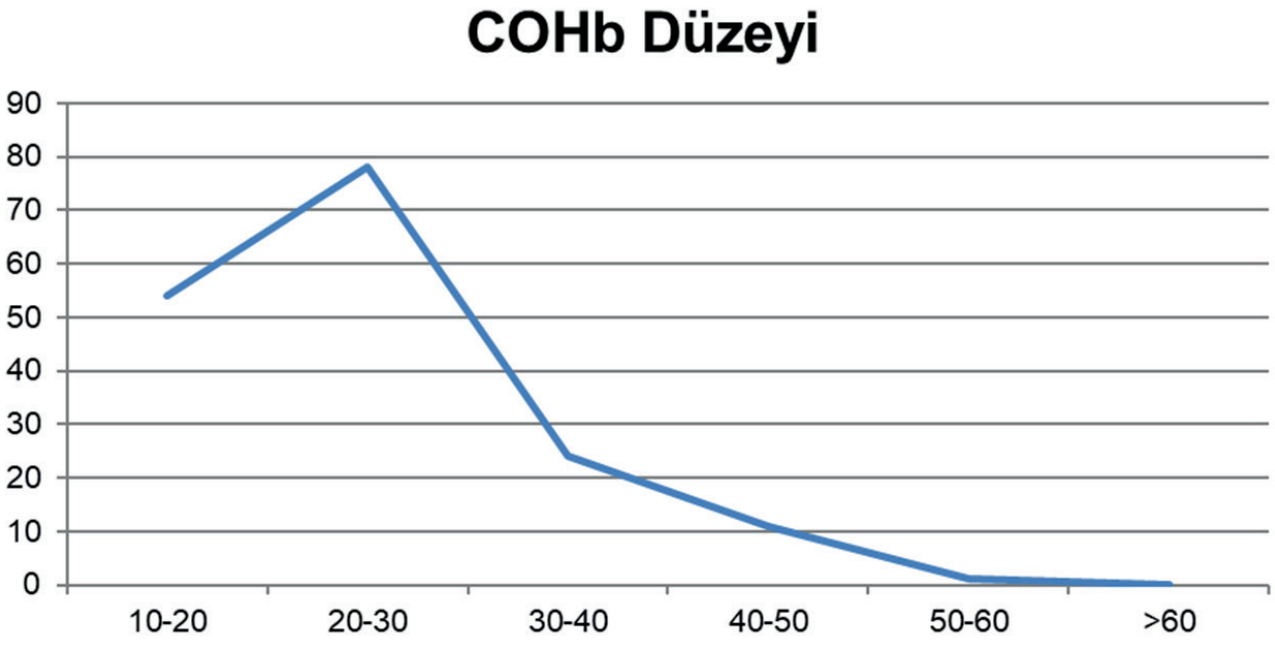


Grafik 1: Karbon Monoksit Zehirlenmesi İle Başvuran Hastaların Aylara Göre Dağılımı



Grafik 2: Karboksihemoglobin Düzeylerine Göre Hasta Sayılarının Dağılımı

genelde zehirlenme olduğunun farkında değildir ve spesifik olmayan semptomlarla başvurmaktadırlar. Hafif zehirlenmelerde bulantı, baş ağrısı, baş dönmesi kırgınlık gibi semptomlar daha çok görülmektedir (5). Ancak ileri düzey zehirlenmelerde bilinç kaybı, koma gibi durumlar görülür (5,6). Bu şekilde gerçekleşen başvurularda en önemli tanı yöntemi CO zehirlenmesinden şüphe duyulmasıdır. Tanı koymada kullanılan en önemli tetkik kan gazıdır. Karboksihemoglobin değerinin yüksek bulunması tanı için yeterli bir kriterdir (7). Tedavide ise normobarik veya hiperbarik oksijen tedavisi kullanılmaktadır (7,8).

Meteoroloji biliminde ise rüzgâr yönleri derece olarak şu şekilde sınıflandırılmaktadır: Yıldız rüzgârları 000°, poyraz rüzgârları 045°, gün doğusu rüzgârları 090°, keşişleme rüzgârları 135°, kıble rüzgarları180°, lodos rüzgârları 225°, gün batısı rüzgârları 270°, karayel rüzgârları 315º dir. Bu verilere göre 000º-090º arası poyraz, 090º-180º arası keşişleme, 180º-270º arası lodos, 270º-360º arası karayel rüzgârları olarak değerlendirilir (9). Ayrıca rüzgar hızlarını da şu şekilde sınıflandırmıştır; sakin (C): 0.0-0.2 m/sn, esinti: 0.3-1.5 m/sn, hafif rüzgar 1.6-3.3 m/sn, tatlı rüzgar: 3.4-5.4 m/sn, orta rüzgar: 5.5-7.9 m/sn, sert rüzgar: 8.0-10.7 m/sn, kuvvetli rüzgar: 10.8-13.8 m/sn, fırtınamsı rüzgar: 13.9-17.1 m/sn, fırtına:17.2-20.7 m/sn, kuvvetli fırtına: 20.8-24.4 m/sn), tam fırtına: 24.5 - 28.4 m/sn, çok şiddetli fırtına: 28.5-32.6 m/sn, Harikeyn (Orkan): 32.7 m/sn ve fazlasını ifade eder (9).

Bu çalışmanın amacı acil serviste CO zehirlenmesi teşhisi konulan hastaların analizini yapmak ve zehirlenmelerin hangi vakitlerde ve hava koşullarında sık meydana geldiğini analiz ederek vakaların önüne geçilmesini artırmak adına veriler elde etmektir.

GEREÇ VE YÖNTEM

Çalışma, 01.01.2021 ile 31.12.2021 tarihleri arasında 1 yıllık veriler analiz edilerek ikinci basamak acil serviste CO zehirlenmesi tanısı konulan hastalarda retrospektif arşiv taraması ile yapılmıştır. Çalışmaya Nevşehir Hacıbektaş Veli Üniversitesi 12.12.2022 tarih ve 2022/112 sayılı etik kurul onayı alındıktan sonra başlanmıştır. Karbon monoksit teşhisi kesinleştirilen ve kan gazında COHb değeri 10'un üzerinde olan hastalar CO zehirlenmesi kabul edilmiştir. Hastalarda demografik veriler, klinik veriler ve meteoroloji genel müdürlüğünden alınan rüzgâr yönü, hızı ve günlük yağış miktarı verileri karşılaştırılmıştır. Verileri analiz etmekte Statistical Packagefor Social Sciences for Windows 21,0 (SPSS 21,0) programı kullanılmıştır. İstatistiksel analiz olarak tanımlayıcı istatistikler (frekans, yüzde dağılımı) ve iki grup arasında kategorik değişkenlerin karşılaştırılmasında ki kare testi kullanılmıştır. Sonuçlar ortalama ± SS, veya frekans (yüzde) şeklinde verilmiştir. Yüzde 95 güven aralığında $p < 0.05$ istatistikî olarak anlamlı kabul edilmiştir.

BULGULAR

Çalışmada çocuk acil ve erişkin acil kliniği değerlendirilmiş olup 169 hastaya CO zehirlenmesi teşhisi konulmuştur. Hastaların %61,9 u kadındı. Yaş aralığı değerlendirdiğinde ise en düşük 2 ve en yüksek 89 yaşında hasta olduğu görüldü. Yaş ortalaması ise 35,20±22,58 di. Hasta başvurularının daha çok kış aylarında olduğu görülmekle beraber en çok başvuru %22,6 oranı ile Mart ayındadır. Yaz aylarında ise hiç başvuru olmamıştır (Grafik 1). Hastaların başvuru saatleri incelendiğinde 00:00-06.00 saatleri arasında 24, 06:00-12:00 saatleri arasında 75, 12:00-18:00 saatleri arasında 47, 18:00-24:00 saatleri arasında 23 hasta başvurmuştur. En çok başvuru %44,3 oranla 06:00-12:00 saatleri arasındadır. Hastaların COHb değerleri incelendiğinde en düşük 10,20 ve en yüksek 55,90 değerlerine ulaşılmıştır. Ortalama değer ise 24,29±8,81dir. Değerler aralıklı olarak detaylı incelendiğinde ise COHb değeri;10-20 arası 54 hasta (%32,1), 20-30 arası 78 hasta (%46,4), 30-40 arası 24 hasta (%14,3), 40-50 arası 11 hasta (%6,5), 50-60 arası 1 hasta (%0,6) olduğu görüldü (Grafik 2). Kanda laktat düzeyleri incelendiğinde en düşük değer 0,75mmol/L, en yüksek değer ise 18,10mmol/L dir. Ortalama kan laktat düzeyi 2,82±1,98 mmol/L dir. Değerler aralıklı olarak incelendiğinde ise 0-2 aralığında 60 (%35,7) hasta, 2-4 aralığında 84 hasta (%50), 4-6 aralığında 14 hasta (%8,3), 6-8 aralığında 6 hasta (%3,6), 8-10 aralığında 2 hasta (%1,2), 10 ve üzerinde ise 2 hasta (%1,2) sonucuna varılmıştır (Grafik 3). Karboksihemoglobin değerleri ve laktat düzeyleri arasındaki ilişki analiz edildiğinde iki grup arasında anlamlı ilişki olduğu görüldü (Ki Kare 165,829, $p<0.001$). Çalışmada zehirlenme vakalarının görüldüğü günlerde, rüzgâr yönleri derece olarak analiz edilmiştir. Çalışmaya göre vakaların görüldüğü günlerdeki rüzgâr yönü ortalaması 209,84º±94,3º dir. Zehirlenme vakalarının görüldüğü günler ve rüzgâr yönleri karşılaştırması yapıldığında anlamlı sonuçlar ortaya çıkmıştır (Ki Kare 840.000, $p<0,001$). Bu sonuca göre ortalama en fazla vaka 99 hasta ile %58,9 oranıyla 180º-270º arasında olduğu günlerdedir. İstatistiksel olarak rüzgâr yönleri ve vaka sayıları tablo 1 de verilmiştir. Vakaların görüldüğü günlerde görülen rüzgâr hızı karşılaştırması yapılmıştır. En düşük hız 0,7 m/sn, en yüksek hız ise 5,5 m/sn dir. Ortalama rüzgâr hızı ise 2,53±1,33 m/sn dir. Rüzgâr hızlarına göre sınıflandırma yapıldığında ise en fazla %41,7 oranıyla 3,4-5,4 m/sn aralığında görülmüştür. Genel olarak değerlendirme yapılırsa %97 oranında 1,6-7,9 m/sn aralığında vaka sayısı daha fazladır. Vakaların görüldüğü günler ile rüzgâr hızı karşılaştırıldığında iki grup arasında anlamlı fark görülmedi (Ki Kare 4368, $p>0,05$). Zehirlenme vakalarının görüldüğü günlerdeki yağış miktarı analiz edilmiştir. Buna göre vakaların görüldüğü günlerde en düşük 0 kg/m², en yüksek ise 29 kg/m² yağış görülmüştür. Ortalama yağış miktarı ise 4,69±6,89 kg/m² dir. Vakaların görüldüğü günler ile yağış miktarı karşılaştırıldığında iki grup arasında anlamlı fark görülmedi (Ki Kare 2434,95, $p>0,05$). Rüzgâr yönü ile kanda COHb düzeyleri arasında ilişki karşılaştırılmış olup anlamlı sonuçlar elde edilmedi (Ki Kare 32,743, $p> 0,05$). Rüzgâr hızı ile kanda COHb düzeyi arasında anlamlı ilişki yoktur (Ki Kare 94,165, $p>0,05$).Yağış miktarı ile COHb düzeyi arasında anlamlı ilişki yoktur (Ki Kare 60,790, $p>0,05$). Çalışmada değerlendirilen hasta grubunda 4 hasta takip amaçlı servise yatırılmış, 5 hastaya ise hiperbarik oksijen tedavisi için sevk talebinde bulunulmuştur. Çalışma kapsamına alınan hasta grubunda ölümle sonlanan vaka yoktur.

Tablo 1: Rüzgâr Yönü ve Vaka Sayıları

Rüzgâr Yönü	Hasta Sayısı (N)	Yüzde (%)
000º	0	0
000º- 045º	22	13,1
045º- 090º	0	0
090º- 135º	0	0
135º- 180º	9	5,4
180º- 225º	66	39,3
225º- 270º	33	19,6
270º- 315º	14	8,3
315º- 360º	24	14,3
Toplam	169	100

TARTIŞMA

Karbon monoksit zehirlenmeleri özellikle soğuk havalarda ve kış aylarında acil servislerde sık görülen vakalar arasındadır(2). Kokusuz ve renksiz olan CO gazı farkındalık yaratmadan zehirlenmelere neden olabilmekte ve erken fark edilmediği takdirde ölümle sonuçlanabilmektedir (1,2,13). Karasal iklimin olduğu ve özellikle kış aylarının daha sert hava koşulları ile geçtiği bölgelerde ısınma kaynaklı olarak kullanılan yakıtların yeterli derecede yanmaması ve/veya hava koşullarının olumsuz olması nedeniyle zehirlenme oranları artmaktadır (13,15).

Çalışmada vaka yaşı ortalama 35,20±22,58 olarak görülmüş ve çoğunluk %61,9 oranla kadınlardan oluşmuştur. Yaş ortalamasını; Arıcı ve ark. 30,2±15,4 (1), Yılmaz ve ark. 39,5±16,3 (3) ve Topçu ve ark 37,5±17,8 (10) olarak analiz etmiş olup bu çalışmadakine benzer yaş ortalaması değerleri görülmüştür. Amerika'da yapılan bir çalışmada ise yaş ortalaması 30±20 çıkmıştır (14). Karbon monoksit zehirlenmeleri genelde ev ortamında olmakla beraber acil servislere başvurular aile şeklinde olmaktadır. Çocuk ve yaşlıların da olduğu göz önüne alınırsa genel olarak çalışmalarda benzer yaş ortalaması değeri ortaya çıkmaktadır. Cinsiyet dağılımı da bazı çalışmalarda bu çalışmada olduğu gibi zehirlenmenin daha çok kadınlarda görüldüğünü gösterirken (1,3), Eskişehir'de yapılan bir çalışma erkeklerde daha çok zehirlenme görüldüğünü belirtmiştir (13). Topçu ve ark. yaptığı çalışmada olguların %50 sinin erkek olduğunu belirtmişlerdir (10). Yunanistan'da yapılan bir çalışmada erkek oranı çok daha yüksek çıkmıştır (4). Yapılan çalışmalara göre cinsiyet dağılımında anlamlı bir fark yoktur. Çalışmadan elde edilen verilere göre vakaların tamamına yakını kış aylarında görülmüştür. Benzer çalışmalarda da kış aylarında CO zehirlenmesi vakalarının artığı görülmektedir (1,3,10,13-15). Bu çalışmada en çok Mart ayında vaka görülmüştür. Amerika'da yapılan bir çalışma en çok Aralık ayında vakaların görüldüğünü belirtmiştir (14). Ülkemizde yapılan farklı iki çalışmada ise en çok Ocak ayında vaka görüldüğü belirtilmiştir (3,11,12). Çalışmaların büyük bir kısmı CO zehirlenmelerinin kış aylarında daha çok olduğunu vurgulamaktadır. Aylar arasındaki vaka sayısındaki fark bölgesel olarak hava şartlarının değişmesine bağlı olarak ortaya çıkmaktadır. Hastaların başvuru saatlerine bakıldığında en çok sabah saatlerinde (06:00-12:00) başvuru yapılmıştır. Topçu ve ark. nın yaptığı bir çalışmada en çok başvuru 20:00-08:00 saatleri arasında olarak %97,3 oranında verilmiş olup (10), Tursun ve ark. yaptıkları yaptığı çalışmada ise saatler arasında anlamlı fark görülmemiştir (11). Bu çalışmadaki verilere göre hastaların büyük çoğunluğunun uyku anında semptomların farkına varmadığını ve özellikle sabah saatlerinde başvuru yaptığı düşünülmektedir. Uykuda geçirilen sürede CO zehirlenmelerinin farkında olma durumu düşebilir ve geç kalınmış durumlarda ölüm ihtimali artabilir.

Başvuru anında kanda COHb değeri bu çalışmada ortalama 24,29±8,81 di. Karboksihemoglobin seviyesini ortalama Topçu ve ark. 23,7±9,2 (10), Usul ve ark. 20,9±10,9 (16), Özdemir ve ark. 25,35±8,31(17), Emektar ve ark. 27,2±8,9 (18) olarak ölçmüşlerdir. Ancak bir çalışmada ise 53,5±17,3 olarak daha yüksek seviyelerde olduğu görülmüştür (13). Kanda COHg düzeyi, hastaların CO gazına maruziyetine, acil servise zehirlenme sonrası geçen başvuru sürelerine, kan gazı cihazlarının kalibrasyonuna göre farklılıklar gösterebilir. Bu çalışmadaki ortalama değer literatür verilerine yakın değerlerde olmuştur. Hastaların laktat düzeyleri incelendiğinde ortalama değer 2,82±1,98mmol/L olarak elde edilmiştir. Karbon monoksit zehirlenmesi görülen vakalarda kan laktat düzeyi araştırılan benzer çalışmalarda ortalama değerlerin bu çalışmadakine yakın seviyelerde olduğu görülmüş olup ortalama laktat düzeyini Tursun ve ark. yaptıkları çalışmada 1,94 mmol/l (11), Usul ve ark. 2,4±1,8 (16), Özdemir ve ark. 2,3 mmol/L (17) olarak ölçmüşlerdir. Zehirlenme görülen vakalarda kanda COHb düzeyi ve laktat düzeyleri arasında bu çalışmada olduğu gibi yapılan benzer çalışmalarda iki değer arasında korelasyon olduğu görülmüştür (16-19).

Çalışmada hava koşulları ile zehirlenme vakalarının sıklığı incelendi. Vakaların olduğu günlerdeki rüzgâr yönü ortalaması 209,84º±94,3º olmakla beraber en fazla vaka %58,9 oranıyla 180º-270º arasında olduğu günlerde görüldü. Çalışmadaki vakaların büyük çoğunluğu (%58,9) lodos rüzgârları olan günlerde, ikinci sıklıkta ise karayel rüzgârları (%22,6) olduğu günlerdeydi. Yılmaz ve ark. Ankara ilinde CO zehirlenmelerinde meteorolojik verilerle ilgili bir çalışma yapmışlardır. Bu çalışmadan farklı olarak vakalar en sık kuzey ve kuzeydoğu yönündeki rüzgârlarda görülmüştür (3). İki çalışma arasındaki farkın bölgesel farklılıktan kaynaklandığı öngörülmektedir. Vakaların olduğu günlerde rüzgâr analizi yapılmış olup ortalama rüzgâr hızı ise 2,53±1,33 m/sn olup, rüzgâr hızlarına göre sınıflandırma yapıldığında ise en fazla vaka %41,7 oranıyla 3,4-5,4 m/sn aralığındaydı. Bu çalışmada en çok vaka tatlı rüzgâr aralığında görülmüş olup rüzgâr hızları ile zehirlenme vakaları arasında anlamlı ilişki bulunamadı (Ki Kare 4368, p>0,05). Vakaların görüldüğü günler ile yağış miktarı karşılaştırıldığında iki grup arasında anlamlı fark görülmedi (Ki Kare 2434,95, p>0,05). Analiz sonuçlarına göre rüzgâr yönü ile zehirlenme vakaları arasında ilişki olduğu görülmekle beraber rüzgâr hızı ve yağış miktarının anlamlı derecede etkili olmadığı kanaatine varıldı. Ayrıca meteorolojik faktörler ve hastaların kanda COHb ve laktat düzeyleri arasında ilişki olup olmadığı analiz edilmiş ve veriler arasında anlamlı farklar görülmemiştir. Literatürde CO zehirlenmeleri ile ilgili çok sayıda çalışma olmakla beraber meteoroloijk verilerin karşılaştırıldığı çalışma sayısı nadirdir. Bu nedenle verileri karşılaştırma konusunda yeterli kaynak bulunamamıştır. Önümüzdeki zamanlarda farklı bölge ve iklimlerde bu tarz çalışmaların yapılması literatüre yeni veriler katma adına faydalı olacaktır.

Kısıtlılıklar

Hiperbarik oksijen tedavisi amacıyla sevk edilen hastaların mortalitesi değerlendirilemedi.

SONUÇ

Karbon monoksit zehirlenmesi en sık kış aylarında görülmektedir. Çalışma sonuçlarına göre lodos rüzgârları olduğu günlerde anlamlı derecede vaka sayısında artış olmuştur. Zehirlenmelerin önüne geçilmesi için hava koşullarının takibi yapılmalı ve gerekli uyarılar yapılarak

tedbirler alınmalıdır. Ayrıca acil servislerde çalışan hekimlerin özellikle kış aylarında CO zehirlenmesini ayırıcı tanıda mutlaka düşünmesi gerekir. Erken teşhis mortaliteyi azaltmaktadır.

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Fon: Bu çalışma için hiçbir kurum veya kuruluştan finansal destek alınmamıştır.
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REFERENCES

1. Akgün Arıcı A, Demir Ö, Özdemir D, Ünverir P, Tunçok Y. Acil Servise Başvuran Karbon monoksit MaruzKalımları: On Dört Yıllık Analiz. Dokuz Eylül Üniversitesi Tıp Fakültesi Dergisi. 2010;24(1):25-32.
2. Kandiş H, Katırcı Y, Karapolat B S. Karbon monoksit Zehirlenmesi. Duzce Medical Journal. 2009;11(3):54-60.
3. Yılmaz D, Çavuş U, Yıldırım S, Çat BG, Besi G, Yılmaz O, et al. The Effect of Carbon monoxide Sources and Meteorologic Changes in Carbon monoxideI Intoxication: A Retrospective Study. Acta Med Nicomedia. 2020;3(1):1-4.
4. Stefanidou ME, Maravelias CP, Dona AA, Pistos CM, Spiliopoulou CA, Athanaselis SA. Carbon monoxide related deaths in Greece: a 23 year survey. Am J Forensic Med Pathol. 2012;33(2):128.
5. Harper A, Croft-Baker J. Carbon monoxide poisoning: undetected by both patients and their doctors. Age and Ageing. 2004;33:105-109.
6. Kao LW, Nañagas KA. Carbon monoxide poisoning. Emerg Med Clin North Am. 2004;22:985-1018.
7. Roth D, Herkner H, Schreiber W, Hubmann N, Gamper G, Lagner AN, et al. Accuracy of noninvasive multiwave pulse oximetry compared with carboxyhemoglobin from blood gas analysis in unselected emergency department patients. Ann Emerg Med. 2011;58:74-79.
8. Buckley NA, Juurlink DN, Isbister G, Bennet MH, Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database of Syst Rev. 2011;13;(4) CD002041.
9. https://mevbis.mgm.gov.tr/mevbis/ui/index.html#/MeteorologyDictionaryPublic. Erişim tarihi: 03/01/2023
10. Topcu H, Karakus Yılmaz B, Carus M. Karbon monoksit Zehirlenmesi Nedeniyle Acil Tıp Kliniğine Başvuran Hastaların Değerlendirilmesi. Phnx Med J. 2021;3(3):135-138.
11. Tursun S, Alpcan A, Karahan İ. Bir üniversite hastanesi çocuk acil servisine başvuran karbon monoksit zehirlenmelerinin geriye dönük incelenmesi. Kırıkkale Üniversitesi Tıp Fakültesi Dergisi. 2020;22(2):199-207.
12. Giniş T, Gürsoy C, Mısırlıoğlu ED, Kocabaş CN. Sekiz Yıllık Dönemde Karbon monoksit Zehirlenmelerinin Değerlendirilmesi. Türkiye Çocuk Hast Derg. 2014;8(2):55-58.
13. Yetiş Y, Karbeyaz K, Güneş A. Eskişehir'de Karbonmonoksit Zehirlenmesine Bağlı Ölümlerin 20 Yıllık Analizi. ADYÜ Sağlık Bilimleri Derg. 2017;3(1):396-406.
14. Partrick M, Fiesseler F, Shih R, Riggs R, Hung O. Monthly variations in the diagnosis of carbon monoxide exposures in the emergency department. Undersea Hyperb Med 2009;36:161-167.
15. Türkoğlu A, Tokdemir M, Şen M, Börk T, Tunçez FT, Yaprak B. Elazığ'da 2006-2012 yılları arasında otopsisi yapılan karbon monoksit zehirlenmesine bağlı ölümlerin değerlendirilmesi. Adli Tıp Bülteni. 2012;17(1):21-26.
16. Usul E, Halıcı A, Hoke M. TheRelationship of Lactate Levels with Carboxyhemoglobin Levels and Clinical Findings in Patients Admitted with Acute Carbon Monoxide Poisoning. Duzce Med J. 2021;23(1):41-46.
17. Özdemir S, Altunok İ, Eroğlu SE. Karbon Monoksit Zehirlenmesi Laktat ve Kardiyak Belirteç İlişkisi Van Tıp Derg. 2019;26(3):285-288.
18. Emektar E, Ramadan H, Yüzbaşıoğlu Y, Vural S, Coşkun F. Use of lactate clearance ındetermının serum lactate levels and effectıveness of treatment ın carbonmonoxıd epoısonıngs. Kırıkkale Üni Tıp Derg. 2017;19(2): 60-65.
19. Doğan NÖ, Savrun A, Levent S, Günaydın GP, Çelik GK, Akküçük H, et al. Can initial lactate level spredict the severity of unintentional carbon monoxide poisoning? Hum Exp Toxicol 2015;34(3):324-329.

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B12 Deficiency and Helicobacter Pylori Enfections in Adolescents

Adolesanlarda B12 eksikliği ve Helikobakter Pylori Sıklığı

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ABSTRACT

Objective: *Low intake of Vitamin B12 (vit B 12) with malabsorptions are the most critical factors causing the deficiency. Vit B 12 deficiency has also been associated with Helicobacter pylori (HP) gastritis in previous studies. This study's main goal is to find a similar relation with recent studies or an opposite conclusion. For this purpose we choose the most suitable group; patients with the same two diseases HP gastritis and vit B 12 deficiency.*

Methods: *The whole study was conducted retrospectively. İn the study we included 19 patients (mean age: 15.6 ± 1.3 years). The B12 levels of patients undergoing upper gastroscopy for any reason were studied. We tried to figure out whether B12 deficiency and HP positivity were statistically significant. The Electrochemiluminescence immunoassay method has been used for serum vit B12 level measurement.*

Results: *There are 15 (62.5%) patients with neurological symptoms and 6 (25.0%) patients with fatigue and weakness. Only 3 (12.5 %) patients have no symptoms. There was no statistical significance between these groups (p=0.224). There are 18 (75%) patients with HP positivity. HP positive and negative patients have levels of B12 108.6 ± 31.1 pg/mL and 113.5 ± 41.2 pg/mL respectively (p=973).*

Conclusion: *There were no statistical significance with vitamin B 12 levels in HP-positive patients and HP-negative patients. İt sure be beneficial to use a bigger aspect patients group to have better results between HP infection and vitamin B 12 deficiency relation.*

ÖZET

Amaç: *Malabsorbsyon B12 eksikliği sebeplerindendir. B12 vitamin eksikliğine neden olan beslenme yetersizliği yada uygunsuz diyet sebeplerden sayılabilir. Yapılan pek çok çalışmada B12 vitaminin eksikliği Helikobakter pilori (HP) ile ilişkilendirilmiştir. Bu çalışmadaki amacımız eksikliği olan adolesanlarda B12 ve HP birlikteliğinin araştırılmasıdır.*

Yöntem: *Çalışma kaynak teşkil eden veriler retrospektif olarak hasta dosyalarının meslektaşlarımız tarafından taranması yolu ile elde edilmiştir. Meslektaşlarımızın çalışmakta bulunduğu merkezlerde üst gastrointestinal sistem endoskopisi ve hızlı üreaz testleri ile HP tanısı almış hastaların B12 düzeyleri taranarak çalışmaya dahil edilmişlerdir. Çalışmaya 19 hasta (ortalama yaş: 16.2 ±2.3 yıl) dâhil olmuş bu hastaların B12 vitamini düzeyi elektrokemiluminesens immunoassay ile ölçülmüştür.*

Bulgular: *Çalışmamızda hastaların 17'sinin (%58.5) nörolojik semptomlar ile başvurduğu görüldü. Başka sebepler ile tetkik edilen diğer hastaların üçünde (%13.5) B12 vitamini eksikliği tespit edildi.Bazı hastalarda ise 8 (%25.0) yorgunluk ve halsizlik şikâyetlerin ana şikayetlerini oluşturduğu görüldü. B12 düzeyleri kıyaslandığında semptomatik ve asemtomatik hasta gruplarının B12 vitamini düzeyleri arasındaki fark anlamlı bulunmadı. (p=0.224). Hastaların onsekizinde (%75) HP pozitifliği saptanırken HP pozitif hastaların vitamin B12 düzeyleri ile HP negatif hastaların B12 düzeyleri kıyaslandığında sırasıyla 103.4 ± 34.3 pg/mL ve 117.5 ± 43.2 pg/mL değerlerine ulaşıldı. (p=973).*

Sonuç: *B12 vitamini düzeyleri kıyaslandığında HP enfeksiyonu pozitif olan çocuklarda düzeyler daha düşük olmakla beraber HP negatif hastalarla arasındaki fark anlamlı bulunmamıştır. Bu birlikteliğin gösterilebilmesi için geniş hasta grupları ile daha büyük ölçekte çalışmaların yapılması yararlı olabilir.*

Keywords:
Adolescents
Vitamin B 12
Helicobacter pylori

Anahtar Kelimeler:
Adolesan
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INTRODUCTION

Helicobacter pylori (HP) is a gram-negative bacterium that is common throughout the world. While its prevalence in the adult population is about 50% in developed countries, it reaches 90% in developing countries. Infection is acquired in childhood and may be lifelong if not treated. (1) HP Infection can lead to gastritis, gastric ulcers, gastric cancer, and micronutrient deficiencies. Vitamin B12 deficiency has also been seen in patients with HP gastritis. Vitamin B12 cannot be synthesized in the human body (2).

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It is available only in animal foods. Dairy products, meat, eggs, poultry, fish, and shellfish are foods rich in vitamin B12. There are many studies investigating the molecular biology of vitamin B12 deficiency. In vitamin B12 deficiency, purine and pyrimidine cannot be synthesized, resulting in megaloblastic anemia (3). The accumulation of methylmalonyl- CoA may be responsible for neurological findings (4). Vitamin B12 deficiency is usually due to malabsorption, it can also occur in the elderly, vegans, and strict vegetarians due to low intake. The aim of this study is to determine if there is a relationship between HP and vitamin B12 deficiency.

MATERIAL AND METHODS

This is a retrospective study. Adolescent patients with vitamin B12 deficiency who underwent endoscopy were our study group. After the local ethics commetee aproval study begin. (12/11/21) Vitamin B12 levels were measured by the electrochemiluminescence immunoassay method. Vitamin B12 deficiency was defined as a serum vitamin B12 level < 150 pmol/L (< 200 pg/mL) with two measurements repeated on different days and concurrent hematologic or neurologic findings of vitamin B12 deficiency. Patients with known vitamin B12 deficiency due to chronic illness such as Crohn's disease, celiac disease, and gastric or intestinal resection were excluded from the study. Patients with familial cobalamin metabolic disorders and IF-related deficiencies who had received vitamin B12 or multivitamin therapy in the past year were also excluded from the study. Their diets included animal products and were not vegans or vegetarians. Patient age and sex, complaints at presentation, and vitamin B12 levels were obtained from medical and computer records. Endoscopy of the upper gastrointestinal tract was performed in all patients. Endoscopically, two biopsies were taken from the esophagus, corpus, antrum, and duodenum. A biopsy specimen from the antrum was placed in a preparation containing urea agar and a pH indicator for the rapid urease test (CLO test duo, Kimberly-Clark-Ballard Medical Products, Draper, UT). The other specimens were placed in 10% formalin immediately after collection and examined histopathologically. The cases with positive urease test and HP, detected by histopathological examination, were accepted as HP positive. Patients in whom HP was not found on either examination were considered HP negative.

All data were collected using the SPSS v11.0 program, and statistics were generated using this program. Numerical data were expressed as mean ± standard deviation (SD). The chi-square test was used to compare group ratios. When the expected values in the eyes were less than 5, the group ratios were compared using Fisher's exact chi-square test. A comparison of the means of the three groups was performed with the Kruskal-Wallis test. The means of the two groups were compared using the Mann-Whitney U test. A p-value of less than 0.05 was considered significant.

RESULTS

Twenty-four patients (mean age: 15.6 ± 1.3 years), 18 of whom were girls (75.0%), were included in this study. While 15 (62.5%) of the 24 patients included in the study had neurological symptoms such as headache, dizziness, numbness/tingling in the arms and/or legs, 6 (25.0%) patients complained of weakness and fatigue and were examined for hematological findings. . Three (12.5%) patients were referred to our outpatient clinic after an examination for other reasons revealed vitamin B12 deficiency (Table 1).

There was no difference between the vitamin B12 levels of patients who had neurologic or hematologic symptoms and asymptomatic patients (Table I). There was no difference between boys and girls in vitamin B12 levels (119.8 ± 42.9 pg/ml and 106.5 ± 29.8 pg/ml, p= 0.312, respectively). Five patients (20.8%) had dyspepsia, while the remaining patients had no stomach-related symptoms. Two children in one HP positive and the other HP negative group had weight-to-height ratios of 84% and 86%, respectively; all other children had normal values for age and weight-to-height. None of the patients were vegan or vegetarian. There were no patients with inadequate or imbalanced nutrition in their dietary history. In 18 (75%) of 24 patients with B12 deficiency, HP was positive in the rapid urease test (Table I). All of these patients were histopathologically positive for HP. Endoscopically, gastritis was present in 23 (96%) of 24 patients (endoscopic erosive pangastritis in one (4%) patient, endoscopic hyperemic antral gastritis in 4 (18%) patients, endoscopic hypertrophic pangastritis in two (8.7%) patients, and in the remaining 16 (69.3%) patients.), endoscopic erythematous pangastritis) was noted in one patient, whereas normal endoscopic findings were observed in 1 patient. Antral atrophic gastritis with HP was detected histopathologically in two of our patients (8.3%), and HP -positive chronic gastritis was found in 16 (67%) patients (Table I). While the mean vitamin B12 level of HP -positive patients was 108.6 ± 31.1 pg/ml, the mean B12 level of HP -negative patients were 113.5 ± 41.2

Table 1: Demographic, anthropometric, hematological and endoscopic characteristics of patients with vitamin B12 deficiency

	Neurological (n= 15)	hematological (n=6)	asymptomatic (n= 3)	p *
Age	15.2 ± 1.3	16.5 ± 1.3	16.0 ± 1.0	0.191
Girl/Boy	11 /4	5 / 1	2 / 1	0.837
Height for Age	98.6 ± 4.5	99.0 ± 5.6	98.0 ± 3.2	0.575
Weight for Height	110.6 ± 13.6	89.9 ± 5.9	92.9 ± 4.9	0.425
B12 vit. (pg/mL)	110.1 ± 37.0	97.5 ± 16.7	129.3 ± 31.4	0.224
Athrophic gastritis, n(%)	1 (6.7)	1 (16.7)	0 (0.0)	0.646
HP (+) patients, n (%)**	9 (60)	6 (100)	3 (100)	0.091

**Kruskal Wallis test*

pg/ml, and no statistical difference was found (p=973).

DISCUSSION

In this study, an upper gastrointestinal tract endoscopy was performed to investigate the frequency of HP in children with vitamin B12 deficiency (5). HP was found in 75% of children with various clinical symptoms and vitamin B12 deficiency. Although serum vitamin B12 levels were lower in patients with HP positivity, no statistically significant difference was found (6). Many studies in adults have reported vitamin B12 deficiency in patients with HP gastritis in the literature (7). The mechanisms by which Helicobacter pylori infection causes B12 deficiency are not fully known (8).

Vitamin B12 ingested with food is bound to proteins. Vitamin B12, separated from proteins in the acidic environment of the stomach, binds to the transporter haptocorin (protein-R), also called transcobalamin I, which is found in saliva. About 80% of circulating vitamin B12 is bound to haptochorin (9). In the acidic environment of the stomach, haptochorin has a greater affinity for vitamin B12 than intrinsic factor (IF). After the haptochorin-vitamin B12 complex enters the small intestine, it is partially digested by pancreatic enzymes and combines with IF, which has a higher affinity for vitamin B12 in the alkaline environment of the intestine. In addition, IF is resistant to digestion by pancreatic enzymes (10). The vitamin B12- IF complex that reaches the terminal ileum is taken up into the cell by phagocytosis by binding to its specific receptors (5,9,10). Because of these pathogenetic mechanisms, the stomach plays an important role in vitamin B12 metabolism, and B12 metabolism is also affected in gastric diseases. Although vitamin B12 levels were low in the HP-positive group in our study, the difference between HP-negative patients was not significant. It is suggested that this is due to the small number of patients in our study. In the literature, there are few studies and case reports of children investigating the relationship between HP and vitamin B12 deficiency (4,6,7). In all these case reports and studies, HP positivity was found to be associated with B12 deficiency (11). On the other hand, there are also studies in the literature that show that there is no correlation between HP infection and B12 levels (12). Because dietary habits, polymorphisms in B12 metabolic pathways, and the frequency of HP may vary from country to country, new studies with large groups of patients are needed on this topic. In our study, the detection rate of HP positivity in children with B12 deficiency was 75% (13). In a study of adults conducted by Kaptan et al, the rate of HP positivity in patients undergoing endoscopy for B12 deficiency was 56%. In this study, the elimination of HP resulted in an increase in B12 levels in 40% of patients, and the researchers found that performing endoscopy in patients with B12 deficiency and treating HP was sufficient to increase B12 levels in many cases. Although all children in our study were diagnosed with B12 deficiency, the rate of atrophic gastritis was low (14). In a study of adults, Tamura et al. showed that the HP-positive group had a higher atrophic gastritis score and lower vitamin B12 levels than the HP-negative group. In this study, it was hypothesized that the low vitamin B12 level was related to the decrease in gastric acid secretion due to atrophic gastritis. However, although the rate of atrophic gastritis was low in our study, the HP positivity was high. In other words, an infection of HP can cause vitamin B12 deficiency without causing atrophic gastritis. A similar result was seen in the study by Elsaghier et al. (15). Although a significant association was demonstrated between infection of HP and vitamin B12 levels, it proved to be independent of the presence of atrophic gastritis. Similarly, it is noted that the only endoscopic finding in patients with B12 deficiency may be HP-positive gastritis.

CONCLUSION

Studies on children performed in larger numbers may shed more light on this issue. In conclusion, although vitamin B12 levels in children with HP infection in our study were lower than in patients with vitamin B12 deficiency, no significant difference was found between patients with HP -negative disease. It would be useful to conduct larger studies to show the relationship between HP infection and vitamin B12 deficiency.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: Ethical permission was obtained from the Univesity of Afyon, Medical Faculty Clinical / Human Research Ethics Committee for this study with date 10.12.2021 and number 119, and Helsinki Declaration rules were followed to conduct this study.

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REFERENCES

1. Choe YH, Kwon YS, Jung MK, Kang SK, Hwang TS, Hong YC. Helicobacter pylori–associated iron-deficiency anemia in adolescent female athletes. The journal of Pediatrics. 2001;139(1):100-4.
2. Mehata S, Parajuli KR, Pant ND, Rayamajhee B, Yadav UN, Mehta RK, et al. Prevalence and correlates of Helicobacter pylori infection among under-five children, adolescent and non-pregnant women in Nepal: Further analysis of Nepal national micronutrient status survey 2016. PLoS neglected tropical diseases. 2021;15(6):e0009510.
3. Mišak Z, Hojsak I, Despot R, Jadrešin O, Kolaček S, Konjik V, et al. Recommendation on diagnosis and treatment of Helicobacter pylori infection in children and adolescents. Liječnički vjesnik. 2022;144(7-8):197-206.
4. Kato S, Gold BD, Kato A. Helicobacter pylori-Associated Iron Deficiency Anemia in Childhood and Adolescence-Pathogenesis and Clinical Management Strategy. Journal of Clinical Medicine. 2022;11(24):7351.
5. Mubaraki MA, Alalhareth AS, Aldawood E, Albouloshi A, Aljarah MS, Hafiz TA, et al. The iron deficiency anemia in association to Helicobacter pylori infection in Najran city, Saudi Arabia. Journal of King Saud University-Science. 2022;34(8):102353.

6. Ding S-Z. Global whole family based-Helicobacter pylori eradication strategy to prevent its related diseases and gastric cancer. World Journal of Gastroenterology. 2020;26(10):995.
7. Hussain A, Nadeem M, Khan R, Khalid M, Iqbal K, Ishfaq M. Prevalence of Iron Deficiency Anemia Amongst Patients Infected with Helicobacter Pylori at Tertiary Care Hospital. Pakistan Journal of Medical & Health Sciences. 2022;16(07):919.
8. Mehrabani S. Helicobacter pylori infection in children: a comprehensive review. Maedica. 2019;14(3):292.
9. Borka Balas R, Meliț LE, Mărginean CO. Worldwide Prevalence and Risk Factors of Helicobacter pylori Infection in Children. Children. 2022;9(9):1359.
10. Patel RR, Sachdeva PD. A Systematic Review of Anemia among Adolescents Girls. National Journal of Medical Research. 2021;11(03):109-13.
11. Liu C, Wang Y, Shi J, Zhang C, Nie J, Li S, et al. The status and progress of first-line treatment against Helicobacter pylori infection: a review. Therapeutic Advances in Gastroenterology. 2021;14:17562848211989177.
12. Elsaadany E, Amin S, Abdel-Hafez M, El Amrousy D, Kasem S, Abd Elaziz D, et al. Study of Serum Ferritin, Zinc, and Copper Levels in Children With Helicobacter pylori Gastritis and the Effect of the Treatment. Journal of Pediatric Gastroenterology and Nutrition. 2022;75(5):e88-e93.
13. Anaya-Loyola MA, Brito A, Vergara-Castañeda H, Sosa C, Rosado JL, Allen LH. Low serum B12 concentrations are associated with low B12 dietary intake but not with Helicobacter pylori infection or abnormal gastric function in rural Mexican women. Nutrients. 2019;11(12):2922.
14. Sadiq A, Hameed JA, Khan MR, Mushtaq M, Yasmin R, Khan MS. Frequency of Iron Deficiency Anemia (IDA) Among Patients with Helicobacter Pylori Infection. Pakistan Journal of Medical & Health Sciences. 2022;16(10):885.
15. Elsaghier AM, Abdel Aal FH, Abu Faddan NH, Farghaly HS, Hassan MA-E, Sherif MF. Serum level of some micronutrients in children infected with Helicobacter pylori. Egyptian Pediatric Association Gazette. 2020;68(1):1-14.

ORIGINAL ARTICLE

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Vertebral Osteomyelitis: What has Changed in Last 10 Years?

Vertebral Osteomiyelit: Son 10 Yılda Neler Değişti?

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ABSTRACT

Objective: *This study was conducted to describe the demographic, clinical, and microbiological characteristics of vertebral osteomyelitis in the last decade, mainly by comparing literature and the previous case series performed in our center.*

Material and Methods: *This is a retrospective, observational, descriptive study performed between 2009-2019 at Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine. All patients were divided into three main groups: pyogenic, tuberculous and brucellar.*

Results: *A total of 100 cases were included in this study. Of these 100 patients, 59 had pyogenic, 15 had brucellar and 26 had tuberculous spondylodiscitis. The disease developed postoperatively in 22 (37.4%) of the 59 pyogenic vertebral osteomyelitis cases. The common isolated microorganism was Staphylococcus aureus (n = 11), followed by coagulase negative staphylococci (n = 6). Brucellar vertebral osteomyelitis rate was lower than previous case series (15 vs. 24). The median time to improvement in the laboratory findings after the administration of the appropriate treatment was 14 days. PET-CT was diagnostic in 81.8% of pyogenic vertebral osteomyelitis patients, similar to MRI. However, PET-CT diagnosis rate was significantly low in tuberculous spondylodiscitis (3 out of 9, p = 0.040).*

Conclusion: *S. aureus remained the most common etiologic agent. Coagulase negative staphylococci infection rate, mainly related to spinal surgery, and postoperative spondylodiscitis rate is higher than before. Brucellar vertebral osteomyelitis rate is lower, which is mostly related to effective animal vaccination and pasteurization. Although, MRI is the gold standard, PET-CT is a promising technique in diagnosis for pyogenic vertebral osteomyelitis.*

ÖZET

Amaç: *Bu çalışmada, vertebral osteomyelit vakalarının son 10 yıldaki demografik, klinik ve mikrobiyolojik özelliklerindeki değişimlerin saptanması, bu bulguların mevcut literatür ve hastanemizde yapılan bir önceki vaka serisi ile karşılaştırılması amaçlanmıştır.*

Gereç ve Yöntem: *2009-2019 yılları arasında İstanbul Üniversitesi-Cerrahpaşa Cerrahpaşa Tıp Fakültesi'nde vertebral osteomyelit tanısı ile takip edilen hastaların verileri retrospektif olarak tarandı. Tüm hastalar piyojenik, tüberküloz ve brusellar vertebral osteomyelit olmak üzere üç ana gruba ayrıldı.*

Bulgular: *Çalışmaya toplam 100 vaka dahil edildi. Bu 100 hastanın 59'unda piyojenik, 15'inde brusella ve 26'sında tüberküloz vertebral osteomyeliti saptandı. Piyojenik vertebral osteomyelit vakalarının 22'si (%37.4) postoperatif olarak gelişti. En sık izole edilen mikroorganizma Staphylococcus aureus (n = 11), ardından koagülaz negatif stafilokoklar (n = 6) idi. Brusella vertebral osteomyeliti oranı önceki vaka serilerinden daha düşüktü (15'e karşı 24). Uygun antimikrobiyal tedavinin ardından laboratuvar bulgularında düzelmeye kadar geçen medyan süre 14 gündü. PET-CT, MR'a benzer şekilde piyojenik vertebral osteomyelit hastalarının %81.8'inde tanı koydurucuydu. Ancak tüberküloz vertebral osteomyeliti hastalarında PET-CT tanı oranı anlamlı olarak düşük saptandı (9'da 3, p=0,040).*

Sonuç: *S. aureus en sık izole edilen mikroorganizma olmaya devam etti. Koagülaz negatif stafilokok enfeksiyon oranı artmış olup, temelde postoperatif enfeksiyon ile ilişkilendirilmiştir. Brusella vertebral osteomyeliti oranı daha düşük olarak saptanmıştır. Bu durumun etkili hayvan aşılama programları ve pastörizasyon ile ilişkili olduğu düşünülmüştür. MR tanıda altın standart olmasına rağmen, PET-CT özellikle piyojenik vertebral osteomyelit tanısında umut vericidir.*

Keywords:
Spondylodiscitis
Vertebral osteomyelitis
Pyogenic
Brucellar
Tuberculous

Anahtar Kelimeler:
Spondilodiskit
Vertebral Osteomyelit
Piyojenik
Bruselloz
Tüberküloz

INTRODUCTION

Vertebral osteomyelitis (VO) is an infection of vertebrae and intervertebral disc with an etiology that might be pyogenic, granulomatous (i.e., tuberculous, brucellar, fungal), or parasitic. Such a condition occurs most commonly via a hematogenous route, followed by spreading from adjacent tissues or direct inoculation (1).

Risk factors related to VO include diabetes mellitus (DM), immunosuppression, chronic heart disease, cirrhosis, intravenous drug use, HIV infection, previous spinal surgery, the presence of foreign bodies, chronic renal failure, the presence of an intravascular catheter, or previous bacteremia (2). The VO incidence is rising because of higher life expectancy, higher prevalence

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of chronic diseases, increased spinal surgery, and other invasive procedures that result in bacteremia (3).

Clinical findings are mostly insidious. The most common symptom is pain which is consistent with the level of the involved vertebra. Pyogenic vertebral osteomyelitis (PVO) is usually monomicrobial, and the most common causative agent is Staphylococcus aureus. Additionally, Gram-negative enteric bacilli, coagulase-negative staphylococci (CoNS), Pseudomonas aeruginosa, streptococci, and other rare microorganisms might be included in VO etiology (4,5).

Imaging findings are fundamental for diagnosis, and magnetic resonance imaging (MRI) is considered the most accurate technique due to its high sensitivity and specificity. Computed tomography (CT) is especially useful for detecting bony sequestra and soft tissue abscesses (6). Recently, 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) was indicated promising to diagnose spondylodiscitis when MRI is unavailable or unfeasible (7,8).

This study was conducted to describe the characteristics of the disease in the last decade, mainly by comparing literature and the previous 100-case study performed in our center (9). Specifically, we focused on the following outcomes: comorbidities, etiology, the role of diagnostic modalities, and follow-up parameters.

MATERIALS AND METHODS

In this retrospective observational study, the files of 100 spondylodiscitis cases followed up between 2009–2019 at the Istanbul University Cerrahpaşa, Cerrahpasa Medical Faculty, Department of Infectious Diseases, were evaluated. The study was approved by the Istanbul University Cerrahpasa Medical Faculty Ethics Committee with protocol number 83045809–604.01.02. We collected the data of the patients who were followed with spondylodiscitis diagnosis. The patients with insufficient records were excluded. The cases were divided into three groups: pyogenic, tuberculous, and brucellar spondylodiscitis.

We accepted the VO diagnosis as definite, either when a microorganism was isolated from affected vertebral area, a polymerase chain reaction (PCR) for the Mycobacterium tuberculosis complex was positive, or a typical histopathological pattern of tuberculosis (TB) was observed in aspirated materials with a CT-guided fine-needle aspiration biopsy (FNAB). A homemade nested PCR using primers targeting the MPB 64 proteins of M. tuberculosis was performed as described by Therese et al (10). Diagnosis of brucellar vertebral osteomyelitis (BVO) was established when high serological titers of brucella antibodies (1/160 for Wright's seroagglutination) were reported. Diagnosis was considered as probable when we observed histopathological inflammatory patterns that may suggest it in FNAB. The diagnosis was also considered probable when such patterns were combined with clinical, radiological pictures compatible with VO and when a microorganism was isolated from a blood culture or another coexistent infection site. Their responses to antibacterial treatment supported the probable cases.

We considered as a laboratory response any minimum 25% decrease in baseline C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) values (or both) after antibiotic treatment. Clinical and laboratory data of the patients were collected from the medical records retrospectively. The patients were followed-up as outpatients for one year after therapy completion.

Statistical Analysis

IBM-SPSS-20 package program was used for statistical analysis. Descriptive data was presented as frequency (n) and percentage (%) for categorical variables and median with interquartile range (IQR). We provided data as mean ± standard deviation. Pearson chi-square test and Fisher's exact test were used for comparing categorical data and the Kruskal–Wallis test was used to compare the nonnormally distributed numeric data. A p value of <0.05 was considered statistically significance level.

RESULTS

One hundred patients were included in this study. The cases consisted of 59 PVO cases, 26 tuberculous vertebral osteomyelitis (TVO) cases, and 15 BVO cases. The diagnosis was definite in 29% of PVO patients and 69% of TVO patients. Fifty-two patients were male and 48 female. The age of the patients ranged from 19 to 90 years; median age (IQR) was 58.5 (46.5-66.8) years. The disease developed postoperatively in 22 (37.4%) of the 59 PVO cases. In the study population, 13 patients were followed up with a misdiagnosis before diagnosing VO. The most common misdiagnosis was lumbar disc hernia (n = 5), followed by myeloproliferative diseases (n = 3), metastasis (n = 2), sarcoidosis (n = 1), pneumonia (n = 1), and gonarthrosis exacerbation (n = 1).

The demographics and clinical features of the patients are shown in Table 1. The age distribution, sex, and baseline clinical findings, except for fever and night sweats, were similar between the study groups. While fever was significantly most common in the BVO patients, weight loss was more frequent in the TVO patients ($p = 0.031$ and $p = 0.005$, respectively). Among the predisposing conditions, DM and previous spine surgery prevalence were significantly higher in the PVO group ($p = 0.027$ and $p = 0.005$, respectively). The TB disease history was statistically higher in TVO patients ($p = 0.019$). Thoracic involvement was significantly higher in the TVO patients ($p = 0.031$). Otherwise, the frequencies of cervical, lumbar, and sacral involvements were similar between groups. Abscess formation was detected in at least one site in 47 of the 100 patients. In TVO patients, abscess existence was significantly higher compared to the other groups ($p = 0.002$). While paravertebral, epidural, paraspinal, and intradural abscess frequencies were similar among the groups, psoas abscesses were more common in the TVO patients ($p = 0.046$; Table 1). Drainage was performed in four patients, and surgical intervention was performed in four patients who developed abscesses.

Mean diagnostic delay value (MDD) was 20.4 (± 41.5) weeks. MDD was 172 (± 256) days for PVO, 193 (± 169) days for TVO and 281 (± 580) days for BVO. There was no statistically significant difference between the sub-groups.

The median leukocyte count was 8600/mm3, median serum CRP level was 30 mg/L, median ESR was 62 mm/h, and median hematocrit (Hct) was 35.0% (± 5%) in

Table 1: Demographics and clinical features of the patients

Characteristics	PVO (n = 59)	TVO (n = 26)	BVO (n = 15)	Total (n = 100)	p
Age (years), median (IQR)	59.0 (51.0-67.0)	53.5 (31.5-66.5)	59.0 (41.0-61.0)	58.5 (46.5-66.8)	0.317[a]
Sex, n (%)					
Female	27 (45.8)	16 (61.5)	5 (33.3)	48 (48.0)	0.190[b]
Male	32 (54.2)	10 (38.5)	10 (66.7)	52 (52.0)	
Baseline findings, n (%)					
Pain	54 (91.5)	25 (96.2)	14 (93.3)	93 (93.0)	0.861[c]
Neurological symptoms	18 (30.5)	5 (19.2)	5 (33.3)	28 (28.0)	0.500[b]
Fever	16 (27.1)	8 (30.8)	9 (60.0)	33 (33.0)	0.031[b]
Fatigue	12 (20.3)	5 (19.2)	5 (33.3)	22 (22.0)	0.513[b]
Weight loss	7 (11.9)	11 (42.3)	5 (33.3)	23 (23.0)	0.005[b]
Night sweating	4 (6.8)	6 (23.1)	3 (20.0)	13 (13.0)	0.070[c]
Predisposing conditions, n (%)					
Cancer history	5 (8.5)	1 (3.8)	0 (0.0)	6 (6.0)	0.594[c]
Rheumatic disease	4 (6.8)	2 (7.2)	1 (6.7)	7 (7.0)	>0.999[c]
DM	15 (25.4)	4 (15.4)	0 (0.0)	19 (19.0)	0.027[c]
Osteomyelitis history	0 (0.0)	1 (3.8)	0 (0.0)	1 (1.0)	0.410[c]
TB disease history	0 (0.0)	3 (11.5)	0 (0.0)	3 (3.0)	0.019[c]
VO history	0 (0.0)	0 (0.0)	1 (6.7)	1 (1.0)	0.150[c]
UTI history	2 (3.4)	1 (3.8)	0 (0.0)	3 (3.0)	>0.999[c]
Any type of infection history	10 (16.9)	6 (23.1)	4 (26.7)	20 (20.0)	0.633[b]
Trauma history	4 (6.8)	2 (7.7)	0 (0.0)	6 (6.0)	0.718[c]
Spine surgery history	23 (39.0)	2 (7.7)	2 (13.3)	27 (27.0)	0.005[b]
Involvement site, n (%)					
Cervical	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.0)	>0.999[c]
Thoracic	11 (18.6)	12 (46.2)	4 (26.7)	27 (27.0)	0.031[b]
Lumbar	51 (86.4)	18 (69.2)	13 (86.7)	82 (82.0)	0.167[c]
Sacral	15 (25.4)	4 (15.4)	5 (33.3)	24 (24.0)	0.399[b]
Multilevel	18 (30.5)	8 (30.8)	7 (46.7)	33 (33.0)	0.474[b]
Abscess formation, n (%)					
Any site	21 (35.6)	20 (76.9)	6 (40.0)	47 (47.0)	0.002[b]
Psoas	4 (6.8)	7 (26.9)	2 (13.3)	13 (13.0)	0.046[c]
Paravertebral	13 (22.0)	12 (46.2)	5 (33.3)	30 (30.0)	0.078[b]
Epidural	6 (10.2)	4 (15.4)	2 (13.3)	12 (12.0)	0.684[b]
Paraspinal	2 (3.4)	1 (3.8)	0 (0.0)	3 (3.0)	>0.999[c]
Intradural	1 (1.7)	0 (0.0)	0 (0.0)	1 (1.0)	0.474[b]

PVO: Pyogenic vertebral osteomyelitis, TVO: Tuberculosis vertebral osteomyelitis, BVO: Brucellar vertebral osteomyelitis, IQR: Interquartile range, DM: Diabetes mellitus, TB: Tuberculosis, VO: Vertebral osteomyelitis, UTI: Urinary tract infection.
a Kruskal-Wallis test was used.
b Pearson chi-square test was used.
c Fisher's exact test was used.
d Osteomyelitis involving bones other than vertebra.
Bold values are statistically significant

our study population. However, there was no statistically significant difference in these parameters among the three study groups (Table 2).

The imaging results of the patients are shown in Table 2. Whereas the MRI results allowed us to observe similar features and achieve high diagnostic success in all study groups, the CT results was diagnostic only one-third of the study group. The diagnostic success obtained with both imaging methods was statistically similar in all groups. However, while PET-CT allowed for a successful diagnosis in 81.8% of PVO patients, successful diagnostic levels decreased significantly in TVO patients (p = 0.040; Table 3).

CT-guided FNAB was performed on 76 patients (47 PVO, 26 TVO, and 3 BVO). In PVO patients, microbiological evaluation was performed in 26 non-postoperative and 15 postoperative patients. The microbiological analysis could not be done in six non-postoperative cases due to

Table 2: Laboratory findings of the patients

Characteristics	PVO	TVO	BVO	Total	p
WBC (/mm3), median (IQR)	8790 (6950-11125)	7820 (6400-9800)	7150 (5675-9450)	8600 (6500-10300)	0.180[a]
CRP (mg/L), median (IQR)	25.0 (13.0-90.0)	30.0 (17.0-98.0)	80.5 (24.8-110.3)	30.0 (15.0-90.5)	0.297[a]
ESR (mm/h), median (IQR)	57.0 (42.5-95.0)	71.0 (38.5-89.5)	72.0 (26.5-99.5)	62.0 (40.0-93.0)	0.946[a]
Hct (%), median (IQR)	35.0 (30.0-39.0)	34.4 (31.5-37.5)	35.5 (31.8-38.8)	35.0 (30.8-39.0)	0.792[a]

WBC: White blood cell count, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, Hct: Hematocrit, PVO: Pyogenic vertebral osteomyelitis, TVO: Tuberculosis vertebral osteomyelitis, BVO: Brucellar vertebral osteomyelitis.
a Kruskal-Wallis test was used.

Table 3: Imaging features of the patients

Imaging wtechnique	PVO n (%)	TVO n (%)	BVO n (%)	Total n (%)	p
MRI					
Negative	0 (0.0)	0 (0.0)	1 (7.1)	1 (1.1)	0.161[a]
Positive	52 (100.0)	21 (100.0)	13 (92.9)	86 (98.9)	
CT					
Negative	6 (66.7)	5 (62.5)	1 (100.0)	12 (66.7)	>0.999[a]
Positive	3 (33.3)	3 (37.5)	0 (0.0)	6 (33.3)	
PET-CT					
Negative	2 (18.2)	6 (66.7)	1 (100.0)	9 (42.9)	0.040[a]
Positive	9 (81.8)	3 (33.3)	0 (0.0)	12 (57.1)	

MRI: Magnetic resonance imaging, CT: Computerized tomography, PET-CT: Positron emission tomography/computed tomography, PVO: Pyogenic vertebral osteomyelitis, TVO: Tuberculosis vertebral osteomyelitis, BVO: Brucellar vertebral osteomyelitis.
a Fisher's exact test was used.
Bold values are statistically significant

Table 4: Fine needle aspiration biopsy results of TVO patients

Characteristics	TVO (n = 26)
Microbiological, n (%)	
AFB staining positivity	1 (3.8)
TB culture positivity	8 (30.8)
PCR positivity	13 (50.0)
Histopathological, n (%)	
Granulomatous reaction	9 (31.7)
Nonspecific inflammatory findings	11 (42.3)
Diagnosis, n (%)	
Solely Microbiological	11 (42.3)
Solely Histopathological	2 (7)
Microbiologically and histopathological	5 (19.2)
Upon empirical treatment response	8 (30.7)

TVO: Tuberculosis vertebral osteomyelitis, AFB: Acid-fast bacillus, TB: Tuberculosis, PCR: Polymerase chain reaction.

insufficient samples. The positivity of biopsy specimens was 12 out of 26 and five out of 15 patients for non-postoperative and postoperative patients, respectively. In TVO patients, one of them (3.8%) was positive for acid-resistant bacilli (ARB) staining, eight (30.8%) were TB culture positive, and 13 (50.0%) were TB PCR positive. Histopathological examinations were performed on 20 TVO patients. Granulomatous changes were detected in nine patients, while non-specific inflammatory changes were observed in 11 ones. The diagnosis of the 26 TVO patients was made by microbiological or histopathological findings (or both) and upon empirical treatment response (Table 4).

Within the pyogenic group, the microbiological diagnosis was established in 20 out of 41 patients (48.7%). Eight (40%) of these 20 patients were methicillin-sensitive Staphylococcus aureus (MSSA), and the remaining were as follows: six CoNS (four of them were methicillin-resistant and two of them were methicillin-sensitive), three were methicillin-resistant S. aureus (MRSA), one was Escherichia coli, one was Pseudomonas aeruginosa, and one was viridans group streptococci. The remaining patients did not yield any bacteria in the blood culture or biopsy culture (Table 5).

The median time to improvement in the laboratory findings of the study population after the administration of the appropriate treatment was 14 days. Follow-up inflammatory markers were not obtained before four weeks of therapy in six patients. The median treatment response times in the laboratory parameters were statistically similar among the three groups. While the median time for pain relief for the entire study group was 21 days, it was statistically significantly reduced to 14 days in the BVO patients (p = 0.034; Table 6). After treatment completion, relapse was observed in one BVO and one PVO patient. There were no deaths among the patients.

Table 5: Microorganisms isolated from the patients with pyogenic vertebral osteomyelitis

Culture results	Non-postoperative PVO (n = 37)	Postoperative PVO (n = 22)	Total (n = 59)
MSSA	7	1	8
MRSA	3	0	3
MSCoNS	2	0	2
MRCoNS	1	3	4
Viridans group streptococci	1	0	1
Pseudomonas aeruginosa	0	1	1
Escherichia coli	1	0	1

PVO: Pyogenic vertebral osteomyelitis, MSSA: Methicillin-sensitive Staphylococcus aureus, MRSA: Methicillin-resistant Staphylococcus aureus, MSCoNS: Methicillin-sensitive coagulase-negative staphylococci, MRCoNS: Methicillin-resistant coagulase-negative staphylococci.

Table 6: Response time after treatment

Treatment response	PVO (n = 59)	TVO (n = 26)	BVO (n = 15)	Total (n = 100)	p
Improvement in laboratory findings (days), median (IQR)	10.0 (3.0-21.0)	14.0 (7.0-30.0)	14.0 (7.0-30.0)	14.0 (5.0-30.0)	0.097
Pain relief (days), median (IQR)	21.0 (14.0-30.0)	30.0 (26.3-82.5)	14.0 (14.0-30.0)	21.0 (14.0-30.0)	0.034

Bold values are statistically significant

DISCUSSION

Although VO is not a frequent disease, its annual hospitalization incidence has been increasing up to 5.4 per 100,000 (11) because of the population aging, increasing the number of immunocompromised patients, bacteremia due to intravascular devices, and spinal instrumentation (9). The male ratio was reported in the related literature from 52 percent of the patients up to twice as often as women (1,11) and the male ratio (52%) was similar in our study. Most VO cases occur in patients > 50 years old. Likewise, the mean age in our series at the time of diagnosis was 55 ± 14 years (mean ± standard deviation).

The primary clinical manifestation of VO is insidious spinal pain in the affected area. Spinal pain was reported in 67–100% of the patients in some studies (5,12,13). Fever is a much less frequent symptom. Chelsom et al. showed that only 37.5% of the patients in their study had a fever, regardless of the etiology (14). The fever frequency was reported in a range of 35–60% in another study (3). Similarly, 93% and 33% of our patients suffered from spinal pain and fever, respectively. A wide range of neurological symptoms might also be observed, from mild limited motion to paralysis (11). As in the previous studies, neurologic involvement was detected in 28% of the patients in our study.

The range of MDD was reported as two to 36 weeks (9,15,16). In our study, the MDD was 20.4 weeks. For patients with TB VO, MDD was reported up to 22 months in one study (17). Contrarily, there were no significant differences in our patient groups. Despite improving the imaging modality and increasing awareness and incidence, the MDD results were similar to the previous studies.

Although most of the studies showed significantly high inflammatory markers in PVO, (18–20) there were no significant differences among the three groups in our study. In addition, 64% and 17% of the patients had normal WBC and ESR levels, respectively. These findings are consistent with previous studies (20,21). Although CRP and ESR are usually elevated in VO, (14) normal inflammatory marker levels cannot rule out the diagnosis (22).

Spinal MRI is recommended as the first choice of radiologic modality for diagnosis. When MRI is not available, a combination of spine gallium and Tc99 bone scan, computed tomography, or PET scan can be performed (7). Although CT is useful for detecting bony sequestra and adjacent soft tissue abscesses, it is inferior to MRI for VO diagnosis (6). In this study, MRI and CT were diagnostic in 94.5% and 33% of the patients, respectively. Previously, the 18F-FDG PET/CT accuracy rates were reported as 94% (23). Here, the 18F-FDG PET/CT was performed in 21 patients; only 12 (57%) of them were diagnosed with VO, and five (24%) were misdiagnosed with metastasis. But since the number of patients having performed CT or PET/CT is low, the results should be evaluated cautiously.

CT-guided FNAB was performed in 76% of patients. This rate is consistent with that reported in the literature (48–100%) (5,9).

The lumbar vertebral bodies are most often involved, followed by thoracic and, less commonly, cervical vertebrae (11). The most common infection site in this study was the lumbar spine (49%), followed by the lumbosacral (22%) and thoracic (16%) sites, which is consistent with a previous report from our institute (9).

In our series, PVO was the most frequent disease (n = 59), and 37% of cases had a spinal surgery history. The number of postoperative case was 10 out of 44 PVO cases in the study previously conducted in our center (9). Several studies reported that 19–47% of patients had undergone spinal surgery before PVO diagnosis (24). Lumbar involvement was the most frequently infected area (56%), similar to other previously conducted studies (3). Our study confirmed that DM is a predisposing factor for pyogenic spondylodiskitis, as observed in many other studies (14,17,19).

The PET-CT diagnostic value was significantly higher (81.8%) in PVO patients. The study comparing 18F-FDG PET and MRI for VO diagnosis showed similar accuracy,

75% vs. 81%, respectively. Hence, 18F-FDG PET could be used as an alternative diagnostic modality for PVO if diagnostic doubt remains after MRI or when MRI is unavailable (25).

Microbiological evaluation of biopsies was done in 41 PVO cases. Of these, 41.4% had significant growth. Similarly, Colmenero et al. reported 49% bone biopsy culture positivity in PVO patients (19). Although S. aureus was still the most common organism (15%), the proportion of CoNS (8%) was higher than that previously reported in our center (n=0) (9). Coagulase-negative staphylococci, frequently associated with postoperative infection or intracardiac device-related sepsis, (26) were found in 5–16% of the PVO cases. Such an increasing rate of CoNS in our center might be explained by the growing rate of postoperative vertebral osteomyelitis in all instances (n = 22 vs. n = 10).

An adequate response manifests as both resolution of fever and back pain with a weekly 50% decrease in CRP levels (27). Furthermore, in a retrospective analysis of 61 patients treated with shorter antibiotic courses, the only independent predictor of the early switch to oral antibiotics was a lower CRP at two weeks than at baseline (28). Similarly, in our study, the median time to improve laboratory findings after administering the appropriate treatment was 14 days.

Brucellar VO is common in Turkey and other Mediterranean countries (22). The spondylodiscitis incidence due to brucellosis was reported as 2–58% (29). In this study, the rate of BVO (15%) was lower than in the previous 10 years (24%) in the same center (9). Such a decrease is likely related to the decreasing brucellosis cases in Turkey (30).

Fever was significantly more common in BVO patients than in other patients, and this finding is similar to the series reported by Horasan et al. (31).

In endemic countries, TB remains a significant cause of spinal infection. The spine is one of the most commonly affected sites of extrapulmonary TB (32). As in previous studies, thoracic vertebral involvement was significantly higher in the TVO group in our study (33). Previous studies reported a relatively higher frequency of paraspinal, epidural (19), and psoas abscesses (20) among patients with TVO. We observed in our data that TVO patients had significantly higher psoas abscesses, while paravertebral, epidural, paraspinal, and intradural abscesses frequencies were similar among the groups.

Although PET-CT looks promising for spondylodiscitis diagnosis,(8,34) its diagnostic success was significantly low (33.3%) for TVO patients in our study. Differential diagnosis could not be made between TVO and metastasis (n = 2), myeloproliferative disease (n = 1), and sarcoidosis (n = 1). However, the number of patients was small (n = 9).

This study is limited by its observational and retrospective design; thus, it cannot account for potential unmeasured confounding effects. Additionally, this is a single-center study; hence, both local microbial patterns and clinical practice may vary in other regions. Finally, our center is a tertiary teaching hospital with spinal surgery units represent a referral bias.

CONCLUSION

In conclusion, VO is a typical disease in elderly patients and the male gender. In endemic areas, both TVO and BVO should be kept in mind in the differential diagnosis. Symptoms might be insidious, and diagnosis requires a high index of suspicion. The lumbar vertebral level is mainly involved in each patient group, whereas thoracic involvement is more prominent in TVO group. Although MRI is the gold standard for diagnosing spinal infections, PET-CT is a promising technique, especially for PVO. Although PET-CT diagnostic rate was lower in TVO patients in our study, there is a need for large-scale studies. S. aureus remains the most common organism causing VO, and methicillin-resistant CoNS is mainly related to postoperative infection. Postoperative spondylodiscitis rate is higher, and BVO rate is lower than before. Lower BVO rate is mostly related to effective animal vaccination and pasteurization.

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REFERENCES

1. Nickerson EK, Sinha R. Vertebral osteomyelitis in adults: An update. Br Med Bull. 2016;117(1):121–38.
2. Akiyama T, Chikuda H, Yasunaga H, Horiguchi H, Fushimi K, Saita K. Incidence and risk factors for mortality of vertebral osteomyelitis: a retrospective analysis using the Japanese diagnosis procedure combination database. BMJ Open. 2013;3(3):e002412.
3. Mustapić M, Višković K, Borić I, Marjan D, Zadravec D, Begovac J. Vertebral osteomyelitis in adult patients--characteristics and outcome. Acta clinica Croatia. 2016;55(1):9–15.
4. Corrah TW, Enoch DA, Aliyu SH, Lever AM. Bacteraemia and subsequent vertebral osteomyelitis: a retrospective review of 125 patients. QJM. 2011;104(3):201–7.
5. Mylona E, Samarkos M, Kakalou E, Fanourgiakis P, Skoutelis A. Pyogenic vertebral osteomyelitis: a systematic review of clinical characteristics. Semin Arthritis Rheum. 2009;39(1):10–7.
6. An HS, Seldomridge JA. Spinal infections: diagnostic tests and imaging studies. Clin Orthop Relat Res. 2006;444:27–33.
7. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, Schmitt SK, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clinical Infectious Diseases. 2015;61(6):e26-46.
8. Bassetti M, Carnelutti A, Muser D, Righi E, Petrosillo N, Gregorio F Di, et al. 18F-Fluorodeoxyglucose positron emission tomography and infectious diseases: current applications and future perspectives. Curr Opin Infect Dis. 2017;30(2):192–200.
9. Mete B, Kurt C, Yilmaz MH, Ertan G, Ozaras R, Mert A, et al. Vertebral osteomyelitis: eight years' experience of 100 cases. Rheumatol Int.

2012;32(11):3591–7.
10. Therese KL, Jayanthi U, Madhavan HN. Application of nested polymerase chain reaction (nPCR) using MPB 64 gene primers to detect Mycobacterium tuberculosis DNA in clinical specimens from extrapulmonary tuberculosis patients. Indian J Med Res. 2005;122(2):165–70.
11. McDonald M (2020) Vertebral osteomyelitis and discitis in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA.
12. Kehrer M, Pedersen C, Jensen TG, Lassen AT. Increasing incidence of pyogenic spondylodiscitis: a 14-year population-based study. J Infect. 2014;68(4):313–20.
13. Loibl M, Stoyanov L, Doenitz C, Brawanski A, Wiggermann P, Krutsch W, et al. Outcome-related co-factors in 105 cases of vertebral osteomyelitis in a tertiary care hospital. Infection. 2014;42(3):503–10.
14. Chelsom J, Solberg CO. Vertebral osteomyelitis at a Norwegian university hospital 1987-97: clinical features, laboratory findings and outcome. Scand J Infect Dis. 1998;30(2):147–51.
15. Gouliouris T, Aliyu SH, Brown NM. Spondylodiscitis: update on diagnosis and management. J Antimicrob Chemother. 2010;65 Suppl 3:iii11-24.
16. Beronius M, Bergman B, Andersson R. Vertebral osteomyelitis in Göteborg, Sweden: a retrospective study of patients during 1990-95. Scand J Infect Dis. 2001;33(7):527–32.
17. Perronne C, Saba J, Behloul Z, Salmon-Céron D, Leport C, Vildé JL, et al. Pyogenic and tuberculous spondylodiskitis (vertebral osteomyelitis) in 80 adult patients. Clinical Infectious Diseases. 1994;19(4):746–50.
18. Weisz RD, Errico TJ. Spinal infections. Diagnosis and treatment. Bull Hosp Jt Dis. 2000;59(1):40–6.
19. Colmenero JD, Jiménez-Mejías ME, Sánchez-Lora FJ, Reguera JM, Palomino-Nicás J, Martos F, et al. Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases. Annals of rheumatic diseases. 1997;56(12):709–15.
20. Gök SE, Kaptanoğlu E, Celikbaş A, Ergönül O, Baykam N, Eroğlu M, et al. Vertebral osteomyelitis: clinical features and diagnosis. Clinical microbiology and infection. 2014;20(10):1055–60.
21. Lemaignen A, Ghout I, Dinh A, Gras G, Fantin B, Zarrouk V, et al. Characteristics of and risk factors for severe neurological deficit in patients with pyogenic vertebral osteomyelitis: A case-control study. Medicine (Baltimore). 2017;96(21):e6387.
22. Saeed K, Esposito S, Ascione T, Bassetti M, Bonnet E, Carnelutti A, et al. Hot topics on vertebral osteomyelitis from the International Society of Antimicrobial Chemotherapy. Int J Antimicrob Agents. 2019;54(2):125–33.
23. Altini C, Lavelli V, Niccoli-Asabella A, Sardaro A, Branca A, Santo G, et al. Comparison of the Diagnostic Value of MRI and Whole Body 18 F-FDG PET/CT in Diagnosis of Spondylodiscitis. J Clin Med. 2020;9(5):1581.
24. Kwon JW, Hyun SJ, Han SH, Kim KJ, Jahng TA. Pyogenic Vertebral Osteomyelitis: Clinical Features, Diagnosis, and Treatment. Korean J Spine. 2017;14(2):27–34.
25. Skanjeti A, Penna D, Douroukas A, Cistaro A, Arena V, Leo G, et al. PET in the clinical work-up of patients with spondylodiscitis: a new tool for the clinician? The quarterly journal of nuclear medicine and molecular imaging. 2012;56(6):569–76.
26. Fantoni M, Trecarichi EM, Rossi B, Mazzotta V, Giacomo G Di, Nasto LA, et al. Epidemiological and clinical features of pyogenic spondylodiscitis. Eur Rev Med Pharmacol Sci. 2012;16 Suppl 2:2–7.
27. Grados F, Lescure FX, Senneville E, Flipo RM, Schmit JL, Fardellone P. Suggestions for managing pyogenic (non-tuberculous) discitis in adults. Joint Bone Spine. 2007;74(2):133–9.
28. Flury BB, Elzi L, Kolbe M, Frei R, Weisser M, Schären S, et al. Is switching to an oral antibiotic regimen safe after 2 weeks of intravenous treatment for primary bacterial vertebral osteomyelitis? BMC Infect Dis. 2014;14:226.
29. Unuvar GK, Kilic AU, Doganay M. Current therapeutic strategy in osteoarticular brucellosis. North Clin Istanb. 2019;6(4):415–20.
30. Republic of Turkey Ministery of Health, Turkish Public Health Institution, Department of Zoonotic and Vector Borne Diseases. Brucellosis Statistical Data. https://hsgm.saglik.gov.tr/tr/zoonotikvektorel-bruselloz/istatistik (Accessed on March 26, 2021).
31. Horasan ES, Colak M, Ersöz G, Uğuz M, Kaya A. Clinical findings of vertebral osteomyelitis: Brucella spp. versus other etiologic agents. Rheumatol Int. 2012;32(11):3449–53.
32. Jain AK, Rajasekaran S. Tuberculosis of the spine. Indian J Orthop. 2012;46(2):127–9.
33. Colmenero JD, Ruiz-Mesa JD, Sanjuan-Jimenez R, Sobrino B, Morata P. Establishing the diagnosis of tuberculous vertebral osteomyelitis. European Spine Journal. 2013;22 Suppl 4(Suppl 4):579–86.
34. Kouijzer IJE, Scheper H, Rooy JWJ de, Bloem JL, Janssen MJR, Hoven L van den, et al. The diagnostic value of 18 F-FDG-PET/CT and MRI in suspected vertebral osteomyelitis - a prospective study. Eur J Nucl Med Mol Imaging. 2018;45(5):798–805.

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Clinical Experiences in Patients Treated with the Diagnosis of COVID-19

COVİD-19 Tanısıyla Tedavi Edilen Hastalarda Klinik Deneyimler

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ABSTRACT

Objective: *All over the world, a specific antiviral and immunomodulatory treatment method that can affect COVID-19 infection has not been found, and research is ongoing. Our goal is to share our clinical experience in patients receiving in patient treatment in our clinic.*

Materials and Methods: *Patients whose symptoms were compatible with COVID-19 and whose microbiological findings and/or tomography findings were compatible between March 11 and May 31, 2020 were included in the study.*

Results: *Among 180 patients included in the study; It was found that favipiravir treatment was added to 45 (25.0%) patients after HCQ treatment. A significant difference was found between treatment groups concerning; age, occupation, oxygen saturation, presence of diabetes mellitus, hypertansion and lung disease, and CT findings (p <0.05).*

Conclusion: *In patient groups; Switching to favipiravir treatment and getting a response in patients aged 65 and over, with comorbidities, widespread CT involvement at admission, and Sat O2≤94 may be predictive in treatment selection.*

ÖZET

Amaç: *Tüm dünyada COVID-19 enfeksiyonunu etkileyebilecek spesifik bir antiviral ve immünomodülatör tedavi yöntemi bulunamamıştır ve araştırmalar devam etmektedir. Amacımız kliniğimizde tedavi gören COVID-19 hastalarındaki klinik deneyimlerimizi paylaşmaktır.*

Gereç ve Yöntem: *11 Mart – 31 Mayıs 2020 tarihleri arasında semptomları COVID-19 ile uyumlu olan ve mikrobiyolojik bulguları/ tomografi bulguları uyumlu olan hastalar çalışmaya alındı.*

Bulgular: *Çalışmaya dahil edilen 180 hasta arasında; 45 (%25.0) hastaya HCQ tedavisi sonrası favipiravir tedavisi eklendiği saptandı. Tedavi grupları arasında; yaş, meslek, oksijen satürasyonu, diabetes mellitus, hipertansiyon ve akciğer hastalığı varlığı ve BT bulguları arasındaki ilişki bu idi. (p <0.05).*

Sonuç: *Hasta gruplarında; 65 yaş ve üzeri, komorbiditesi olan, başvuruda yaygın BT tutulumu olan, Sat O2≤94 olan hastalarda favipiravir tedavisine geçilmesi ve yanıt alınması tedavi seçiminde belirleyici olabilir.*

Keywords:
COVID-19
Treatment
Favipiravir
Hydroxychloroquine

Anahtar Kelimeler:
COVID-19
Tedavi
Favipiravir;
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INTRODUCTION

Coronavirus Disease (COVID-19) continues to be widely seen worldwide as a cause of a serious and severe pandemic (1-4). Currently, there is noeffective and eliable therapeutic agent in the treatment of COVID-19. Various antimicrobial agents have been used as emergency treatment options in the treatment experience of variousc ountries (4,-8). However, the evidence for the efficacy and safety of these drugs is limited and research on the subject continues (7,9).

In Türkiye, hydroxychloroquine (HCQ), favipiravir, combination of lopinavir and ritonovirarere commended molecules in the treatment of COVID-19 disease by the Ministry of Health (10). Countriesusing HCQ among these drugs have different clinical experiences.In some of the studies, it has been reported that this drug may be preferred in thetreatment and prophylaxis of COVID-19 infection because it is thought to have antiviral, anti-inflammatory and immunomodulatory properties against the virus and it is cheaper (7,9,11). In addition, there are studies showing that it has no effect, and information confusion about the use of the drug continues (12). In COVID-19 infection, which needs to be treated urgently all over the world, it is thought that countries sharing their own clinical experiences may be beneficial for COVID-19 infection studies, which are still in search of specific and reliable antimicrobial agents. Our aim is to contribute to the literature by presenting our clinical experiences of our patients for whom HCQ and-or favipiravir therapy was initiated.

MATERIALS AND METHODS

This retrospective, descriptive study was carried out by the inclusion of patients treated and followed up using the COVID-19 Clinical and Therapeutic Assessment Form at the Infectious Disease and Clinical Microbiology Departments of Rize Research and Training Hospital and Rize State Hospital between 11 March and 31 May 2020.

Inclusion criteria: Patients aged > 18 years hospitalized due to PCR or CT findings consistent with COVID-19 infection were included if they did not have critical clinical course, received HCQ and/or favipiravir, and completed their prescribed treatment at the infectious disease unit. In

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addition, patients with clinical symptoms, PCR and/or CT findings compatible with COVID-19, who were initiated HCQ and/or favirapir treatment, hospitalized, followed by the infectious diseases clinic, aged 18 years and older were included.

Patients classification: Patients were classified into subgroups based on clinical, microbiological, and radiological findings.

Symptomatic classification: Clinical classification of the patients based on symptoms at presentation was performed according to the COVID-19 Diagnostic and Therapeutic Guidelines issued by the Turkish Ministry of Health (10). In this guidelines, patients are divided into three groups as follows: 1) Uncomplicated disease (high fever, muscle and joint pain, cough, sore throat without shortness of breath; respiration rate < 24/min, SpO2 > 93%) without lung involvement; 2) mild-to-moderate pneumonia (high fever, muscle and joint pain, cough, sore throat together with a respiration rate of < 30/min and SpO2 > 90%, plus lung involvement); and 3) severe pneumonia (high fever, muscle and joint pain, cough, sore throat with SpO2 < 90, respiration rate ≥ 30/min, and widespread lung involvement).

Radiologic Classification: Based on computed tomography images, 4 patient groups were defined: 1) no specific signs or atypical signs; 2) unilateral involvement consistent with COVID-19 disease; 3) bilateral involvement consistent with COVID-19 disease; and 4) bilateral diffuse involvement consistent and presence of consolidations.

Clinical classification: Patients were classified into three groups based on clinical, microbiological, and radiological findings: 1) negative PCR at admission, but clinical symptoms or tomographic findings consistent with COVID-19; 2) positive PCR at admission, with clinical symptoms and tomographic findings inconsistent with COVID-19; and 3) positive PCR at admission with clinical symptoms and tomographic findings consistent with COVID-19.

Treatment Protocol: Treatments were administered following the Diagnostic and Therapeutic Guidelines for COVID-19 issued by the Turkish Ministry of Health (10). Initially, treatment with HCQ was started in uncomplicated patients with mild to moderate pneumonia, and the primary endpoint was negative PCR at 6 days. The second endpoint consisted of drug side effects, lack of clinical improvement

Table 1: Demographic characteristics and risk factors for COVID-19 disease of patients (n=180)

		n	%			n	%
Sex	Female	89	49.4	**Occupation**	Healthcare worker	37	20.6
	Male	91	50.6		Non-healthcare worker	143	79.4
PCR	Positive	91	50.6	**Contact with COVID**	Present	104	57.8
	Negative	89	49.4		Absent	76	42.2
Group	PCR(+)/ BT(+)	62	34.4	**Travel history**	Absent	94	52.2
	PCR(+) / BT(-)	29	16.1		Present	42	23.3
	PCR(-) / BT(+)	89	49.4		Contact individuals	44	24.4
Preferred treatment group	1	12	6.7	**CT findings**	1	28	15.6
	2	48	26.7		2	49	27.2
	3	75	41.7		3	49	27.2
	4	45	25.0		4	54	30.0
Smoking	Yes	33	18.3	**Anticoagulant use**	Yes	142	78.9
	No	147	81.7		No	38	21.1
Alcohol use	Yes	4	2.2	**C vit use**	Yes	92	51.1
	No	176	97.8		No	88	48.9
Diabetes	Yes	38	21.1	**CT progression**	Present	29	16.1
	No	142	78.9		Absent	151	83.9
HT	Yes	76	42.2	**Antibacterial use**	Present	25	13.9
	No	104	57.8		Absent	155	86.1
Pulmonary findings	Yes	33	18.3				
	No	147	81.7				

Based on CT findings: 1) CT normal or no typical involvement; 2) unilateral involvement; 3) bilateral involvement; 4) bilateral involvement and consolidation (diffuse involvement)

Based on treatment groups: Hydroxychloroquine (1), Hydroxychloroquine- Azithromycin (2), Hydroxychloroquine- Oseltamivir-Azithromycin (3), Hydroxychloroquine-Azithromycin-Favipiravir (4)

despite 48 to 72 hours of treatment, or switch in therapy due to worsening condition. On the other hand, favipiravir was given to patients with severe pneumonia at admission, prolonged QT at or after admission, no improvement or worsening in symptoms despite 48-72 hours of treatment with HCQ, and congenital long QT syndrome (basal QTc > 480 msec). HCQ treatment consisted of an initial 800 mg dose on the first day of treatment, continued with 400 mg/day for 5 days, with the total dose not exceeding 2400 mg, while favirapir was given at a dose of 3200 mg on the first day, followed by 1200 mg for the next 4 day, for a total treatment duration of 5 days. Treatment groups: for statistical evaluation, treatment groups divided into two parts according to the drug which have been used: Non-favipiravir group (Groups 1, 2, and 3) and Favipiravir group (Group 4)

Data Analysis: Study data were analyzed using IBM SPSS 21.0 software pack (Chicago, US). The level of significance was set at < 0.05. Descriptive statistics (percentage, frequency, mean, standard deviation) were used for data assessment. To evaluate CT findings and treatment groups (more than 2) ANOVA test was used for numerical values, and the Kruskal-Wallis test was used for non-numerical values.

Ethical considerations: The study protocol was approved by the Scientific Research Committee, General Directorate of Health Services, Turkish Ministry of Health (Permission no: 2020-05-17T01_18_25)and Ethics Committee for Non-Interventional Research, Recep Tayyip Erdogan University (Permission no: 2020/129).

RESULTS

A total of 180 patients were included with a mean age of 55.5 ± 19.8 years (range: 18-89 y). There were 91 male patients (50.6%), and 86 (47.7%) with a history of travel. One-hundred and four patients (57.8%) had a positive history for contact with an individual with COVID-19 diagnosis, 18.3% (n=33) were smokers. The most frequent comorbidity was hypertansion (HT) in 42.2% (n=76). Table 1 summarizes the sociodemographic characteristics and COVID-19 risk factors in the patient group. Rates of PCR positivity, 81.1% (n=158) Table 1). PCR positivity rate was 50.6% (n = 91), and CT involvement rate was 81.1% (n = 158). In our study population, which consisted of patients with mild to moderate and severe pneumonia, oxygen saturation at admission was 95.4% ± 2.9 (90-99), 138 patients (76.7%) had a SatO2 of > 93%, the QTc at admission was 408.1 ± 19.4 msec (357-480), and the mean duration of hospital stay was 10.7 ± 3.9 days (7-21). Two patients required intensive care during the subsequent course of their illness, and one of these subjects died. A comparison of sociodemographic characteristics among treatment groups showed significant differences (p<0.05)

Table 2: Distribution of demographic characteristics and risk factors according to treatment groups

		Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Group 4 n (%)	Test and p value
Age (y)		34.8±4.2 (26-53)	53.8±2.9 (20-89)	54.6±2.2 (22-88)	63.0±2.9 (23-88)	KW=18.95 p=0.000
Sex	Female	8 (9)	23 (25.8)	42 (47.2)	16 (18)	$\chi2$=6.23 p=0.101
	Male	4 (4.4)	25 (27.5)	33 (36.3)	29 (31.9)	
Occupation	Healthcare worker	9 (24.3)	5 (13.5)	15 (40.5)	8 (21.6)	$\chi2$=25.03 p=0.000
	Non-healthcare worker	3 (2.1)	43 (30.1)	60 (42)	37 (25.9)	
Travel history	Absent	6 (6.4)	31 (33)	36 (38.3)	21 (22.3)	$\chi2$=4.06 p=0.256
	Present	6 (6.4)	17 (19.8)	39 (45.3)	24 (27.9)	
Contact individuals	Absent	2 (1.1)	32 (30.8)	44 (42.3)	26 (25)	$\chi2$=9.89 p=0.020
	Present	10 (13.2)	16 (21.1)	31 (40.8)	19 (25)	
Diabetes	Yes	0 (0)	8 (21.1)	19 (50)	11 (28.9)	$\chi2$=4.88 p=0.181
	No	12 (8.5)	40 (28.2)	56 (39.4)	34 (23.9)	
HT	Yes	0 (0)	18 (23.7)	32 (42.1)	26 (34.2)	$\chi2$=13.68 p=0.003
	No	12 (11.5)	30 (28.8)	43 (41.3)	19 (18.3)	
Pulmonary disease	Yes	0 (0)	7 (21.2)	11 (33.3)	15 (45.5)	$\chi2$=10.58 p=0.014
	No	12 (8.2)	41 (27.9)	64 (43.5)	30 (20.4)	
Smoking	Yes	4 (12.1)	9 (27.3)	9 (27.3)	11 (33.3)	$\chi2$=4.94 p=0.176
	No	8 (5.4)	39 (26.5)	66 (44.9)	34 (23.1)	
Sat O2 (%)	> 93	11 (33.3)	38 (21.1)	66 (36.7)	23 (25.8)	KW=23.36 p=0.000
	≥ 90-93	1 (0.6)	10 (13.2)	9 (27.3)	22 (12.2)	
Treatment duration(d)		7.2±0.2 (7-10)	8.5±0.4 (7-21)	10.1±0.3 (7-14)	14.9±0.6 (10-21)	$\chi2$=78.03 p=0.000

Treatment groups: Group 1. Hydroxychloroquine, Group 2. Hydroxychloroquine- Azithromycin, Group 3. Hydroxychloroquine- Oseltamivir-Azithromycin, Group 4. Hydroxychloroquine-Azithromycin-Favipirav

in terms of age, history of contact with a COVID-19 positive subject, oxygen saturation, duration of treatment, presence/absence of HT, presence/absence of pulmonary conditions, and treatment types according to CT findings. The mean duration of hospital stay was 10.7 ± 3.9 days (7-21), and the longest mean duration of hospital stay was recorded in Group 4, with 14.9 ± 0.6 days (10-21) (r=0.528, p < 0.001). Table 2 shows the sociodemographic characteristics and risk factor distribution in the study population. Examination of the pre-admission clinical data showed significant (p<0.05) differences in terms of baseline lymphocyte count, neutrophil count, lymphocyte/neutrophil ratio, CRP, D-dimer, and Troponin values. Lymphocyte count (1372 ± 72; 300-3430) and lymphocyte/neutrophil ratio (0.35 ± 0.06; 0.03-2.47) were lowest in Group 4, patients with more severe CT findings were more likely to be in Group 4. Table 3 shows a comparison of patients in terms of CT and laboratory findings according to the treatment group. A linear regression analysis for the association between clinical parameters and treatment duration showed significant positive correlation between age and the duration of treatment (R2=0.274, p=0.003). Also, HT, diabetes mellitus (DM), and pulmonary conditions were found to be significantly correlated with the treatment duration and treatment type (R=.246, R2= 0.60, p < 0.05; and R=.298, R2=.089, p<0.05, respectively).

The t test for the significance of regression coefficients did not confirm a significant association between the duration of treatment and HT, DM, and pulmonary disease, while the significant correlation with the type of treatment was retained. Also, there was a significant correlation between treatment duration and administration of treatment containing favipiravir (R=.336. R2=.113. p<0.05). Two groups of patients were defined on the basis of favipiravir use (favipiravir group vs. non-favipiravir group), and a regression analysis was performed to examine the relationship between treatment groups and epidemiologic data as well as comorbidity. When significance (p<0.05) was found in the initial univariate analysis, a multivariate analysis performed (although p was 0.224 for smoking, it was still included in the analysis due to its importance as a risk factor). Accordingly, no significant correlations were found between favipiravir use and smoking, being a healthcare worker, travel history, and history of COVID-19 contact. However, favipiravir treatment was associated with age, gender, CT findings, low saturation, HT, and pulmonary disease. A multivariate analysis, on the other hand, showed an association only between low saturation and having favipiravir treatment (p<0.001) (Table 4). When a ROC analysis was performed for the low saturation values in the favipiravir treatment group, the sensitivity and specificity of a SatO2 of ≤ 94% for receiving favipiravir containing treatment were 60% and 76.3%, respectively (p < 0.01, 95% CI=0.638-0.775).

During the 3 month follow up of patients receiving

Table 3: Comparison of treatment groups according to laboratory and CT findings

	Group 1 (n=12)	Group 2 (n=48)	Group 3 (n=75)	Group 4 (n=25)	Test value p value
Lymphocyte count (/uL)	2344±450 (1000-4700)	1378±91 (370-2900)	1518±78 (290-3070)	1372±72 (300-3430)	KW=10.54 p=0.015
Neutrophil count (/uL)	3248±336 (1500-6090)	6037±486 (770-14800)	4748±330 (1330-14300)	5495±468 (720-18000)	KW=12.69 p=0.005
Lymphocyte/Neutrophil ratio	0.83±0.18 (0.19-2.28)	0.35±0.04 (0.05-1.38)	0.41±0.03 (0.2-1.0)	0.35±0.06 (0.03-2.47)	KW=18.42 p=0.000
CRP (mg/L)	5.6±4.7 (1-15)	51.4±18.5 (1-462)	73.7±24.4 (2-358)	50.9±8.6 (10-113)	KW=19.33 p=0.000
D-Dimer (mg/L)	0.33±0.15 (0.1-0.6)	1.33±0.43 (0.1-11.5)	1.53±0.67 (0.1-12.0)	0.77±0.19 (0.2-2.5)	KW=12.53 p=0.006
Troponin (pg/ml)	4.67±3.67 (1-12)	50.3±22.7 (2-600)	194.4±95.9 (1-1447)	44.7±10.1 (1-135)	KW=7.79 p=0.050
CT findings n (%)					
1	12 (6.7)	1 (0.6)	1 (0.6)	1 (0.6)	
2	0 (0)	27 (15.0)	16 (8.9)	6 (3.4)	χ^2=192.7 p=0.000
3	0 (0)	12 (6.7)	23 (12.8)	14 (7.8)	
4	0 (0)	8 (4.5)	22 (12.2)	24 (13.4)	
PCR and CT positivity n (%)					
PCR(+)-BT(+)	0 (0)	5 (2.8)	31 (17.2)	26 (14.4)	
PCR(+)-BT(-)	10 (5.6)	3 (1.7)	15 (8.3)	1 (0.6)	χ^2=28.53 p=0.000
PCR(-)-BT(+)	2 (1.1)	40 (22.2)	29 (16.1)	18 (10.0)	

Based on CT findings: 1) CT normal or no typical involvement; 2) unilateral involvement; 3) bilateral involvement; 4) bilateral involvement and consolidation (diffuse involvement)

Treatment Groups: Group 1. Hydroxychloroquinine, Group 2. Hydroxychloroquinine- Azithromycin, Group 3. Hydroxychloroquinine- Oseltamivir-Azithromycin, Group 4. Hydroxychloroquinine-Azithromycin-Favipiravir

Table 4: Regression analysis of epidemiological data for favipiravir containing treatment group

	Univariate Analyses			Multivariate Analyses		
Variable	**p value**	**Logistic Regression**	**95% Cl**	**p value**	**Logistic Regression**	**95% Cl**
Sex (male)	0.033	2.134	1.062-4.289	0.064	2.065	0.957-4.452
Age	0.003	1.029	1.010-1.048	0.867	0.998	0.973-1.024
Presence of CT findings	0.020	11.000	1.450-83.460	0.110	5.396	0.682-42.684
Smoking	0.224	1.662	0.733-3.769	0 .787	0.868	0.311-2.423
Healthcare worker	0.595	1.265	0.531-3.013	-	-	-
Travel history	0.390	1.346	0.684-2.647	-	-	-
Contact individual	1.000	1.000	0.505-1.980	-	-	-
Presence of DM	0.528	0.773	0.347-1.720	-	-	-
Presence of HT	0.016	0.430	0.216-0.854	0.315	0.626	0.251-1.559
Presence of pulmonary disease	0.004	0.308	0.139-0.681	0.057	2.358	0.974-5.709
Low oxygen saturation	0.000	0.759	0.673-0.856	0.000	0.799	0.706-0.904

HCQ treatment, bradycardia was observed in two, and arrhythmia with QT prolongation in one patient, requiring discontinuation of HCQ treatment. Although gastrointestinal complaints such as nausea, vomiting, and/or diarrhea was the most common side effect of HCQ, treatment was continued due to improvement of symptoms with subsequently better drug tolerance. Following the initiation of favipiravir treatment, three patients had rash, four had mild elevation of liver function tests, two had diarrhea, and five had hypomagnesemia, all of which improved with replacement therapy.

DISCUSSION

The global search for effective and safe treatments for COVID-19 infection continues, with no specific treatments with confirmed efficiency currently available. Clinical experience is being continuously reported from different countries (4,7,8). It is thought that sharing experiences by exchanging ideas can be useful in fighting the COVID-19 pandemic. In our research, which we think may contribute to the fight against pandemic, our clinical experiences with our patients treated have been shared. We observed no life-threatening side effects occurred in patients receiving HCQ or favipiravir during their hospital stay. Although initial reports on HCQ use described some benefits, the need for in vivo and randomized controlled studies was also underscored. Also, HCQ is thought to be ineffective in those with persistently elevated viremia (4,7,8,13-15). In Cortegiani et al.'s review involving studies from China, France, Italy, Holland, and Guandong, it was reported that HCQ could be used for the treatment of COVID-19 infection, with therapeutic effects such as reduced body temperature, improved CT signs, and delayed disease progression (9).

However several limitations of these studies have also been emphasized, including the limited sample size, preliminary nature of the data, and absence of randomization and control groups. On the other hand, in a multi-center observational study across Belgium, supportive therapy alone was compared with HCQ + supportive therapy in terms of mortality, and the latter treatment was associated with reduced mortality rates (4). In the first results of the studies on the use of HCQ, which is one of the drugs recommended at the beginning of the pandemic, although the drug was reported to be beneficial, it was reported that its effectiveness was not sufficient in studies published afterwards and it was not effective in patients with persistently high viremia (4,7,8,13,14,15). In the review of Cortegiani et al., It was reported that COVID-19 treatment reduced fever, improved tomography findings, and showed theropathic effects such as delaying the progression of the disease (9). In these studies, various limitations such as limited number of data and presenting them as preliminary data, and lack of non-randomized controlled studies were also mentioned. However, in a multi-center observational study conducted in Belgium, patients who received only supportive treatment and HCQ + supportive treatment were compared in terms of mortality and mortality was found to be lower in the group using HCQ (4). Conversely, in the SOLIDARITY study endorsed by UK-based Recovery and WHO, HCQ was administered at a high dose (9200-9600 mg) for 10 days, but the treatment was halted due to cardiotoxic effects. However, it should be noted that the doses utilized in that study were much higher compared to the generally recommended dose of 2400 mg, possibly causing the observed side effects. Similarly, in a publication by Catteau et al., another study was mentioned that was withdrawn from publication due to side effects associated with high doses. These authors observed no significant cardiotoxic side effects at a dose of 2400 mg in their study (4). The doses used in our study were similar to those reported by Catteau et al., and except for three patients (1.6%) no significant side effects occurred. These findings support the view that HCQ with a long history of use as safe antimalarial and anti-rheumatic agent may also be used in appropriately selected COVID-19 patients. Also presence clinical, laboratory, and radiologic responses to HCQ among mildly ill patients as well as the low rate of cardiotoxic effects and complications suggest that HCQ should not be disregarded in the first place. When one

also considers the low cost of the drug, HCQ may also be used as an emergency treatment option in selected patients, particularly in developing countries where drug availability is low (4,8,12). Reporting of clinical experience with HCQ treatment in real-life conditions may also assist in eliminating some of the confusion surrounding HCQ use.In the recent WHO-led SOLIDARITY and UK- based Recovery study, HCQ therapy was given a high dose of 9200-9600 mg for 10 days, and the study was stopped due to cardio toxiceffects. administering at a dose much above there commended weekly dose of 2400 mg in the treatment of COVID-19 may be associated with side effects due to the high dose. They also reported that they did not experience any significant cardiotoxicside effects at a dose of 2400 mg given weekly in their studies (4). In our study, the weekly dose given was similar to the study of Catteau et al. No significant cardiotoxic side effects were observed excep for three patients (1.6%). Although favipiravir is another recommended agent for the treatment of COVID-19 infection, literature data regarding this agent is relatively scarce. In one study comparing favipiravir and a combination of lopinavir-ritonavir in these patients, favipiravir was associated with more rapid viral clearance, earlier improvement in CT signs, and lower rate of side effects (15). On the other hand, pre-clinical animal models have not yielded clear-cut results, and further and larger double blind studies are warranted. Furthermore, despite pharmacokinetic concerns such as low serum concentrations, it was also reported that this agent may be used as a safe treatment option (7,16). Although it was found effective in our study, it should be supported by long-term data that more patients were followed up.

Studies reported that both agents were used in this study have a relatively good safety profile, with no significant side effects when used in appropriate dose and duration in selected patients (7). While favipiravir could be associated with elevation in liver enzymes, HCQ may lead to gastrointestinal side effects such as nausea, vomiting, and diarrhea; on the other hand longer treatment with higher doses may result in retinopathy or cardiomyopathy (4). In multi-center nationwide studies in China and Belgium, the most frequently reported side effect was diarrhea, and no life-threatening or cardiotoxic complications were observed (4,17). In our study, the most common side effects were found to be gastrointestinal symptoms in patients who were treated similarly, and nosignificant cardiotoxic sideeffects were observed. This situation may be related to the administration of the treatment in the appropriate patient group at the appropriate dose. However, it is thought that it may be more beneficial to monitor the long-term sideeffects of the patients and to share the results.

It is very important to determine how the clinical course of a disease will develop, in which conditions the prognosis may be poor, and to determine the prognostic factors at the time of application in order to take precautions against these situations. When the laboratory data and treatment groups of the patients were examined at the time of first application; the fact that parameters such as low lymphocyte counts (KW = 10.54 and p = 0.015), high neutrophil count (KW = 12.69 and p = 0.005), low lymphocyte / neutrophilratio (KW = 18.42 and p = 0.000), CRP, D –Dimer and troponin elevation (KW = 19.33 and p = 0.000, KW = 12.53 and p = 0.006 and KW = 7.79 and p = 0.050, respectively.) show statistical significance to wards Group 4 (thegroupreceiving Favipiravir). This may provide an idea for the treatment selection in patients. A similar situation can be stated for CT involvement at the time of admission (2 = 192.7 and p = 0.000).

When examined which parameter showed the strongest correlation with clinical progression among thepatients comorbidity conditions; Multivariate Analysis was applied and it was found that there is a significant relationship between low oxygen saturation. In the Roc Analysis performed after wards, it was determined that the SatO2≤94 value was 60% sensitive and 76.3% specific for starting the treatment group containing favipiravir. These parameters are thought to be useful in determining the treatment method of the patient at the time of application.

In conclusion, response to favipiravir treatment observed in elderly patients (≥ 65 y), in those with comorbid conditions, or in those with diffuse CT involvement at presentation may provide insights for the clinician regarding the choice of therapy. In this context, we believe that appropriate treatments may be administered to carefully selected patients by considering physical examination and laboratory findings as well as comorbid conditions prior to initiation of therapy. However, our results should be corroborated with larger and randomized, controlled studies. As a result; responseto favipiravir treatment in patients aged 65 and over, with comorbidities, and extensive involvement in CT at hospitalization, especially Sat O2≤94, may provide an idea for treatment selection. The prominence of favipiravir treatment in our patient group has concluded that the treatment should be initiated in the appropriate patient group ands electively

Conflict of Interest: No conflict of interest was declared by the authors.
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REFERENCES

1. Bahceci I, Yildiz I E, Duran O F, Soztanaci US, KirdiHarbawi Z, Senol FF, et al . Secondary Bacterial Infection Rates Among Patients With COVID-19. Cureus. 2022;14(2):e22363. doi:10.7759/cureus.22363.
2. Bahceci I, Senol FF. Post-vaccination COVID-19 positivity and clinical situation analysis in healthcare professionals. Annals of Clinical and Analytical Medicine. 2022 13(9), 959-962. doı: 10.4328/ACAM.21139
3. Bahçeci I, Yıldız S, İbik YE, Duran OF, Arslan N, Sahin K. Determination of HBsAg, Anti-HCV and Anti-HIV Reactivity in Covid-19 Patients

Evaluation. Journal of Immunology and Clinical Microbiology. 2022; 7(3), 51-57.
4. Catteau L, Dauby N, Montourcy M, Bottieau E, Hautekiet J, Goetghebeur E, et al. Low-dose Hydroxychloroquine Therapy and Mortality in Hospitalized Patients with COVID-19: A Nationwide Observational Study of 8075 Participants. International journal of antimicrobial agents. 2020:106144. doi: 10.1016/j.ijantimicag.2020.106144
5. Çakırca D, Bal T. Relationship between COVID-19 infection and ABO and Rh blood group systems. Cukurova Medical Journal. 2022 : 1485-1491. doi: 10.17826/cumj.1134928
6. Şenol FF, Bahçeci I, Arslan N, Aytaç Ö, Öner P, Aşcı Toraman Z. Comparison of respiratory tract pathogens and antibiotic susceptibility profiles of patients diagnosed with COVID-19 with pre-COVID-19. Journal of Health Sciences and Medicine. 2022; 5(2): 510-516. doi.org/10.32322/jhsm.1010249
7. Drożdżal S, Rosik J, Lechowicz K, Machaj F, Kotfis K, Ghavami S, et al. FDA approved drugs with pharmacotherapeutic potential for SARS-CoV-2 (COVID-19) therapy. Drug Resistance Updates. 2020; 53:1 00719. doi: 10.1016/j.drup.2020.100719.
8. Singh AK, Singh A, Shaikh A, Singh R, Misra A. Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries. Diabetes & metabolic syndrome. 2020;14: 241-6. doi: 10.1016/j.dsx.2020.03.011
9. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. Journal of critical care. 2020;57: 279-83. doi: 10.1016/j.jcrc.2020.03.005
10. The Republic of Turkey Ministry of Health Directorate General of Public Health. Müdürlüğü SBHSG. COVID-19 (SARS-CoV-2 Infection) Adult Patient Treatment. Ankara. 2 August 2020.
11. Schrezenmeier E, Dörner T. Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatology. Nature reviews Rheumatology. 2020; 16:155-66.
12. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell research. 2020; 30:269-71.
13. Kaptein SJ, Jacobs S, Langendries L, Seldeslachts L, ter Horst S, Liesenborghs L, et al. Antiviral treatment of SARS-CoV-2-infected hamsters reveals a weak effect of favipiravir and a complete lack of effect for hydroxychloroquine. Bio R xiv. 2020:2020.06.19.159053. doi: https://doi.org/10.1101/2020.06.19.159053
14. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International journal of antimicrobial agents. 2020; 56:105949. doi: 10.1016/j.ijantimicag.2020.105949
15. Cai Q, Yang M, Liu D, Chen J, Shu D, Xia J, et al. Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study. Engineering. 2020. DOI: 10.1016/j.eng.2020.03.007
16. Du Y-X, Chen X-P. Favipiravir: Pharmacokinetics and Concerns About Clinical Trials for 2019-nCoV Infection. Clinical Pharmacology & Therapeutics. 2020; 108: 242-7. doi: 10.1002/cpt.1844
17. Chen C, Zhang Y, Huang J, Yin P, Cheng Z, Wu J, et al. Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial. medRxiv. 2020. doi:10.1101/2020.03.17.20037432

ORIGINAL ARTICLE

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Determining Risk Factors for Delirium Among Elderly Patients in The Emergency Care Settings

Acil Servise Başvuran Yaşlı Hastalarda Deliryum İçin Risk Faktörlerinin Belirlenmesi

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ABSTRACT

Objective: *Delirium is reported as a common clinical state among elderly patients seeking care in the emergency departments (ED). However, it is commonly underdiagnosed in the ED. This study aimed to evaluate delirium prevalence and determine the risk factors for developing delirium in elderly patients in ED.*

Material and Methods: *The study included 238 patients who were ≥65 years old and visited the emergency department (ED). The emergency specialist used the 'Confusion assessment method (CAM)' to screen for delirium in the patient group. A psychiatrist then evaluated the patients according to DSM-5 criteria for delirium. Demographic data, vital signs, and laboratory findings of the patients were also recorded as part of the study.*

Results: *Delirium was identified in 10.9% of the patients through CAM and 11.8% of the patients according to DSM-5 criteria. No statistically significant difference was found between the groups with and without delirium in terms of age, gender, comorbidities, presence of dementia, and use of polypharmacy. A positive correlation between mean arterial blood pressure (MABP) (r=0.373, p<0.001), pulse rate (r=0.208, p<0.001), and respiratory rate (r=0.284, p<0.001) and a negative correlation between CRP levels (r=-0.139, p=0.032) and the presence of delirium were found. Logistic regression analysis showed that MABP>99 mmHg and respiratory rate>19/min are associated risk factors for delirium.*

Conclusion: *High MABP and respiratory rate could be related to delirium risk. Although the hemodynamic risk factors could contribute to the recognition of delirium, practical clinical screening tools are still the most important and reliable methods to detect delirium.*

ÖZET

Amaç: *Deliryum, acil servislere başvuran yaşlı hastalarda sık görülen bir klinik durum olmakla birlikte, tanısı genellikle atlanmaktadır. Bu çalışmada acil servise başvuran yaşlı hastalarda deliryum prevalansının değerlendirilmesi ve deliryum için risk faktörlerinin belirlenmesi amaçlanmıştır.*

Gereç ve Yöntemler: *Acil servise başvuran 65 yaş üstü 238 hasta çalışmaya dahil edildi. Hasta grubu acil servis uzmanı tarafından 'Konfüzyon Değerlendirme Yöntemi (KDY)' kullanılarak deliryum açısından tarandı. Hastalar daha sonra bir psikiyatrist tarafından DSM-5 kriterlerine göre deliryum açısından değerlendirildi. Hastaların demografik verileri, vital bulguları ve laboratuvar bulguları kaydedildi.*

Bulgular: *KDY ile hastaların %10,9'unda, DSM-5 kriterlerine göre hastaların %11,8'inde deliryum tanısı saptandı. Deliryum olan ve olmayan gruplar arasında yaş, cinsiyet, ek hastalık, demans ve polifarmasi varlığı açısından istatistiksel olarak anlamlı bir fark saptanmadı. Ortalama arteriyel kan basıncı (OAKB) (r=0,373, p<0,001), nabız (r=0,208, p<0,001) ve solunum sayısı (r=0,284, p<0,001) ve deliryum arasında pozitif, CRP düzeyleri (r=-0,139, p=0,032) ve deliryum varlığı arasında ise negatif korelasyon saptandı. Lojistik regresyon analizi sonuçları, OAKB> 99 mmHg ve solunum hızı> 19/dk'nın üzerinde olmasının deliryum için risk faktörü olabileceğini gösterdi.*

Sonuç: *Yüksek OAKB ve solunum hızı deliryum riski ile ilişkili olabilir. Hemodinamik risk faktörleri deliryumun tanınmasına katkıda bulunabilse de, pratik klinik tarama araçları deliryumu saptamak için hala en önemli ve güvenilir yöntemlerdir.*

Keywords:
Delirium
Emergency department
Elderly
Related factors

Anahtar Kelimeler:
Deliryum
Acil servis
Yaşlı
İlişkili faktörler

INTRODUCTION

Delirium is an acute neuropsychiatric syndrome characterized by various psychomotor disturbances and cognitive symptoms. It is a state of alteration in consciousness, and disorientation that can occur suddenly and fluctuate during the day and is often accompanied by changes in behavior and perception. Delirium is generally caused by an underlying medical condition and can not be caused by a preexisting or established neurocognitive disorder such as dementia (1).

Delirium is known to have a higher incidence in elderly patients, with the prevalence increasing with age. It is estimated that up to 50% of hospitalized elderly patients may experience delirium (2). Elderly patients are more susceptible to delirium due to age-related changes in the central nervous system, which include alterations in neurotransmitter functions, neurodegenerative changes, and reduced cerebral blood flow. Additionally, the prevalence of comorbidities, cognitive loss, and polypharmacy increases with age, which further increases

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the risk of delirium (3, 4).

Delirium is also a prevalent condition among elderly patients in emergency services. Several studies have reported the incidence of delirium in the emergency department (ED) ranging from 7 to 20% (5, 6). Delirium in emergency services is associated with longer hospital stays, higher healthcare costs, poorer functional outcomes, and increased mortality rates (7). However, it is often underdiagnosed in emergency settings due to the complexity of patient assessment and the lack of awareness among healthcare professionals (8). It is reported that the mortality rate in patients discharged from the ED with unrecognized delirium diagnosis is 3 times higher than in patients for whom delirium is detected, which shows that unidentified delirium in emergency care settings results in poor outcomes in elderly patients (9).

Determining the risk factors for delirium can allow the rapid recognition and management of this clinical state in emergency services and is crucial to improving patient outcomes and reducing the burden of it on healthcare systems. Therefore, this study aims to assess the delirium prevalance and determine the associated risk factors for developing delirium in geriatric patients admitted to emergency care settings.

MATERIAL AND METHODS

This study was conducted with elderly patients, 65 years and older, applied to the ED during weekdays for 6 months period. The patients were assessed by the psychiatrist within the working hours (from 9 am to 6 pm). All the patients able to undergo a psychiatric examination and whose informed consent was obtained were included in the study. The unconscious patients, who have unstable cardiovascular or respiratory conditions, severe burns or trauma, or refuse to involve in the study were excluded.

The Short Portable Mental Status Questionnaire (SPMSQ) was administered to determine the capacity of patients to give informed consent. The SPMSQ has 10 items to detect cognitive impairment by evaluating orientation, memory, and concentration (10). If the patient had 4 or fewer mistakes in the SPMSQ, informed consent was directly asked of the patient. For patients with more than 4 mistakes in the test, informed consent was taken from the caregiver of the patient.

Patients' sociodemographic characteristics, the reason for the application to the ED, medical history, number of medications used by the patient, presence of polypharmacy (≥5 drugs), vital values (body temperature, systolic and diastolic arterial blood pressure (SABP and DABP), mean arterial blood pressure ([SABP+2xDABP] / 3), pulse, respiratory rate), laboratory findings (sedimentation rate, C-reactive protein (CRP), and neutrophil/lymphocyte ratio (NLR)) and follow-up time in ED were recorded. The patients were examined first by the emergency physician using Clinical Assessment Method (CAM) to screen for delirium. CAM is a semi-structured tool that is sensitive and widely used to assess delirium in clinical settings (11). The patients were also examined by the psychiatrist to detect delirium according to the DSM-5 delirium criteria (reduced ability to focus or shift attention, disturbance of consciousness, the disturbance develops over a short period, tends to fluctuate during the day, and not due to dementia) (1). If there is a diagnosis of depression, psychosis, or dementia in the medical history, the differential diagnosis of delirium from the primary psychiatric condition was determined according to the psychiatric examination of the patient. The study adhered to the guidelines set forth in the Helsinki Declaration, and the research protocol was approved by the Clinical Research Ethics Committee of Bolu Izzet Baysal University (date: 22.05.2019 no:236).

Statistical Analysis

The statistical analysis was conducted using IBM SPSS 25.0 (Armonk, NY: IBM Corp.) and MedCalc 15.8 (MedCalc Software bvba, Ostend, Belgium) software packages. For the qualitative data, the Chi-Square ($\chi 2$) test was utilized, along with descriptive statistical methods including frequency, percentage, mean, standard deviation, median, min-max, and IQR. The distribution of data was assessed using the Kolmogorov-Smirnow test, skewness-kurtosis, and graphical methods such as histogram, Q-Q plot, stem and leaf, and boxplot. Independent Samples t-test was employed to analyze data with normal distribution, whereas the Mann-Whitney U test was used for data without normal distribution. The ROC curve (Receiver Operating Characteristic) analysis was performed to assess variable distinctiveness, and Binary Logistic Regression was used to estimate risk ratios. Finally, Spearman's Rho Correlation test was conducted to evaluate the relationships between variables. The significance level was set at $\alpha=0.05$.

Power analysis was made with the statistical package program G*Power 3.1.9.7 (Franz Foul, Universitat Kiel, Germany). Power was found as 99% with n1=210(91.6 ± 11.1), n2=28(106.9 ± 11.7), $\alpha=0.05$, effect Size (d)=1.2.

RESULTS

There were 238 patients included in the study. 55.5% of the patients were female (n=132), and the mean age was 76.0 ± 8.1 years. The mean follow-up time of the patients at the ED was 16.8±9.7 hours. Delirium is detected in 10.9% of the patients (n=26) by using CAM. Meanwhile, it was found that 11.8% of patients (n=28) had delirium according to DSM-5 criteria.

Table 1 presents a comparison of the sociodemographic characteristics and medical records of patients with and without delirium. The results showed that there were no statistically significant differences between the groups in terms of age, gender, place of residence, number of comorbid diseases, presence of dementia, number of drugs used, and presence of polypharmacy ($p>0.05$ for all). Furthermore, no significant differences were observed between the groups in terms of the reasons for their admission to the emergency department ($p>0.05$). Notably, metabolic, cardiovascular, and neurological disorders were identified as the most common problems leading to ED admission for both groups of patients.

Table 2 presents the vital signs and laboratory values of patients upon admission to the ED. The results showed that patients diagnosed with delirium had significantly higher systolic arterial blood pressure (SABP), diastolic arterial blood pressure (DABP), mean arterial blood pressure (MABP), pulse rate, and respiratory rate values ($p<0.001$ for all), while CRP values were significantly lower ($p=0.032$) compared to patients without delirium.

Table 1: Comparison of the sociodemographic and medical status of the patients with and without delirium

		Delirium		p
		No (n=210)	Yes (n=28)	
Sex	Female	115 (54.8%)	17 (60.7%)	0.694 a
	Male	95 (45.2%)	11 (39.3%)	
Age (year)		76.4 ± 8.1	73.1 ± 7.2	0.054 b
	65-74 Year-old	83 (39.5%)	16 (57.1%)	0.205 a
	75-84 Year-old	82 (39.0%)	7 (25.0%)	
	≥85 Year-old	45 (21.4%)	5 (17.9%)	
Residence	Home alone	49 (23.3%)	3 (10.7%)	0.248 a
	Home with others	126 (60.0%)	21 (75.0%)	
	Nursing homes	35 (16.7%)	4 (14.3%)	
Number of chronic diseases		2.0 (1.0 – 3.0)	3.0 (1.0 – 4.0)	0.185 c
Dementia Diagnosis	No	186 (88.6%)	24 (85.7%)	0.753 a
	Yes	24 (11.4%)	4 (14.3%)	
Total number of patient's medication		3.0 (1.0 – 5.0)	5.0 (2.0 – 6.0)	0.090 c
Polypharmacy	No	130 (61.9%)	12 (42.9%)	0.085 a
	Yes	80 (38.1%)	16 (57.1%)	
Reason for Application to Emergency Department	Metabolic disease	43 (20.5%)	6 (21.4%)	0.969 a
	Cardiovascular disease	32 (15.2%)	4 (14.3%)	
	Neurological disease	31 (14.8%)	5 (17.9%)	
	Respiratory disease	23 (11.0%)	3 (10.7%)	
	Urinary tract disease	19 (9.0%)	3 (10.7%)	
	Infection	18 (8.6%)	3 (10.7%)	
	Multiple	19 (9.0%)	2 (7.1%)	
	Malignancy	10 (4.8%)	0 (0.0%)	
	Trauma	8 (3.8%)	1 (3.6%)	
	Others	7 (3.3%)	1 (3.6%)	

a: Chi-Square Test (n (%)), b: Independent Samples t Test (Mean ± SD), c: Mann-Whitney U test (Median (Q1 – Q3))

Table 2: Comparison of vital signs and laboratory findings of the patients with and without delirium upon admission to the emergency department

	Delirium		p
	Yes (n=210)	No (n=28)	
Systolic arterial blood pressure (mmHg)	116.0 (107.8 – 126.0)	135.0 (128.0 – 138.0)	<0.001 c
Diastolic arterial blood pressure (mmHg)	77.0 (71.0 – 84.0)	93.0 (86.0 – 103.3)	<0.001 c
Mean arterial blood pressure (mmHg)	90.0 (83.0 – 97.0)	106.5 (101.3 – 114.8)	<0.001 c
Pulse rate (/min)	91.0 ± 17.8	102.5 ± 13.1	<0.001 b
Respiratory rate (/min)	17.4 ± 3.0	21.0 ± 4.4	<0.001 b
Temperature (°C)	36.6 (36.2 – 37.1)	36.7 (36.3 – 37.2)	0.514 c
C-reactive protein (CRP) (mg/l)	4.0 (1.7 – 10.3)	0.4 (0.1 – 5.9)	0.032 c
Sedimentation (mm/h)	16.0 (6.0 – 24.0)	18.5 (3.0 – 28.0)	0.899 c
Neutrophil/leukocyte ratio (NLR)	2.4 (1.7 – 3.1)	2.6 (1.6 – 3.2)	0.638 c
Follow-up time in the ED (hours)	14.0 (9.0 – 21.0)	17.0 (9.5 – 23.0)	0.300 c
Mortality rate during follow-up in the ED	7 (%3.3)	2 (%7.1)	0.286 a

a: Chi-Square Test (n (%)), b: Independent Samples t Test (Mean ± SD), c: Mann-Whitney U test (Median (Q1 – Q3)), ED: Emergency Department

However, no significant differences were observed between the groups in terms of body temperature, sedimentation rate, and NLR values (p>0.05 for all). Moreover, there was no statistically significant difference between the groups in terms of mean follow-up time in the ED and mortality rates at the end of the follow-up (p=0.300 and p=0.286, respectively).

Subsequently, a correlation analysis was performed to identify any associations between these variables and the presence of delirium. Results indicated positive correlations between SABP (r=0.368, p<0.001), DABP (r=0.366, p<0.001), MABP (r=0.373, p<0.001), pulse rate (r=0.208, p<0.001), respiratory rate (r=0.284, p<0.001), and the presence of delirium, whereas a negative correlation was found between CRP levels (r=-0.139, p=0.032) and the presence of delirium. Logistic regression analysis including variables that were statistically correlated with the presence of delirium (MABP, CRP, pulse, and respiratory rate) revealed a statistically significant relationship between delirium and MABP and respiratory rates (p<0.001 and p=0.002, respectively) (Table 3). The model indicated that approximately 38% of the presence of delirium could be explained (Nagelkerke R2=0.375) and that the risk of delirium increased by approximately 1.1 times in those with higher MABP values and approximately 1.3 times in those with higher respiratory rates.

The variables identified as risk factors were assessed through ROC analysis, which revealed that MABP had a cut-off point of >99 mmHg (AUC=0.834, p<0.001, 95% CI: 0.781-0.879), while the cut-off point for respiratory rate was >19/min (AUC=0.752, p<0.001, 95% CI: 0.692-0.805) (Figure 1 and 2).

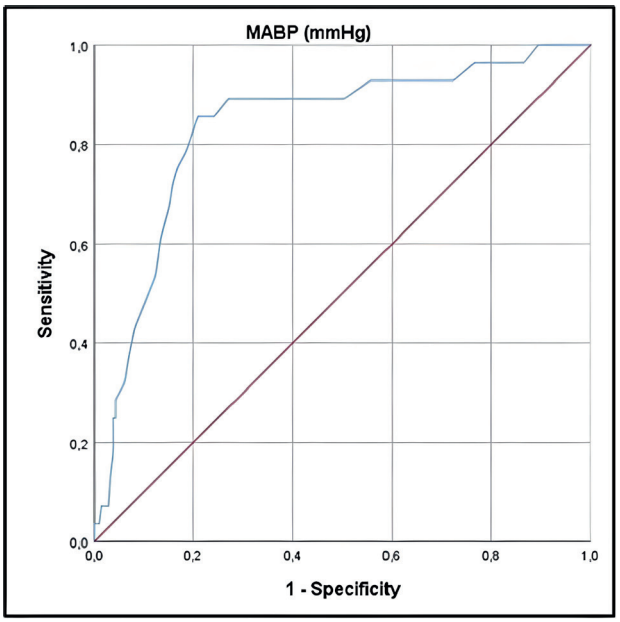

Figure 1: ROC analysis of the mean arterial blood pressure (MABP) to predict delirium

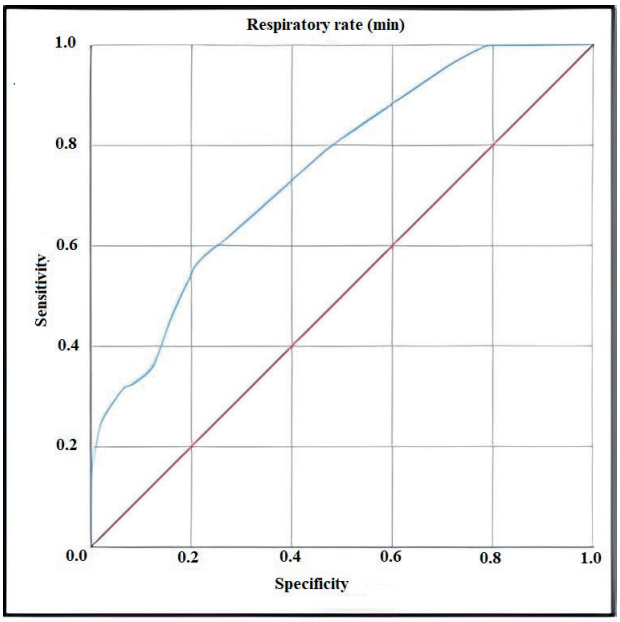

Figure 2: ROC analysis of the respiratory rate to predict delirium

Table 3: Logistic regression analysis of the variables contribute to the presence of delirium

Risk Factor	β	SE	Wald	Odds	%95 GA	p*
MABP (mmHg)	0.081	0.018	20.025	1.08	1.05 - 1.12	<0.001
Pulse rate (/min)	-0.001	0.017	0.007	1.00	0.97 - 1.03	0.932
Respiratory rate (/min)	0.251	0.080	9.796	1.29	1.10 - 1.50	0.002
CRP (mg/l)	-0.042	0.037	1.298	0.96	0.89 - 1.03	0.255
Constant	-14.369	2.275	39.879			

**Binary Logistic Regression Test, Nagelkerke R2 = 0.375, Hosmer and Lemeshow Test = 0.127 MABP: Mean-arterial blood pressure, CRP: C-reactive protein*

Table 4: Accuracy of prediction of the cases according to the created model including MABP and respiratory rate

		Predicted delirium status of the patients with the created model		Accuracy (%)
		No (n)	Yes (n)	
Real patient group	Without delirium (n)	205	5	97,6
	With delirium (n)	20	8	28,6
Overall accuracy of correctly classified cases (%)				89,5

The estimation table was performed according to the created model created with MABP and respiratory rate, and 97.6% of patients without delirium diagnosis and 28.6% of patients with delirium diagnosis were predicted correctly with this model (Table 4). The overall accuracy rate was found to be 89.5%.

DISCUSSION

Our study revealed that delirium is a common condition in elderly patients applied to the ED. While no correlation was found between sociodemographic features, comorbid diseases, presence of polypharmacy or dementia, and delirium; it was shown that there was a positive correlation between delirium and MABP, pulse rate, respiratory rate, and a negative relationship with CRP levels. In the model established with MABP and respiratory rate, the sensitivity for detecting delirium was 28.6%, while the specificity was 97.6%. Furthermore, logistic regression analysis shows that MABP>99 mmHg and respiratory rate>19/min are associated risk factors for delirium.

In this study, delirium was diagnosed in 11.8% of the patients based on DSM-5 criteria. A recent meta-analysis reported a prevalence of 15.2% among elderly patients in the ED (12). In the same meta-analysis, a negative correlation was found between the sample size of the study and the prevalence of delirium, therefore, the prevalence of delirium may be lower in our study. The ability of emergency physicians to identify delirium using the CAM was also assessed, and it was found that most patients with delirium could be identified using this screening tool. Previous research has shown that up to one-third of patients with delirium can be identified by emergency physicians in the absence of a screening tool (13). Although there are several different tools developed for the assessment of delirium, their superiority to each other has not been proven (14). CAM is accepted as a very sensitive and practical tool that can determine the patient's delirium status (11). The use of such assessment tools facilitates the recognition of patients and the necessary interventions for patients.

When the conditions that contribute to the development of delirium in elderly patients who apply to the ED are examined, different risk factors are reported in the literature. In a meta-analysis, being a nursing home resident, cognitive impairment, hearing loss, and a history of stroke are the factors associated with delirium in ED (15). Some studies also showed that pain, urinary catheterization, dehydration, the presence of infection, and a chaotic ED environment may also cause delirium (16). However, our study did not reveal any difference in terms of the rate of nursing home residents or the presence of cognitive decline. The reason for this result may be that some cases with a diagnosis of neurocognitive disorder were not diagnosed yet or the diagnosis was missed due to lack of confident anamnesis. In addition, improvements in nursing home conditions with regular supervision policies may have improved the quality of care for elderly patients and therefore did not affect the risk of delirium.

The most frequent reasons for seeking medical attention in patients with delirium were metabolic, neurological, and cardiovascular diseases, although there was no significant difference in terms of the reason for admission between the two groups. Metabolic and neurological disorders were the most commonly associated medical conditions with delirium. These conditions are believed to cause delirium either by directly damaging the central nervous system (CNS) or indirectly by causing functional disturbances and altering neuronal transmission (17).

The laboratory findings and vital signs at admission were evaluated, and it was found that SABP, DABP, MABP, CRP values, and respiratory rate were correlated with the presence of delirium. However, the logistic regression analysis revealed that higher MABP and respiratory rate are associated with delirium. Specifically, a MABP higher than 99 mmHg and a respiratory rate greater than 19/min were found to be related to delirium. Previous studies have reported that vital signs such as heart rate, SABP, respiratory rate, body temperature, and oxygen saturation at the triage have moderate effects on delirium clinics. (15). Another study included low SABP, high DABP, low (<16/min), and high (>24/min) respiratory rates in a model to estimate delirium risk. (18). Additionally, another study showed that a respiratory rate greater than 20/min is related to an increased risk of delirium (19).

However, the model created based on MABP and respiratory rate higher than the determined cut-off levels have unfavorable results in detecting delirium. Whereas, it has a high specificity to exclude non-delirium cases. The direct effect of hypertension on cerebral vascular structure is known as an important risk factor for delirium (20). Moreover, hemodynamic changes in different clinical states could cause dysfunction in cerebral autoregulatory functions and may lead to hypoxia. Hypoxia is also reported as an important clinical finding related to delirium (21).

Although there are some sensitive prediction models related to delirium, the selected variables vary considerably, and accessing information about some of these variables in the ED can be difficult and not accessible (18, 19, 22). Therefore, using delirium assessment tools taking less than a few minutes such as CAM, The 3-Minute Diagnostic Confusion Assessment Method (3D-CAM), The '4A' Test (4AT) is a quick and reliable method to screen the presence of delirium (23).

The study has several limitations that should be considered when interpreting the results. One limitation is that it was conducted in a single center, which may limit the generalizability of the findings to other healthcare settings. Another limitation is that the study participants were recruited during weekdays and working hours, which may not be representative of all elderly patients who visit the ER at different times. Furthermore, clinically unstable patients were excluded from the study, which could lead to an underestimation of the prevalence of delirium since this group is at higher risk for delirium. In addition, the fluctuating symptoms of delirium may have led to some cases being missed. Finally, the medications administered during the ED stay were not taken into account in the analysis, which could have influenced the development of delirium.

In conclusion, delirium is a common clinical syndrome seen in elderly patients in the ED. Vital signs such as higher

MABP and respiratory rate are related to the increased risk of delirium. Although the hemodynamic risk profile of the individuals could contribute to the recognition of delirium, practical clinical screening tools are still the most important and reliable methods to assess delirium.

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REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Press Inc; 2013.
2. Inouye S, Westendorp R, Saczynski J. Delirium in elderly people. Lancet. 2014; 383(9920):911–22. DOI: 10.1016/S0140-6736(13)60688-1
3. Hshieh T, Inouye S, Oh E. Delirium in the Elderly. Clin Geriatr Med. 2020;36(2):183–99. DOI: 10.1016/j.cger.2019.11.001
4. Mattar I, Chan M, Childs C. Risk factors for acute delirium in critically ill adult patients: A systematic review. Int Sch Res Not. 2013;2013:1–10. DOI: 10.5402/2013/910125
5. Barron E, Holmes J. Delirium within the emergency care setting, occurrence and detection: a systematic review. Emerg Med J. 2013;30(4):263–8. DOI: 10.1136/emermed-2011-200586
6. Nguyen P, Pelletier L, Payot I, Latour J. The Delirium Drug Scale is associated to delirium incidence in the emergency department. Int Psychogeriatr. 2018;30(4):503–10. DOI: 10.1017/S1041610217002538
7. Reynish E, Hapca S, De Souza N, Cvoro V, Donnan P, Guthrie B. Epidemiology and outcomes of people with dementia, delirium, and unspecified cognitive impairment in the general hospital: prospective cohort study of 10,014 admissions. BMC Med. 2017;15(1):1–2. DOI: 10.1186/s12916-017-0899-0
8. Boucher V, Lamontagne M, Nadeau A, Carmichael P, Yadav K, Voyer P, et al. Unrecognized incident delirium in older emergency department patients. J Emerg Med. 2019;57(4):535–42. DOI: 10.1016/j.jemermed.2019.05.024
9. Kakuma R, Du Fort G, Arsenault L, Perrault A, Platt R, Monette J, et al. Delirium in older emergency department patients discharged home: effect on survival. J Am Geriatr Soc. 2003;51(4):443–50. DOI: 10.1046/j.1532-5415.2003.51151.x
10. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J Am Geriatr Soc. 1975;23:433–41.
11. Inouye S, van Dyck C, Alessi C, Balkin S, Siegal A, Horwitz R. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113:941–8.
12. Chen F, Liu L, Wang Y, Liu Y, Fan L, Chi J. Delirium prevalence in geriatric emergency department patients: A systematic review and meta-analysis. Am J Emerg Med. 2022;59:121–8. DOI: 10.1016/j.ajem.2022.05.058
13. Han J, Zimmerman E, Cutler N, Schnelle J, Morandi A, Dittus R, et al. Delirium in older emergency department patients: recognition, risk factors, and psychomotor subtypes. Acad Emerg Med. 2009;16(3):193-200. DOI: 10.1111/j.1553-2712.2008.00339.x
14. LaMantia M, Messina F, Hobgood C, Miller D. Screening for delirium in the emergency department: a systematic review. Ann Emerg Med. 2014;63(5):551–60. DOI: 10.1016/j.annemergmed.2013.11.010
15. Silva L, Berning M, Stanich J, Gerberi D, Murad M, Han J, et al. Risk factors for delirium in older adults in the emergency department: a systematic review and meta-analysis. Ann Emerg Med. 2021;78(4):549–65. DOI: 10.1016/j.annemergmed.2021.03.005
16. Rosen T, Connors S, Clark S, Halpern A, Stern M, DeWald J, et al. Assessment and Management of Delirium in Older Adults in the Emergency Department: Literature Review to Inform Development of a Novel Clinical Protocol. Adv Emerg Nurs J. 2015;37(3):183–96. DOI: 10.1097/TME.0000000000000066
17. Duran L, Aygun D. Evaluation of patients with delirium in the emergency department. Balk Med J. 2012;2012(4):381–5. DOI: 10.5152/balkanmedj.2012.023
18. Oliveira J. e Silva L, Stanich J, Jeffery M, Mullan A, Bower S, Campbell R, et al. REcognizing DElirium in geriatric Emergency Medicine: The REDEEM risk stratification score. Acad Emerg Med. 2022;29(4):476–85. DOI: 10.1111/acem.14423
19. Kennedy M, Enander R, Tadiri S, Wolfe R, Shapiro N, Marcantonio E. Delirium risk prediction, healthcare use and mortality of elderly adults in the emergency department. J Am Geriatr Soc. 2014;62(3):462–9. DOI: 10.1111/jgs.12692
20. Tilley E, Psaltis P, Loetscher T, Davis D, Harrison S, Kim S, et al. Meta-analysis of prevalence and risk factors for delirium after transcatheter aortic valve implantation. Am J Cardiol. 2018;122(11):1917–23. DOI: 10.1016/j.amjcard.2018.08.037
21. Ng K, Lee Z, Ang E, Teoh W, Wang C. Association of obstructive sleep apnea and postoperative cardiac complications: A systematic review and meta-analysis with trial sequential analysis. J Clini Anesth. 2020;62:109731.DOI: 10.1016/j.jclinane.2020.109731
22. Sri-on J, Tirrell G, Vanichkulbodee A, Niruntarai S, Liu S. The prevalence, risk factors and short-term outcomes of delirium in Thai elderly emergency department patients. Emerg Med J. 2016;33(1):17–22. DOI: 10.1136/emermed-2014-204379
23. Pérez-Ros P, Martínez-Arnau F. Delirium assessment in older people in emergency departments. A literature review. Diseases. 2019;7(1):14. DOI: 10.3390/diseases7010014

ORIGINAL ARTICLE

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Evaluation of Hemogram, Biochemistry, Inflammatory Markers and Electrolyte Levels in Patients with Acute Myocardial Infarction

Akut Miyokard İnfarktüslü Hastalarda Hemogram, Biyokimya, İnflamatuar Belirteçler ve Elektrolit Düzeylerinin Değerlendirilmesi

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ABSTRACT

Objective: *Hemogram, biochemistry, serum electrolyte, and inflammatory marker levels are altered in patients with acute myocardial infarction. When diagnosing and monitoring patients with acute myocardial infarction using cardiac-specific biomarkers, the levels of these markers should also be under control. We looked into the diagnostic and therapeutic value of hemogram, biochemistry, inflammatory markers, and electrolyte levels in acute myocardial infarction patients.*

Material and Method: *It is a descriptive epidemiological study. Within the scope of the study, all patients aged 18 years and over and diagnosed with acute myocardial infarction in the Emergency Department and Cardiology Department of Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital between 01.01.2022 - 31.12.2022 were included retrospectively. Hemogram, biochemistry, serum electrolyte and inflammatory marker levels were investigated in acute myocardial infarction patients.*

Results: *Leukocyte, neutrophil, procalcitonin and C-reactive protein values were significantly higher in patients with acute myocardial infarction. Although platelet/lymphocyte ratios were high, no significance was found. In patients with acute myocardial infarction, glucose values measured at the time of stress were found to be high (hyperglycaemia). When we analysed the serum lactate levels of patients with acute myocardial infarction, it was found to be significantly higher.*

Conclusion: *In patients with acute myocardial infarction, hemogram, biochemistry, serum electrolyte and inflammatory marker levels are altered. The levels of these markers should also be controlled during the diagnosis and follow-up of acute myocardial infarction patients with cardiac specific biomarkers. We believe that hemogram, biochemistry, inflammatory markers and electrolyte levels may contribute to the prediction of early serious complications in patients with acute myocardial infarction.*

Keywords:
Myocardial İnfarction
Hemogram
Biochemistry
Electrolic Levels
Inflammatory Markers

ÖZET

Amaç: *Akut myokard infarktüsü hastalarında hemogram biyokimya serum elektrolit ve inflamatuar belirteç düzeylerinde değişiklikler olmaktadır. Akut myokard infarktüsü hastalarının kardiyak spesifik biyobelirteçler ile tanı ve takibi esnasında bu belirteçlerin düzeyleri de kontrol edilmelidir. Bu çalışma ile hemogram, biyokimya, inflamatuar belirteçler ve elektrolit düzeylerinin akut myokard infarktüslü hastaların tanısındaki ve yönetimindeki yerini araştırmayı amaçladık.*

Gereç ve Yöntem: *Çalışma tanımlayıcı tipte bir epidemiyolojik araştırmadır. Çalışma kapsamında retrospektif olarak 01.01.2022 – 31.07.2022 tarihleri arasında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Hastanesi Acil Servis'inde ve Kardiyoloji bölümünde akut myokard infarktüsü tanısı almış 18 yaş ve üstü tüm hastalar dahil edildi. Akut myokard infarktüsü hastalarında hemogram biyokimya, serum elektrolit ve inflamatuar belirteç düzeyleri incelendi.*

Bulgular: *Akut myokard infarktüslü hastalarda lökosit, nötrofil, prokalsitonin, C-reaktif protein değerleri anlamlı derecede yüksek saptandı. Platelet/lenfosit oranlarının yüksek çıkmasına rağmen anlamlılık saptanmadı. Akut myokard infarktüslü hastalarda stres anında ölçülen glikoz değerleri yüksek (hiperglisemi) saptandı. Akut myokard infarktüslü hastaların serum laktat düzeylerini incelediğimizde anlamlı derecede yüksek saptandı.*

Sonuç: *Akut myokard infarktüsü hastalarında hemogram, biyokimya, serum elektrolit ve inflamatuar belirteç düzeylerinde değişiklikler olmaktadır. Akut myokard infarktüsü hastalarının kardiyak spesifik biyobelirteçler ile tanı ve takibi esnasında bu belirteçlerin düzeyleri de kontrol edilmelidir. Akut miyokard infarktüslü hastalarda hemogram, biyokimya, inflamatuar belirteçler ve elektrolit düzeylerinin erken dönem ciddi komplikasyonları önceden belirlemede katkılarının olabileceği kanısındayız.*

Anahtar Kelimeler:
Myokard İnfarktüsü
Hemogram
Biyokimya
Elektrolit Düzeyleri
İnflamatuar Belirteçler

INTRODUCTION

Cardiovascular diseases are currently the main cause of death in industrialized nations, and in the ensuing decades, they are predicted to overtake them in emerging nations. The most prevalent form of cardiovascular disease and the main cause of death is coronary artery disease (CAD). CAD is not only a health problem but also an important social problem because of its economic burden and negative effect on quality of life (1).

Myocardial ischaemia is myocardial damage resulting from a disturbance in the balance between myocardial oxygen supply and demand. Myocardial ischaemia is

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often caused by an atherosclerotic lesion. Acute Coronary Syndrome (ACS) is due to coronary arterial spasm at the site of the atherosclerotic lesion, erosion or rupture of the atherosclerotic lesion and reduced coronary blood flow due to platelet aggregation or thrombus formation. It is responsible for most of the deaths related to CAD and is closely related with its complications (2).

Acute Myocardial Infarction (AMI) is defined as irreversible myocardial cell damage and necrosis caused by severe and prolonged ischaemia. The most often utilized and crucial variables in the diagnostic assessment of patients with AMI symptoms are electrocardiography (ECG) and biochemical markers such troponins, creatine kinases, and myoglobin. Other markers that may aid in the diagnosis include serum electrolytes, ischaemia-modified albumin, cardiac fatty acid binding protein, high-sensitivity C-Reactive Protein (hs-CRP), and Brain Natriuretic Peptide (BNP) (3).

Mg plays a vital role in many cellular processes. It is closely associated with a wide range of enzymes and metabolic activities that control carbohydrate, fat, protein and electrolyte metabolism. Mg is a cardioprotective element that causes systemic and coronary vasodilatation, has antiplatelet activity and protects myocytes from calcium (Ca) influx during reperfusion. Mg deficiency or reduced dietary Mg intake plays an important role in the aetiology of cardiovascular diseases such as thrombosis, atherosclerosis, ischaemic heart disease, AMI, hypertension (HT), cardiac arrhythmias and congestive heart failure (CHF).

Potassium (K) decreases renal vascular resistance, boosts glomerular filtration rate, inhibits platelet aggregation and arterial thrombosis, slows proliferation of vascular smooth muscle cells, and inhibits free radical production among vascular endothelial cells and macrophages (4). It has been reported that cardiovascular diseases are less common in societies consuming primitive diets containing high levels of K and in vegetarians living in industrialised cultures (5). A higher risk of sudden cardiac mortality and ventricular arrhythmias has also been linked to hypokalaemia.

Ca is one of the most important cations in the body and plays a critical role in cardiac contraction, enzymatic activity and electrophysiological properties. Ca flow must be balanced for the maintenance of the steady state in the myocardium (6). High serum Ca levels have also been shown to be an independent risk factor for coronary heart disease such as AMI.

According to the National Health and Nutrition Examination Survey, low sodium (Na) intake is thought to be associated with coronary vascular disease. There are reports that low Na levels activate renin-angiotensin activity and sympathetic nervous system, increase insulin resistance and these increase the risk of cardiovascular disease (7).

Hyperglycaemia that develops during the stress process; The aim of this adaptation, which is the physiological response of the organism to stress, in which increased cytokines, stress hormones with anti-insulin effect and changes in insulin sensitivity are observed, is to provide glucose to vital organs. With acute hyperglycaemia, impairment in leukocyte function, increase in free oxygen radicals, blood pressure changes, increase in vascular permeability, angiogenesis, capillary occlusion, electrolyte changes, acid-base balance disturbances, immunity disorder and acceleration of catabolism may be observed. AMI is one of the events that cause stress hyperglycaemia. In-hospital mortality rate after AMI is even higher in patients with stress hyperglycaemia (8).

C-Reactive Protein (CRP) is an acute phase protein found in serum/plasma and its level increases in the inflammatory process. It is a sensitive marker whose level increases in acute/chronic inflammation and infection. It is secreted from the liver via IL-6 (9). Inflammation and thrombosis play a very important role in the pathophysiology of atherosclerosis. Platelets (PLT) and leukocytes (neutrophils) are essential components of these processes associated with the development of atherosclerosis and acute coronary syndromes. In patients with AMI and other inflammatory diseases, CRP, procalcitonin (PCT), "white blood cells count, neutrophil, lymphocyte, platelet and the ratios of these values to each other (neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR))" among complete blood count parameters are used as inflammatory markers (10, 11).

The role of trace elements in cardiovascular diseases has been the subject of many studies. High copper (Cu) and low zinc (Zn) levels have been found in patients with AMI. Iron (Fe) levels are at normal levels. A close relationship between high copper levels and haemodynamic parameters has been found. It was concluded that serum copper and zinc levels are valuable in terms of showing the degree of myocardial depression in AMI (12).

According to the literature, higher serum lactate levels indicate a greater extent of myocardial damage/necrosis due to myocardial infarction and more myocardial oedema. It has been reported that the risk of mortality may increase in AMI patients, especially in those with an initial serum lactate >2.5 mmol/L (13).

Although there are several studies on AMI and hemogram, biochemistry, serum electrolytes and inflammatory markers, there are limited data on the value of these markers in patients with AMI. We aimed to investigate the role of hemogram, biochemistry, inflammatory markers and electrolyte levels in the diagnosis and management of patients with AMI.

MATERIAL AND METHOD

It is a descriptive epidemiological study. Within the scope of the study, all patients aged 18 years and over and diagnosed with AMI in the Emergency Department and Cardiology Department of Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital between 01.01.2022 - 31.12.2022 were included retrospectively. No sample was selected within the scope of the study. The study was approved by the decision of Kahramanmaraş Sütçü İmam University Faculty of Medicine Clinical Research Ethics Committee session no: 2022/35, decision no: 03, dated 29.11.2022. The study is consistent with the principles of the Declaration of Helsinki.

Sociodemographic data such as age and gender and laboratory tests such as hemogram, biochemistry, inflammatory markers and electrolyte levels were analysed. Laboratory tests include hemogram,

biochemistry, routine inflammatory markers, C-reactive protein (CRP), procalcitonin, complete blood count parameters, white blood cell count (WBC), neutrophils, lymphocyte, neutrophil lymphocyte ratio, platelet (PLT), platelet lymphocyte ratio, zinc, copper, magnesium, sodium, potassium, calcium, chlorine, phosphate, lactate, pH and glucose levels.

The study's data were statistically evaluated using the SPSS v.23.0 package application (SPSS Inc, Chicago, Illinois, USA). Descriptive statistics, such as frequency and percentage for qualitative data and frequency, mean, and standard deviation for numerical data, were provided for reviewing the study's data. Utilizing both analytical (Kolmogorov Smirnov and Shapiro Wilks tests) and visual (histogram) techniques, the parameters' adherence to a normal distribution was assessed. If parametric assumptions were satisfied, one group t test, student t test, and one-way analysis of variance (ANOVA) were used in the comparison of quantitative data for parameters with a given mean, parameters between two groups, and parameters between more than two groups. For comparisons of parameters with a specific mean, Mann-Whitney U test was utilized if parametric assumptions were not met. Whitney Parameter comparisons between two groups were conducted using the U test, while comparisons involving more than two groups were conducted using the Kruskall Wallis test. To compare qualitative data, the Chi-Square test was applied. The statistical significance level was set at $p<0.05$.

RESULTS

A total of 66 participants were included in the study, of which 59.1% (n=39) were male and 40.9% were female. While 24.2% (n=16) of the participants were between the ages of 65-74, 33.3% (n=22) were over 75 years old. 42.4% (n=28) of the participants who had MI were under the age of 65 (Table 1).

The mean leukocyte count of the patients who applied to the emergency department and had MI was 10.32 (SD: 2.8), and the mean neutrophil count was 7.32 (SD: 2.9). The leukocyte and neutrophil levels of the patients were found to be statistically significantly higher than the normal individuals ($p<0.001$ and $p<0.001$, respectively) (Table 2).

The mean glucose level of the patients who had MI was 173.49 (SD:92.0) and the mean lactate level was 11.39 (SD:8.9). Glucose and lactate levels of the patients were found to be statistically significantly higher than normal individuals ($p<0.001$ and $p<0.001$, respectively) (Table 2).

Some acute phase reactant levels of the participants were examined. The mean c reactive protein value of the participants was 16.62 (SD: 29.4) and the mean procalcitonin level was determined as 0.08 (SD: 0.8). C-reactive protein and procalcitonin levels were found to be statistically significantly higher in patients diagnosed with MI compared to normal individuals ($p=0.002$ and $p=0.022$, respectively) (Table 2).

The mean immature granulocyte level of MI patients admitted to the emergency department was found to be 0.05 (SD:0.05). Although the relevant value was found to be higher than the normal limits, the difference was not statistically significant ($p=0.767$). On the other hand, the mean platelet-lymphocyte ratio of the patients was found to be 170.6 (SD:144.0) and although this value was higher than the normal limits, it did not create a statistically significant difference ($p=0.74$). Other values in the study were within the range of normal values in the literature (Table 2).

The changes in the laboratory values of MI patients admitted to the emergency department by gender were examined. The mean percentage of immature granulocytes was determined as 0.43 (SD:0.49) in men and 0.48 (SD:0.32) in women. The mean percentage of immature granulocytes in women was statistically significantly higher than in men ($p=0.048$). The mean of procalcitonin was determined as 0.095 (SD: 0.10) in men and 0.061 (SD: 0.059) in women. The mean procalcitonin level in men was statistically significantly higher than in women ($p=0.035$) (Table 3).

The pH values of the venous blood gases taken from the patients in the emergency room were checked. The mean pH value was found to be 7.42 (SD:0.02) in men and 7.35 (SD:0.08) in women. The mean pH level in men was statistically significantly higher than in women ($p=0.038$). There was no statistically significant difference between the genders in terms of other parameters (Table 3).

DISCUSSION

Markers have a role in determining the disease process, in diagnosis and follow-up, in determining susceptibility to disease and in determining the appropriateness of specific treatments. Cardiac markers are fragments of cellular structures released into the circulation when myocardial damage occurs. Currently, biomarkers frequently used in the diagnosis of acute coronary syndrome are creatine kinase-MB (CK-MB), myoglobin and cardiac troponins. Various new markers are being investigated in order to diagnose acute coronary syndrome at an early stage and to provide the necessary intervention. We will review the literature by analysing hemogram, biochemistry, inflammatory markers and electrolyte levels in patients with acute myocardial infarction.

Studies have shown that individuals with AMI had significantly lower mean Na, K, and Mg levels and significantly higher mean Ca levels (4, 5, 6, 7). In our study, calcium readings were close to the top limit of

Table 1: Sociodemographic characteristics of AMI patients admitted to the emergency department

		n	%
Gender			
	Female	27	40.9
	Male	39	59.1
	Total	66	100
Age			
	25 – 44	5	7.6
	45 – 64	23	34.8
	65 – 74	16	24.2
	75 – 84	19	28.8
	85 and above	3	4.5
Total		66	100

Table 2: Hemogram, biochemistry, inflammatory markers and electrolyte levels of AMI patients admitted to emergency department

	n	Mean ± SS	Normal Values*	p
WBC (10^9/L)	66	10.32 ± 2.8	3.39 – 8.86	<0,001a
Neutrophil (10^9/L)	66	7.32 ± 2.9	1.5 – 5	<0,001b
Percent neutrophils (%)	66	69.72 ± 13.2	40.1 – 71.4	-
Lymphocyte (10^9/L)	66	2.17 ± 1.2	1.05 – 3.17	-
Lymphocyte percentage (%)	66	21.89 ± 11.1	21.6 – 49	-
Platelet (10^9/L)	66	257.85 ± 67.3	150 – 400	-
IG (#)	66	0.05 ± 0.05	0.01 – 0.04	0.767
IG percentage (%)	66	0.45 ± 0.42	0.16 – 0.62	-
NLR (%)	66	5.28 ± 5.7	0.91 – 5.6	-
PLR (%)	66	170.6 ± 144.0	40 - 140	0.740
Glucose (mg/dL)	66	173.49 ± 92.0	74 – 100	<0,001b
CRP (mg/L)	58	16.62 ± 29.4	<5	0.002b
PCT (µg/L)	58	0.08 ± 0.08	<0.046	0.022b
Albumin (g/L)	66	40.87 ± 5.2	39.7 – 49.4	-
K (mmol/L)	66	4.42 ± 0.7	3.5 – 5.5	-
Ca (mg/dL)	65	8.99 ± 0.8	8.6 – 10	-
Na (mmol/L)	66	137.79 ± 3.1	132 – 146	-
Mg (mg/dL)	66	1.89 ± 0.3	1.6 – 2.6	-
Cu (µg/dL)	49	90.79 ± 26.9	70 – 140	-
Zn (µg/dL)	53	76.41 ± 27.7	50 – 150	-
pH	14	7.38 ± 0.07	7.35 – 7.45	-
Lactate (mmol/L)	43	11.39 ± 8.9	<2	<0,001b

Ca: calcium, CRP: c-reactive protein, Cu: copper, İG: immature granulocyte, K: potassium, Mg: magnesium, Na: sodium, NLR: neutrophil lymphocyte ratio, PCT: procalcitonin, PLR: platelet lymphocyte ratio, SS: standard deviation, WBC: white blood cell count, Zn: zinc
** Related variables were compared with normal values in the literature. When compared with normal values, parameters increasing with MI were compared with the upper normal limit and parameters decreasing with MI were compared with the lower normal limit. No correlation was observed for parameters within normal limits.*
a T-test in one group
b Wilcoxon Signed Rank Test

the reference range, whereas potassium, sodium, and magnesium values were close to the lower limit. The readings for copper and zinc were also discovered to be within the usual range. Although the electrolyte results of some of our patients were similar to the literature, this situation is not similar to the literature when the total number is considered. The reason for this may be the small number of patients in our study. Serum electrolyte levels should be checked during the diagnosis and follow-up of AMI patients with cardiac-specific biomarkers. Changes in serum electrolyte levels, especially Mg, can be used in the follow-up of AMI patients. Serum electrolyte levels may support cardiac-specific biomarkers in the diagnosis of AMI.

Inflammation markers are nonspecific in cardiac diseases, but when combined with cardiac markers, they are reported to provide useful diagnostic information in the diagnosis of ACS in the emergency department (9). Studies have demonstrated that increased CRP levels independently indicate cardiac damages (9). Leukocytes are part of the increased inflammatory process associated with increased cardiovascular risk and mortality in myocardial infarction patients. Low lymphocyte counts have been associated with increased cardiovascular events in patients with coronary artery disease. Increased PLR may lead to increased inflammatory and atherothrombosis response as a result of increased cytokine response. In cardiovascular diseases, PLR and NLR appear to be simple and applicable markers used to evaluate the inflammatory status (10, 11). Hemogram and inflammatory markers were also examined in our study. WBC, neutrophil, procalcitonin and CRP ratios were found to be significantly higher in patients with AMI. Although platelet/lymphocyte ratios were high, no significance was found. Routine hemogram examination in patients with AMI will both accelerate the diagnostic process and support the diagnosis.

Studies have shown that stress hyperglycaemia during AMI, especially in non-diabetic patients, impairs the pump function of the heart and thus leads to an increase in mortality due to heart failure. Patients with stress hyperglycaemia are also at increased risk of other cardiovascular events. Stress hyperglycaemia has been shown to be an independent predictive value in addition to smoking, hypertension, hyperlipidaemia and body mass index which are known risk factors of coronary artery disease (8). In our study, glucose values measured at the

Table 3: Hemogram, biochemistry, inflammatory markers and electrolyte levels of AMI patients admitted to emergency department according to gender

	Gender						
	Female			Male			
	n	Average	SS	n	Average	SS	p
WBC (10^9/L)	27	10.2	2.7	39	10.41	2.8	0.757a
Neutrophil (10^9/L)	27	7.34	2.9	39	7.31	2.9	0.958b
Percent neutrophils (%)	27	70.73	14.1	39	69.03	12.6	0.611a
Lymphocyte (10^9/L)	27	2.14	1.4	39	2.19	1.1	0.379b
Lymphocyte percentage (%)	27	21.92	12.1	39	21.87	10.6	0.986a
Platelet (10^9/L)	27	261.37	71.7	39	255.41	65.0	0.739b
IG (#)	27	0.053	0.048	39	0.048	0.063	0.078b
IG percentage (%)	27	0.48	0.32	39	0.43	0.49	0.048b
NLR (%)	27	5.70	6.7	39	4.99	4.9	0.784b
PLR (%)	27	183.73	155.1	39	161.53	137.1	0.351b
Glucose (mg/dL)	27	201.85	107.4	39	153.85	75.0	0.063b
CRP (mg/L)	25	11.90	10.8	33	20.20	37.7	0.603b
PCT (µg/L)	27	0.061	0.059	31	0.095	0.10	0.035b
Albumin (g/L)	27	40.0	4.4	39	41.48	5.6	0.059b
K (mmol/L)	27	4.34	0.8	39	4.47	0.7	0.231b
Ca (mg/dL)	27	9.02	0.55	38	8.97	0.88	0.645b
Na (mmol/L)	27	137.78	3.41	39	137.80	2.94	0.829b
Mg (mg/dL)	27	1.86	0.27	39	1.92	0.25	0.313b
Cu (µg/dL)	20	96.27	19.5	29	87.02	30.73	0.093b
Zn (µg/dL)	24	67.79	23.07	29	83.55	29.45	0.051b
pH	8	7.35	0.08	6	7.42	0.02	0.038b
Lactate (mmol/L)	22	11.80	10.2	21	10.96	7.6	0.865b

Ca: calcium, CRP: c-reactive protein, Cu: copper, İG: immature granulocyte, K: potassium, Mg: magnesium, Na: sodium, NLR: neutrophil lymphocyte ratio, PCT: procalcitonin, PLR: platelet lymphocyte ratio, SS: standard deviation, WBC: white blood cell count, Zn: zinc
a The p value found using Student's t test
b The p value found using the Mann - Whitney U test

time of stress were found to be high (hyperglycaemia) in patients with AMI; our glucose values were similar to the literature. AMI causes stress hormones secreted during stress with emotions such as stress/anxiety, fear of death, etc. We think that this clinical condition also increases blood glucose. Patients with AMI should have their blood glucose levels monitored, and if clinically appropriate, examinations and therapies for hyperglycemia should start without delay.

Serum lactate level has been reported to be a prognostic factor in patients with AMI (13, 14). In our study, serum lactate levels of patients with AMI were found to be significantly higher. The lactate levels of our patients with AMI are similar to the literature. Therefore, serum lactate levels should be monitored in these patients to reduce the spread of myocardial damage.

CONCLUSION

There are changes in hemogram, biochemistry, serum electrolyte and inflammatory marker levels in AMI patients. The levels of these markers should also be controlled during the diagnosis and follow-up of AMI patients with cardiac-specific biomarkers. We believe that hemogram, biochemistry, inflammatory markers and electrolyte levels may contribute to the prediction of early serious complications in patients with acute myocardial infarction. There is a need for further studies on the importance of markers to be used in the diagnosis and prognosis of AMI patients.

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REFERENCES

1. AHA Statistical Update Heart Disease and Stroke Statistics. A Report From the American Heart Association. 2012 Update.
2. AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association

Joint Committee on Clinical Practice Guidelines. 2022 Update.
3. Bassand JP, Christian WH, Diego A, Eric B. ST Segment Yükselmesi Olmayan Akut Koroner Sendromların Tanı ve Tedavi Kılavuzu. European Heart Journal. 2007; 28: 1598–1660. doi:10.1093/eurheartj/ehm161
4. Macdonald JE, Struthers AD. What is the optimal serum potassium level in cardiovascular patients? J Am Coll Cardiol. 2004 Jan 21;43(2):155-61. doi: 10.1016/j.jacc.2003.06.021.
5. Young B, Lin H, Mc Cabe RD. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology. 1995: 68(4); 825.
6. Eisner D, Bode E, Venetucci L, Trafford A. Calcium flux balance in the heart. J Mol Cell Cardiol. 2013: 58; 110–7.
7. Cohen HW, Hailpern SM, Alderman MH. Sodium intake and mortality follow-up in the Third National Health and Nutrition Examination Survey (NHANES III). J Gen Intern Med. 2008; 23: 1297–1302.
8. Murat K, Çiğdem E, Nizameddin K. Stres Hiperglisemisinin Akut Miyokard Enfarktüsünün Prognozuna Etkisinin Değerlendirilmesi. Metabolik Sendrom Derneği: XVII. Metabolik Sendrom Sempozyumu; 24-28 Kasım 2020, SS-09.
9. Zeynep A, Yusuf T. Acute Coronary Syndrome and Cardiac Markers. İnönü Üniversitesi Sağlık Bilimleri Dergisi. 2016: 5(1); 67-73
10. Özmen Ç, Akray A, İltaş A, Özmen Yıldız P, Yıldız İ, Aktaş H. "Primer perkütan koroner girişim uygulanan ST-segment yükseklikli miyokard infarktüslü hastalarda platelet/lenfosit oranı ile no-reflow oluşumu arasındaki ilişki". Cukurova Medical Journal. 2021: 46; 1441-1448.
11. Boyacı F, Akçay M, Gökdeniz T. Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratio in Predicting Chronic Total Occlusion in ST-Segment Elevation Myocardial Infarction. Harran Üniversitesi Tıp Fakültesi Dergisi. 2022; 19(2): 277-283.
12. Coşkun A, Soysal D, Kılavuz A, Yalçın H, Atay A, Ildız B, et al. İdiopatik dilate kardiyomyopati ve akut myokard infarktüsünde serum bakır, çinko ve demir düzeylerinin hemodinamik parametrelerle ilişkisi. Medical Network Klinik Bilimler ve Doktor. 1997; 3(1): 46-50.
13. Park IH, Cho HK, Oh JH, Chun WJ, Park YH, Lee M, et al. Clinical Significance of Serum Lactate in Acute Myocardial Infarction: A Cardiac Magnetic Resonance Imaging Study. J Clin Med. 2021 Nov 13;10(22):5278. doi: 10.3390/jcm10225278.
14. Chebl RB, Tamim H, Dagher GA, Sadat M, Enezi FA, Arabi YM. Serum Lactate as an Independent Predictor of In-Hospital Mortality in Intensive Care Patients. J Intensive Care Med. 2020; 35 :1257–1264. doi: 10.1177/0885066619854355.

CASE REPORT

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Pansitopeni ile Başvuran Bir Akut Bruselloz Olgusu

A Case of Acute Brucellosis Presenting with Pancytopenia

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ABSTRACT

Brucellosis is a zoonotic disease that is endemic to our country and can cause hematological involvement. Hematological involvements may be seen due to hypersplenism or bone marrow involvement during the course of the disease. In this case report, it was aimed to bring to the literature a case who applied to the hospital with complaints of low back pain and sweating and was found to have pancytopenia as a result of the examinations. A diagnosis of acute brucellosis was made in the patient with splenomegaly who developed fever in the follow-up. Hematological parameters improved with brucellosis treatment. In this case report; we aimed to emphasize that brucellosis should be considered in the differential diagnosis of hematological diseases.

ÖZET

Bruselloz ülkemiz için endemik olan ve hematolojik tutulumlara da yol açabilen zoonotik bir hastalıktır. Hastalık seyri sırasında gelişen hipersplenizme veya kemik iliği tutulumuna bağlı olarak hematolojik tutulumlar görülebilir. Bu olgu sunumunda bel ağrısı ve terleme şikayetleri ile hastaneye başvuran ve yapılan tetkikleri sonucunda pansitopeni saptanan olgunun literatüre kazandırılması amaçlandı. Splenomegalisi olan, takibinde ateş yüksekliği gelişen hastaya akut bruselloz tanısı konuldu. Bruselloz tedavisi ile hematolojik parametreleri düzeldi. Bu olgu sunumunda; hematolojik hastalıkların ayırıcı tanısında brusellozun düşünülmesi gerektiğini vurgulamayı amaçladık.

Keywords:
Brucellosis
Pancytopenia
Leukopenia
Anemia
Thrombocytopenia

Anahtar Kelimeler:
Bruselloz
Pansitopeni
Lökopeni
Anemi
Trombositopeni

GİRİŞ

Bruselloz, özellikle Akdeniz ülkelerinde ve Orta Doğu'da endemik olan, dünya çapında en yaygın bakteriyel zoonozdur (1). Dünya Sağlık Örgütü'ne (DSÖ) göre, dünya çapında her yıl 500.000'den fazla bruselloz olgusu saptanmaktadır (2). Bruselloza boyutları 0,61 ile 1,5 µm arasında değişen küçük, Gam negatif kokobasil olan Brucella spp. cinsi bakteriler neden olur. Küresel olarak en sık ve şiddetli enfeksiyonlardan sorumlu olan türü B. melitensis'tir ve bunu B. abortus, B. suis ve B. canis izler (2).

Bruselloz, çok çeşitli klinik bulgulara neden olabilir, hatta multisistemik tutulum yapan tüm hastalıkları taklit edebilir. Bu hastalık, retiküloendotelyal sistemi tuttuğundan spesifik olmayan çok çeşitli hematolojik anormalliklere de neden olabilir. Dalak ve kemik iliği sıklıkla etkilenir ve bu etki, kan yaymasında hipoplaziye neden olabilir. Lökopeni ve anemi sık görülen bulgular iken, trombositopeni daha nadir saptanır. Brusellozda pansitopeni ise oldukça nadir görülen bir klinik tablodur (3).

Bu olgu sunumunda, pansitopeni ile başvuran, akut bruselloz tanısı alan ve bruselloz tedavisi ile tamamen düzelen bir hastayı literatüre kazandırmayı amaçladık.

OLGU

Özgeçmişindediyabetes mellitus öyküsü bulunan ve oral antidiyabetik ilaçlarla tedavi gören 63 yaşındaki şehir merkezinde ikamet eden erkek hasta, 3 haftadır olan ve ağrı kesicilere cevap vermeyen bel ağrısı ve ara ara olan terleme şikâyetleri ile hastanemize başvurdu. Fizik muayenede genel durumu iyi, vital bulguları olağan olan hastanın lomber bölgede palpasyonla ağrı mevcuttu. Batın muayenesinde splenomegali dışında özelliği yoktu. Kardiyak ve pulmoner oskültasyon normaldi. Hastanın motor ve nörolojik defisiti yoktu. Yapılan labaratuvar tetkiklerinde; Hemoglobin (Hb): 8,6 g/dl, trombosit: 83000 hc/ml ve beyaz kan sayımı (WBC): 2775/mm3 (%55 nötrofil, %42 nötrofil) ile pansitopeni tespit edildi. Laktat dehidrojenaz (LDH): 559 U/L, C reaktif protein (CRP): 7,9 mg/dl olarak bulundu. İleri tetkik için Enfeksiyon hastalıkları yataklı servisine yatış yapıldı. Ayırıcı tanı amaçlı istenen idrar kültürü sterildi ve Hepatit B, Hepatit C ve Human Immunodeficiency Virus / İnsan Bağışıklık Yetmezliği Virüsü (HIV) viral serolojilerinin tümü negatifti. Vitamin B12 ve folik asit seviyeleri normaldi. Periferik yaymada atipik hücre saptanmadı. Batın ultrasonografisinde karaciğerde basit kistik yapı mevcuttu ve dalak 148 mm ile normalden büyüktü; bu bulgu haricinde başka anormal bulguya rastlanmadı. Bel ağrısı tarifleyen hastadan istenen vertebral manyetik rezonans görüntülemede (MRG) lomber disk hernisi dışında patoloji saptanmadı. Yatışı sırasında ondülan ateş seyri saptanan hastadan tekrar ayrıntılı anamnez alındı. Hasta yaklaşık 3-4 ay önce pastörize edilmemiş süt tükettiğini

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bildirdi. Ateş yüksekliği nedeniyle 2 şişe kan kültürü alındı. Bruselloz ekartasyonu için istenen Rose Bengal testi (BioMerieux® Fransa) pozitifti. Brucella Serum Aglütinasyon (Wright) test titresi 1/160 pozitif olarak saptandı. Hastada mevcut sonuçlar değerlendirilerek akut bruselloza bağlı pansitopeni teşhisi konuldu. Kan kültüründe üreme saptanmadı. Rifampisin (900 mg/gün) ve doksisiklin (200 mg/gün) ile 6 haftalık antibiyotik tedavisinden sonra tam kan sayımı normale döndü (Hb: 12,6 g/dl, trombosit: 162.000 hc/ml, WBC: 6500/mm3).

TARTIŞMA

Türkiye'den yayınlanan çalışmalarda bruselloz hastalarının %4,9-9'unda pansitopeni olduğu bildirilmiştir (3-6). Olgumuzda aşikâr lökopeni, anemi ve trombositopeni mevcuttu ve bu tablo pansitopeni olarak değerlendirildi. 6 haftalık tedavi sonrası kan tablosu düzeldi ve pansitopeni geriledi.

İnsanlara brusella bulaşı, enfekte hayvanlara doğrudan temas (deri, enfekte hayvansal materyallere temas veya inhalasyon) sonucu olabilir. Ayrıca kontamine ürünlerin yenmesinden sonra gıda yoluyla dolaylı olarak bulaş da mümkündür (1). Sunulan olguda olası bulaş yolu enfekte sütün tüketilmesi olarak düşünüldü.

Brusellozda akut enfeksiyon seyri sırasında, ondülan ateş, titreme, eklem ve kas ağrısı, terleme gibi tipik şikayetler olabilir. Ancak hastalığın çok farklı klinik sunumları olabilir (3,7,8). Özellikle analjezik ve antipiretiklerin kullanılması, kısmi antibiyotik tedavileri nedeniyle ateş seyrinde ondülan ateş görülme sıklığı azalmıştır. Bel ağrısı, miyalji, atralji, artrit, spondilit, spondilodiskit gibi çok çeşitli osteoartiküler tutulumlar en sık tutulumlardır (9). Sunulan olguda da bel ağrısı mevcuttu, ancak lomber MRG'de lomber disk hernisi dışında tutulum saptanmadı. Bruselloz olgularının yaklaşık %20-40'ında splenomegali görüldüğü bildirilmekle beraber, pansitopenisi olan olgularda %86-88 oranında splenomegali saptandığı bildirilmiştir. Bu hastalardaki hipersplenizmin pansitopeniye neden olabileceği savunulmuştur (3,10). Olgumuzda da hipersplenizme bağlı pansitopeni geliştiği düşünülmektedir. Ancak bruselloza bağlı kemik iliği tutulumu da benzer klinik tabloya sebep olabilir; olguda kemik iliği örneklemesi yapılmadığı için net ayrım yapılamadı.

Brusellozda pansitopeni dahil hematolojik tutulumların antimikrobiyal tedavi ile tamamen düzeldiği bildirilmiştir (3-6,10). Sunulan olguda da benzer şekilde 6 haftalık bruselloz tedavisi ile hastamızın pansitopenisi düzeldi.

SONUÇ

Ülkemiz bruselloz açısından endemik bölgedir. Brusellozda pansitopeni dahil hematolojik tutulumların olabileceği unutulmamalıdır ve hematolojik malignitelerin ayırıcı tanısında bruselloz tanısı da yer almalıdır. Pansitopenili hastalarda anamnez dikkatle alınmalı, epidemiyolojik veriler göz önünde bulundurulmalı ve bruselloz için tetkik edilmelidir.

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KAYNAKLAR

1. Galińska EM, Zagórski J. Brucellosis in humans etiology, diagnostics, clinical forms. Ann Agric Environ Med. 2013;20(2):233-238.
2. WHO. Brucellosis. Erişim tarihi: 01 Mayıs 2022. [Erişim: https://www.who.int/news-room/fact-sheets/detail/brucellosis]
3. Özlü C. Brucellosis from hematology perspective. Dental and Medical Journal - Review. 2022; 4(1): 72-78.
4. Kaya S, Elaldi N, Deveci O, Eskazan AE, Bekcibasi M, Hosoglu S. Cytopenia in adult brucellosis patients. Indian J Med Res 2018;147(1):73-80.
5. Bilek H, Alanbayı Ü, Bal T. Pansitopeni ve Hepatit ile Başvuran Akut Bruselloz Vakası. Dicle Med J. 2018; 45 (1):103-107.
6. Ben Lahlou Y, Benaissa E, Maleb A, Chadli M, Elouennass M. Pancytopenia revealing acute brucellosis. IDCases. 2020;23: e01037. doi: 10.1016/j.idcr.2020.e01037.
7. Alkan Çeviker S, Dindar Demiray EK. A Case of Acute Brucellosis that Presenting With Cutaneous Manifestations. Biotech&Strategic Health Res. 2020; 4(2): 184-187.
8. Alkan S, Dindar Demiray EK, Tarhan N, Önder T. A case of Brucella pyelonephritis: a rare case. Iberoam J Med. 2022;4(2):113-117. doi: 10.53986/ibjm.2022.0012
9. Özlü A. Brucellosis: A perspective from physical therapy and rehabilitation specialist. D J Med Sci. 2021;7(3):323-326.
10. Bektaş MS, Okur M, Aktar F, Temel H, Başaranoğlu M. Akut Brusellozlu Bir Olguda Pansitopeni. Türkiye Çocuk Hastalıkları Dergisi. 2013; 7(3): 145-146.

CASE REPORT

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A Rare Case of Increase in Seizure Frequency After COVID19

Nadir Bir Olgu: COVİD19 Sonrası Nöbet Sıklığında Artış

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ABSTRACT

Tuberous sclerosis complex (TSC) is a rare genetic disease and affected individuals are usually characterized by the triad of cutaneous angiofibroma, mental retardation and epileptic seizures. Different clinical tables may occur due to the inflammatory response after COVID19. Apart from this, there is no article in the literature reporting that the frequency of seizures has increased as stated in the case example presented. A 30-year-old male patient was brought to our emergency room by his relatives with the complaint of epileptic seizures. Relatives of the patients stated that the frequency of seizures increased progressively after having COVID19 a month ago and that he had seizures 10 times in the last 24 hours. As seen in the case we presented, there may be an increase in the frequency of seizures in the late period after COVID19 in patients with epilepsy. For this reason, patients with an increased seizure frequency by emergency medicine physicians should also be evaluated for COVID19.

ÖZET

Tüberoskleroz Kompleksi (TSK) nadir görülen bir genetik hastalıktır ve etkilenen bireyler genellikle epileptik nöbetler, mental retardasyon ve kutanöz anjiyofibroma üçlüsü ile karakterize edilir. COVID19 sonrası inflamatuar yanıta bağlı olarak farklı klinik tablolar ortaya çıkabilir. Bunun dışında literatürde sunulan vaka örneğinde belirtildiği gibi nöbet sıklığının arttığını bildiren bir makale bulunmamaktadır. 30 yaşında erkek hasta epileptik nöbet şikayeti ile yakınları tarafından acil servisimize getirildi. Hasta yakınları, bir ay önce COVID19 geçirdikten sonra nöbet sıklığının giderek arttığını, son 24 saatte 10 kez nöbet geçirdiğini ifade etti. Bizim olgumuzda da görüldüğü gibi epilepsi tanılı hastalarda COVID19 sonrası geç dönemde nöbet sıklığında artış olabilir. Bu nedenle acil tıp hekimleri tarafından nöbet sıklığında artış tanımlayan hastaların COVID19'a yönelik de değerlendirilmesi gerekmektedir.

Keywords:
Complications
COVID19
Drug resistant epilepsy
Epileptic seizure
Tuberous sclerosis complex

Anahtar Kelimeler:
Komplikasyonlar
COVID19
İlaca dirençli epilepsi
Epileptik nöbet
Tüberoskleroz kompleksi

INTRODUCTION

Tuberous sclerosis complex (TSC) is a rare hereditary disease that can affect almost all systems. Its prevalence has been reported to be between 1/6000 and 1/10 000 live births in recent studies (1). Affected individuals are usually characterized by the triad of cutaneous angiofibroma, mental retardation and epileptic seizures seen in the early stages of life; however, less than 30% of TSC patients have this triad while 6% have none of these features (2).

Renal complications and seizure are the most common causes of increased morbidity and mortality in TSC patients compared to the normal population (3,4).

It is indicated that seizures may develop in the acute infectious period in patients with a diagnosis of COVID19. However, only one case has been described of developing status epilepticus after having COVID19. The possible mechanism is thought to be triggered by refractory status epilepticus secondary to the postinfectious inflammatory response. Different clinical tables may occur due to the inflammatory response after COVID19. Isolated symptoms related to the affected organ system can be observed, especially due to systemic or local cytokine increase. Apart from this, there is no article in the literature reporting that the frequency of seizures has increased as stated in the case example presented (5).

In this case report, a 30-year-old patient who had COVID19 a month ago and then presented to the emergency room with the complaint of an increase in the frequency of epileptic seizures and was diagnosed with TSC was evaluated.

CASE REPORT

A 30-year-old male patient was brought to our emergency room by his relatives with the complaint of epileptic seizures which occurred approximately 10 times in the last twenty-four hours. His seizures were in a self-terminating form, lasting two to three minutes. It was learned that the patient had a history of epilepsy and mental retardation, used valproic acid and olanzapine regularly. Relatives of the patients stated that the frequency of seizures, which was once or twice a year, increased progressively to once or twice a day after having COVID-19 a month ago. There was no feature in his family history. His parents did not have a chronic disease or consanguineous marriage. There were no pathological symptoms in his vital signs.

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On physical examination, he had confused consciousness, his cooperation and orientation were limited, pupils were isochoric, indirect and direct light reflexes were bilaterally positive, successful in localizing painful stimuli in all four extremities, and plantar reflexes were bilaterally flexor. In his dermatological examination, there were hypopigmented macules on the back and forehead; Plaques with raised skin, rough surface, and irregular edges, consistent with shagreen patch, in the 3rd-5th rib space on the left thorax and the left lumbar region (Image 1), tiny, erythematous, symmetrically located papules compatible with adenoma sebaceum, a type of angiofibroma, around the nose, cheeks, and chin (Image 2). Routine biochemistry and hemogram tests were normal in the laboratory examination. In contrast-enhanced brain magnetic resonance imaging (MRI), cortical and mild nodular T2 signal increases were observed at the level of high convexity, in the right frontal, parafalcine area, and lateral peripheral level, consistent with the cortical tuber, which is accepted as cortical dysplasia (Image 3). There was no pathological image in the brain computed tomography (CT) and chest CT. In the echocardiography performed by the cardiology specialist, an image compatible with rhabdomyoma, which is the cardiac involvement of the TSC, was not observed. In the urinary system ultrasonography performed by the radiology specialist, an image of angiomyolipoma, cyst, or mass, which is compatible with the renal involvement of TSC, was not observed. In the examination performed by an ophthalmologist, the anterior and posterior segments were assessed as normal. The patient was given phenytoin 750 mg intravenously at a previous hospital before being referred to our hospital. The patient was hospitalized with consultation with the neurology department. After seizure control was achieved, the patient was discharged with the recommendation to continue the same treatment.

DISCUSSION

Mutation in one of the TSC2 or TSC1 genes causes hyperactivation in the mTOR pathway results in the development of hamartomas or benign tumors in many organ systems, including the kidneys, heart, eyes, brain and skin (3, 6).

The criteria for clinical diagnosis of the disease were redefined in 2012 by the International TSC Consensus Group (Table 1) (1).

Hypomelanotic macules are seen in approximately 66.7-97.2%, facial angiofibroma in approximately 57.3-74.5%, and shagreen patches in approximately 22.7-48.1% of patients which are the skin symptoms of TSC (3). While these symptoms were also present in our patient, other skin symptoms were not present.

One of the central nervous system symptoms of TSC, subependymal nodules are seen in approximately 78.2% of patients, while cortical tubers are seen in approximately 88.2% of patients (3). In our patient, there was no subependymal nodule while cortical tubers were present. While seizures affect approximately 62% to 93% of TSC patients, cortical dysplasias have been associated with these seizures and learning difficulties (4, 7).

Our patient had 4 major symptoms including hypomelanotic macules, shagreen patches, angiofibroma, and cortical dysplasia, which are among the major diagnostic criteria,

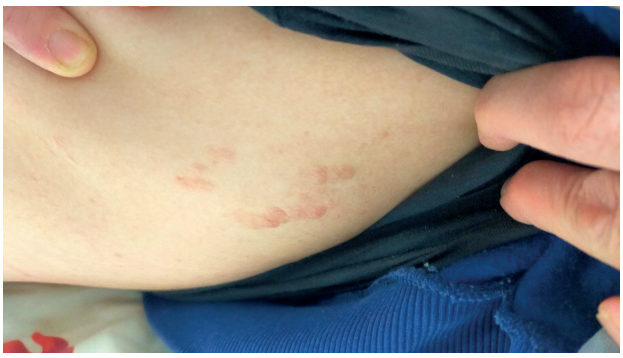

Figure 1: Plaques with raised skin, rough surface, and irregular edges, consistent with shagreen patch (Written consent was obtained from the legal guardian of the patient)

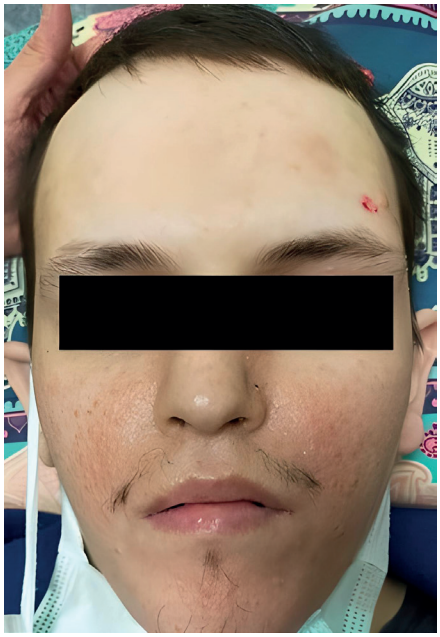

Figure 2: Adenoma sebaceum, a type of angiofibroma, around the nose, cheeks, and chin (Written consent was obtained from the legal guardian of the patient)

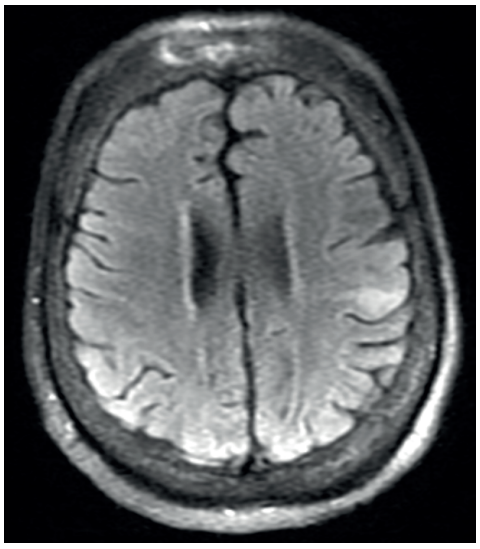

Figure 3: Cortical tuber, which is accepted as cortical dysplasia

Table 1: Criteria for the clinical diagnosis of tuberous sclerosis complex

Major Symptoms	Minor Symptoms
1. Hypomelanotic macules (≥3; at least 5 mm diameter)	1. Confetti skin lesions
2. Angiofibromatous (≥3) or fibrous cephalic plaques	2. Numerous pits in tooth enamel
3. Ungual fibroma (≥2)	3. Intraoral fibroma
4. Shagreen patch	4. Hypopigmented patch on the retina
5. Multiple retinal hamartomas	5. Multiple kidney cysts
6. Cortical dysplasias	6. Extrarenal hamartoma
7. Subependymal nodules	7. Sclerotic bone lesions
8. Subependymal giant cell astrocytomas	
9. Rhabdomyoma of the heart	
10. Lymphangioleiomyomatosis (LAM)*	
11. Angiomyolipoma (≥2) *	
Definitive Diagnosis: 2 major factors or 1 major and ≥2 minor factor	
PossibleDiagnosis: 1 major or ≥ 2 minor factors	

**The presence of lymphangioleiomyomatosis or angiomyolipoma alone is sufficient for a definitive diagnosis.*

and he met the definitive diagnostic criteria.

Various treatment options are available for TSC-related epilepsy and infantile spasms such as antiepileptic drugs, hormone therapy, ketogenic diets, epilepsy surgery and vagus nerve stimulation (4). However, one-third of these patients become resistant to seizures treatments. Drug-Resistant Epilepsy (DRE) carries a significant cognitive, economic and social burden. Therefore, it is necessary to identify risk factors that increase the likelihood of drug-resistant seizures (8). In our case, the possible factor that increased the frequency of seizures and made them resistant was COVID19 infection.

In most studies, it is stated that DRE is proportional to the number of cortical tubers. The presence of epileptiform discharges in EEG increases the risk of resistant seizures. Most of the risk factors cannot be changed, but early recognition of refractory seizures and initiation of appropriate treatment before clinical seizures become more frequent reduces the risk of resistant seizures (8).

Early and resistant seizures have been associated with poor neurological outcomes. Aggressive seizure control can reduce the harmful neurodevelopmental effects of epilepsy. Antiepileptic drugs and steroids and classical can be used for treatment, and seizures can be ceased with everolimus, an mTOR inhibitor. It is stated that cannabinoids may be generally safe and effective for treatment-resistant seizures in children and adults with severe early-onset epilepsy (9).

CONCLUSION

Our case was newly diagnosed with TSC in the emergency department and the increase in seizure frequency was evaluated in relationship with COVID19 infection. For this reason, it is necessary to evaluate especially the dermatological symptoms of patients who apply to the emergency department with the complaint of epileptic seizures and have a history of mental retardation, and besides the diagnosis of TSC should be considered in the differential diagnosis by emergency medicine physicians. As seen in the case we presented, there may be an increase in the frequency of seizures in the late period after COVID19 in patients with epilepsy. For this reason, patients with an increased seizure frequency by emergency medicine physicians should also be evaluated for COVID19.

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REFERENCES

1. Northrup H, Aronow ME, Bebin EM, Bissler J, Darling TN, de Vries PJ, et al. Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations. Pediatr Neurol. 2021; 123: 50-66. DOI: 10.1016/j.pediatrneurol.2021.07.011.
2. Seibert D, Hong CH, Takeuchi F, Olsen C, Hathaway O, Moss J, et al. Recognition of tuberous sclerosis in adult women: delayed presentation with life-threatening consequences. Ann Intern Med. 2011; 154(12): 806-813. DOI: 10.7326/0003-4819-154-12-201106210-00008.
3. Zöllner JP, Franz DN, Hertzberg C, Nabbout R, Rosenow F, Sauter M, et al. A systematic review on the burden of illness in individuals with tuberous sclerosis complex (TSC). Orphanet J Rare Dis. 2020; 15(1): 23. DOI: 10.1186/s13023-019-1258-3.
4. Nabbout R, Belousova E, Benedik MP, Carter T, Cottin V, Curatolo P, et al. Epilepsy in tuberous sclerosis complex: Findings from the TOSCA Study. Epilepsia Open. 2018; 4(1): 73-84. DOI: 10.1002/epi4.12286.
5. Carroll E, Neumann N, Aguero-Rosenfeld ME, Lighter J, Czeisler BM, Melmed K, et al. Post–COVID-19 inflammatory syndrome manifesting as refractory status epilepticus. Epilepsia. 2020; 61(10): e135-e139. DOI: 10.1111/epi.16683.
6. Salussolia CL, Klonowska K, Kwiatkowski DJ, Sahin M. Genetic Etiologies, Diagnosis, and Treatment of Tuberous Sclerosis Complex. Annu Rev Genomics Hum Genet. 2019; 20: 217-240. DOI: 10.1146/annurev-genom-083118-015354.
7. Northrup H, Krueger DA. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 Iinternational Tuberous Sclerosis Complex Consensus Conference. Pediatr Neurol. 2013; 49(4): 243-254. DOI: 10.1016/j.pediatrneurol.2013.08.001.

8. Miszewska D, Sugalska M, Józwiak S. Risk Factors Associated with Refractory Epilepsy in Patients with Tuberous Sclerosis Complex: A Systematic Review. J Clin Med. 2021; 10(23): 5495. DOI: 10.3390/jcm10235495.
9. Curatolo P, Nabbout R, Lagae L, Aronica E, Ferreira JC, Feucht M, et al. Management of Epilepsy Associated with Tuberous Sclerosis Complex: Updated Clinical Recommendations. Eur J Paediatr Neurol. 2018; 22(5): 738-748. DOI: 10.1016/j.ejpn.2018.05.006.

IMAGE PRESENTATION

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Diz Lateralinin Avülsiyon Kırığı: Segond Kırığı

Avulsion Fracture of the Lateral Knee: Segond Fracture

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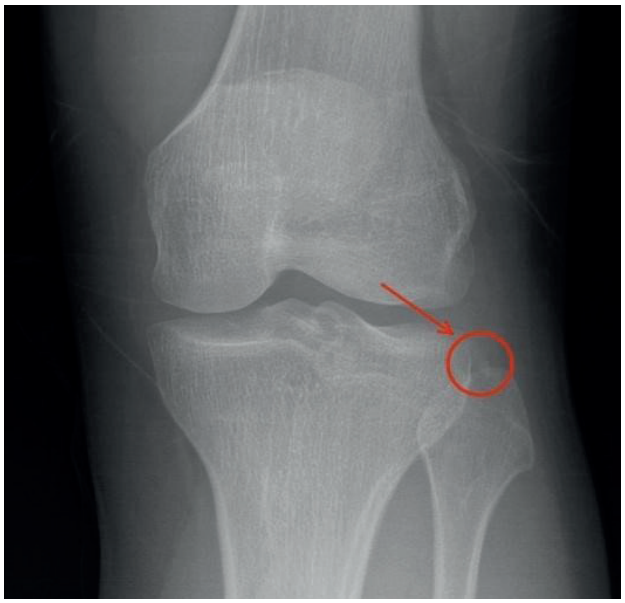
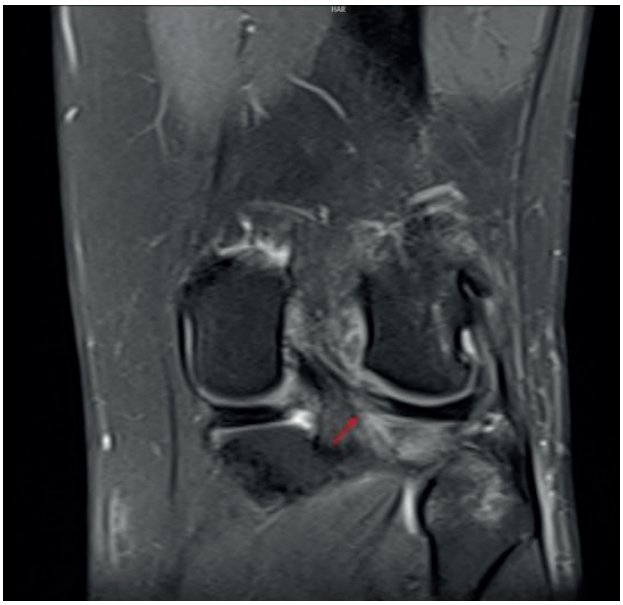


Şekil 1: Diz lateralinde avülsiyon kırığı (segond kırığı) izlenmektedir.



Şekil 2: Anterior cruciate ligament yırtığı.

Acil servise 26 yaşında erkek hasta motosiklet kazası geçirmesi nedeniyle başvurdu. Hasta motosiklet ile birlikte sol tarafına doğru düştüğünü, sol bacağının motosikletin altında sıkıştığını ve sol dizinin döndüğünü belirtti. Başvuruda sol dizine yük veremediği, dizini hafif fleksiyonda ve diz hareket açıklığında tuttuğu görüldü. Bilinci açık, oryantasyon ve kooperasyonu tam olan hastanın vital bulguları olağandı. Fizik muayenede sol dizde ekimoz veya deformite olmaksızın hassasiyet ve diz içinde efüzyon tespit edildi. Diz eklem hareket açıklığı 0-85 derece, hareket arkının tüm derecelerinde ağrısı mevcuttu. Hastanın, patellarinstabilite olmaksızın, tibia platosu lateralinde noktasal hassasiyeti mevcuttu. Ön çekmece testi ağrılı olduğundan yapılamayan hastada Lachmann testi pozitif idi. Dizde ödemli ve ağrı olması sebebi ile pivot shift testi de yapılamadı. Diğer tüm sistemik fizik muayene bulguları normal olan hastanın ek şikâyet veya patolojik bulgusu bulunmamaktaydı. Hastanın yük vermeden çekilen sol diz anteroposterior radyografisinde lateralde bir avülsiyon kırığı tespit edildi (Şekil 1) ve Segond kırığı tanısı kondu. Hastanın diğer sistem muayenelerinde ve tetkiklerinde patoloji saptanmadı. Çekilen sol diz manyetik rezonans görüntülemesinde (MRI), sol ACL de total rüptür olduğu tespit edildi. (Şekil 2) Hastaya erken cerrahi planlandı.

Segond kırığı klasik olarak tibial plato seviyesinin hemen altında, proksimaltibianınlateralinde oluşan avülsiyon kırığı olarak tanımlanmaktadır (1). Genellikle dizin rotasyonu sırasında oluşan travmalarda daha sık görülür ve kompleks diz yaralanmalarında Segond kırığı, anterior cruciate ligament (ACL) yırtığı için patognomik bir bulgudur (2). ACL yaralanması olan hastaların %75-100'üne Segond kırığının eşlik ettiği görülmüştür (3). ACL ile birlikte, lateral kapsül veya lateral menisküs yırtılması ile ilişkilidir ve kronik anterolateral diz instabilitesine neden olabilmesi açısından önemlidir (4). Segond kırığının tanısı direkt radyografi ile konulur iken MRI ile de kemik ödemi görülür ve dizin ligamanları değerlendirilir. Aynı zamanda direkt radyografiye nazaran daha az oranda da olsa Segond kırığının tanısı MRI ile de konulabilir (5).

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KAYNAKLAR

1. Shaikh H, Herbst E, Rahnemai-Azar AA, Bottene Villa Albers M, Naendrup JH, Musahl V, et al. The Segond Fracture Is an Avulsion of the Anterolateral Complex. Am J Sports Med. 2017 Aug;45(10):2247-2252. doi: 10.1177/0363546517704845.
2. Ferretti A, Monaco E, Wolf MR, Guzzini M, Carli A, Mazza D. Surgical Treatment of Segond Fractures in Acute Anterior Cruciate Ligament Reconstruction. Orthop J Sports Med. 2017 Oct;5(10):2325967117729997.
3. Campos JC, Chung CB, Lektrakul N, Pedowitz R, Trudell D, Yu J, Resnick D. Pathogenesis of the Segond fracture: anatomic and MR imaging evidence of an iliotibial tract or anterior oblique band avulsion. Radiology. 2001 May;219(2):381-6. doi: 10.1148/radiology.219.2.r01ma23381. PMID: 11323461.
4. Goldman AB, Pavlov H, Rubenstein D. The Segond fracture of the proximal tibia: a small avulsion that reflects major ligamentous damage. AJR Am J Roentgenol. 1988;151:1163e1167.
5. Porrino, J., Maloney, E., Richardson, M., Mulcahy, H., Ha, A., &Chew, F. S. (2015). The Anterolateral Ligament of the Knee: MRI Appearance, Association Withthe Segond Fracture, and Historical Perspective. American Journal of Roentgenology. 204(2), 367–373. doi:10.2214/ajr.14.12693.

LETTER TO EDITOR

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Akut Kalp Yetmezliğinde Eşlik Eden Akciğer Enfeksiyonu Dilemması

Dilemma of Lung Infection Associated with Acute Heart Failure

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Sayın editör

Derginizin 2022 yılı ikinci sayısında yayınlanan Akça ve arkadaşları tarafından hazırlanan "Pandeminin Dilemması: İlaç Yan Etkisi mi? Ya COVID-19'sa?" isimli yazıyı büyük bir ilgi ile okuduk. Yazarlara ve editöriyel kurula klinik sorunu tartışan bu ilgi çekici yazıdan dolayı teşekkür ederiz (1). Biz de bu yazımızda pnömoni ve özellikle SARS-CoV-2 pnömonisi ile ayırt etmede klinisyenleri zorlayan bir diğer antite olan akut kalp yetmezliğine değinmek isteriz.

Ateş ve diğer nonspesifik inflamasyon belirtileri ve bulguları akut kalp yetmezliği ile acil servise başvuran hastalarda görülebilmektedir (2). Benzer inflamasyon bulguları akciğer enfeksiyonlarında da görülmektedir. Akut kalp yetmezliği kliniği ile birlikte ateş de dâhil olmak üzere sistemik inflamasyon belirtileri olan ve antibiyotik tedavisine başlanması gereken hastaları belirlemek çözümlenmemiş bir klinik ikilemdir. Bakteriyel pnömoni ve özellikle SARS-CoV-2 pnömonisi bu konuda önemli bir endişe kaynağıdır. Akut kalp yetmezliği hastalarına ait toraks konvansiyonel grafileri ve bilgisayarlı tomografileri genel olarak alveolar veya interstisyel ödem ile birlikte plevral efüzyonu gösterir; bunların tümü, eşlik eden pnömoniye bağlı infiltratları maskeleyebilir veya taklit edebilir. Ek olarak, pulmoner konjesyon hem viral hem de bakteriyel pnömoni ihtimalini artırır. Bunula birlikte yalnızca bakteriyel pnömoniler antibiyoterapi gerektirir. Klinisyenlere klinik uygulamada enfeksiyonun varlığı veya yokluğuna ilişkin önemli bir tanısal belirsizlikle karşı karşıya kalmaktadır (3). Özellikle hemodinamik olarak stabil olmayan akut kalp yetmezliği kliniğinde, eşlik eden Pnömosepsis dışlanamadığından; kültür sonuçları ve PCR sonucu gibi tetkiklerin sonuçlanması saatler ve günler sürebildiği ve sepsis kılavuzlarının erken antibiyotik uygulama önerilerinden dolayı klinisyenlere güvenli alanda kalabilmek adına acil serviste erken antibiyoterapiyi hemen her hastaya başlamaktadır.

Akut kalp yetmezliği hastalarının değerlendirilmesinde Stevenson, hastalar klinisyen tarafından tahmin edilen hacim durumuna (ıslak/kuru) ve perfüzyon durumuna (sıcak/soğuk) göre kategorize edilmesini önermiştir (Tablo1). Bu klinik yaklaşıma göre hastalar bir dört gözlü tabloda kliniğine en uygun alana yerleştirilir ve klinik yaklaşım ilgili alana uygun planlanır. Juguler venöz distansiyon, hepatojuguler reflü, ortopne, bendopne (Hasta bir sandalyeye oturur, belini büker ve ayaklarına dokunur. Eğilmeden sonraki 30 saniye içinde dispne meydana gelirse, bendopne mevcut kabul edilir.) gibi klinik bulgular kalp yetmezliği ile ilişkilendirilir (4). Ateş, öksürük, balgam gibi klinik belirtileri olan hastalarda fizik muayene sırasında oskültasyonda ral veya bronşial seslerin duyulması perküsyonda matite alınması pnömoni açısından klinik tanı konulması için yeterlidir. Ancak bu bulguların olmaması pnömoniyi dışlamak için yeterli değildir (5). Özellikle hemodinamisi bozulmuş hastalarda ayırıcı tanıda yatak başı ultrasonografi acil servis pratiğinde gün geçtikçe daha fazla yer tutmaktadır. Lokalize B çizgileri daha çok pnömoni veya lokalize konjesyon lehine değerlendirirlerken yaygın B çizgileri sıklıkla kalp yetmezliği lehine

Tablo 1: Kalp yetmezliği olan hastanın klinik değerlendirmesi

		Konjesyon bulguları Artmış juguler venöz dolgunluk, abdominojüguler reflü, S3, ödem, assit, ral	
		Yok	**Var**
Kötü perfüzyon bulguları Soğuk ekstremiteler, pulsus alternans, daralmış nabız basıncı, bozulmuş renal fonksiyon, artmış laktat	**Yok**	Sıcak / kuru A Beta bloker, ACE inhibitörü, Diüretik	Sıcak / yaş B İntravenöz diüretik (Loop, tiazid)
	Var	Soğuk /kuru L Temelde volüm eksiği söz konusu Volüm replasmanı ± inotrop, ± diüretik	Soğuk /yaş C Dekompanse kalp yetmezliği, kardiyojenik şok İnotrop, O2 desteği, mekanik destek

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değerlendirilmektedir. Bununla birlikte pek çok çalışma yaygın B çizgilerinin görüldüğü klinik senaryoda yatak başı ultrasonografinin pnömoniyi dışlamak için yeterli olmadığını raporlamaktadır (6).

Bu ikilemde klinisyenleri zorlayan bir diğer durum akut kalp yetmezliğine sistemik yanıt olarak verilen akut faz yanıtıdır. Literatürde akut kalp yetmezliğinde akut faz reaktan yüksekliğinden ilgili intrensek spesifik bir inflamatuar süreç sorumlu olabileceği raporlanmıştır. Milo ve arkadaşları, akut kalp yetmezlikli bazı hastalarda interlökin 6 düzeylerinin 2 aylık takipte yüksek kaldığını göstermişlerdir (7).

Akut kalp yetmezliğindeki akut faz reaktan yüksekliği için literatürde önerilen bir diğer mantıklı açıklamada mezenterik hipoperfüzyon teorisidir. Akut kalp yetmezlikli hastalarda bakteriyel endotoksin ve enflamatuar sitokin seviyelerinin invaziv olarak değerlendirildiği bir çalışmada, sol ventriküle kıyasla, hepatik venlerde daha yüksek endotoksin seviyesi olduğu ortaya konulmuştur. Bu durum araştırmacılara akut kalp yetmezliğinde bağırsakta kan akışında azalmanın (mezenterik hipoperfüzyon) bakteriyel veya endotoksin translokasyonu ile sonuçlandığını düşündürdü. Bulgular akut kalp yetmezliği şiddetinin mezenterik hipoperfüzyonla, bağırsaktan kan akışına bakteriyel veya endotoksin translokasyonunun boyutuyla ve akut faz reaktanı seviyeleri ile ölçülen sistemik inflamatuar yanıtın boyutuyla ilişkili olduğu hipotezini ortaya çıkardı (8). Yukarıda izah edilen her iki akut faz reaktan yanıtı mekanizması klinisyenlerin ikilemini daha içinden çıkılmaz bir hale sokmaktadır.

Sonuç olarak; özellikle hemodinamik olarak stabil olmayan akut kalp yetmezliği kliniğinde, erken antibiyotik gerekliliği kararı acil serviste klinisyenlere için bir ikilemdir. Bu karara katkı sağlayacak ve kolaylaştıracak yaygın olarak bulunan, güvenilir ve ucuz parametrelerin keşfi ve araştırmacıların bu alanda çalışma yapmaya teşvik edilmesi önemlidir.

KAYNAKLAR

1. Akça A, Alkan S, Önder T, Güçlü Kayta SB, Vurucu S, Yüksel C. Pandeminin Dilemması: İlaç Yan Etkisi mi? Ya COVID-19'sa? Phnx Med J. 2022; 4(2): 90-91. DOI: 10.38175/phnx.1033918.
2. Özdemir S, Özkan A. RDW and pro-BNP in predicting short-term mortality in geriatric patients presenting to the emergency department with acute decompensated heart failure. Emergency Care Journal. 2022; 18(4): 10747. doi:10.4081/ecj.2022.10747
3. Mueller C, Laule-Kilian K, Christ A, Brunner-La Rocca HP, Perruchoud AP. Inflammation and long-term mortality in acute congestive heart failure. Am Heart J. 2006 Apr;151(4):845-50. doi: 10.1016/j.ahj.2005.06.046.
4. Thibodeau JT, Drazner MH. The Role of the Clinical Examination in Patients With Heart Failure. JACC Heart Fail. 2018 Jul;6(7):543-551. doi: 10.1016/j.jchf.2018.04.005.
5. Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA. 1997 Nov 5;278(17):1440-5.
6. Hacquin A, Putot S, Barben J, Chagué F, Zeller M, Cottin Y, et al. Bedside chest ultrasound to distinguish heart failure from pneumonia-related dyspnoea in older COVID-19 patients. ESC Heart Fail. 2020 Dec;7(6):4424-4428. doi: 10.1002/ehf2.13017.
7. Milo O, Cotter G, Kaluski E, Brill A, Blatt A, Krakover R, et al. Comparison of inflammatory and neurohormonal activation in cardiogenic pulmonary edema secondary to ischemic versus nonischemic causes. Am J Cardiol. 2003 Jul 15;92(2):222-6. doi: 10.1016/s0002-9149(03)00545-9.
8. Peschel T, Schönauer M, Thiele H, Anker SD, Schuler G, Niebauer J. Invasive assessment of bacterial endotoxin and inflammatory cytokines in patients with acute heart failure. Eur J Heart Fail. 2003 Oct;5(5):609-14. doi: 10.1016/s1388-9842(03)00104-1.

LETTER TO EDITOR

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Prognostic Value of SCUBE-1 in Ischemic Stroke

SCUBE-1 in İskemik İnmede Prognostik Değeri

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Dear editor

SCUBE-1 is a newly identified cell surface protein identified during early embryogenesis. SCUBE-1 is known to be involved in the angiogenesis mechanism. SCUBE-1 was first detected in human umbilical vein endothelial cells, so it was said that it originates and is secreted from the vascular endothelium. It is also found in organs and tissues with high vascularization such as kidney, brain, lung, spleen and liver (1).

In addition to embryonic expression, SCUBE-1 is also known to be expressed from endothelium and platelets. In recent studies, it has been shown that it is also secreted from platelets and is a platelet-derived protein. SCUBE-1 is stored in alpha granules of inactive platelets. When platelets are activated by thrombin, SCUBE-1 expression is enhanced and they are secreted as small, soluble particles from the platelet surface (2). It plays a role in platelet agglunitation and activation. It has been shown in the literature that SCUBE-1 levels increase in oxidative stress conditions such as ischemic events, mesenteric ischemia, testicular torsion, pulmonary embolism, cancer diseases, cardiopulmonary arrest and acute coronary syndrome (3).

Stroke was defined by the World Health Organization in 1988 as a focal or global impairment of cerebral function lasting longer than 24 hours or until death without an obvious non-vascular cause. This historically important definition is a general description that includes all stroke types (4). The definition was updated by the American Heart Association in 2013 as a period of neurological dysfunction due to focal cerebral, spinal, or retinal infarction. ischemic stroke; In the "Global Burden of Disease Study 2019" published in 2021, it is still the second most common cause of death in the world and the third most common cause of combined death and disability (5). In our country, the incidence of stroke has been reported as 177 per 100,000 and its prevalence as 254 per 100,000. It is estimated that about 132,000 people have a stroke each year (6).

It has been suggested in the literature that SCUBE-1 can be used as a biomarker in ischemic stroke in which the thromboembolic process plays a key role (7-9). In the first study, Dai et al. compared the SCUBE-1 level of 40 ischemic stroke patients with 40 healthy volunteers, and reported an increased SCUBE-1 level in ischemic stroke (7). Türkmen et al. reported that SCUBE-1 could be used as a biomarker in ischemic stroke in their experimental study with 24 female Sprague Dawley rats (8). Bolayır et al. showed that SCUBE-1 could predict ischemic brain volume in 35 ischemic stroke and 35 control patients and that SCUBE-1 could be a prognostic biomarker in ischemic stroke (9).

In conclusion, SCUBE-1 is promising as a biomarker in ischemic stroke. However, due to the single-center nature of the studies in the literature and their small sample size, their evidence value is low. Researchers should be encouraged to investigate the prognostic value of SCUBE-1 in ischemic stroke.

REFERENCES

1. Sonmez E, Turkdogan KA, Karabacak M, Civelek C, Yilmaz C, Ozer OF, et al. The diagnostic role of signal peptide-C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein 1 in non-ST-elevation acute coronary syndrome. Am J Emerg Med. 2015 Jan;33(1):21-4.
2. Özkan A, Sönmez E, Özdemir S, Özer ÖF, Muharrem N, Gülen B, et al. The Diagnostic Value of SCUBE1 in Unstable Angina Pectoris Patients. Eurasian J Emerg Med. 2016;15:167-171.
3. Yılmaz C, Gülen B, Sönmez E, Akbay D, Söğüt Ö, Özdemir S, et al. Serum SCUBE-1 Levels and Return of Spontaneous Circulation Following Cardiopulmonary Resuscitation in Adult Patients. Avicenna J Med. 2022 Sep 5;12(3):148-153.
4. Özdemir S, Cimilli Öztürk T, Ecmel Onur Ö. Relationship between the national institutes health stroke scale score and bispectral index in patients with acute ischemic stroke. J Exp Clin Med. 2021; 38(4): 440-4.
5. Santomauro DF, Melen S, Mitchison D, Vos T, Whiteford H, Ferrari AJ. The hidden burden of eating disorders: an extension of estimates from the Global Burden of Disease Study 2019. Lancet Psychiatry. 2021 Apr;8(4):320-328.
6. Yigit M, Sogut O, Yigit E, Turkdogan KA, Kaplan O, Dur A, et al. The relationship between anemia and recurrence of ischemic stroke in patients with Trousseau's syndrome: A retrospective cross-sectional study. Turk J Emerg Med. 2016 May 9;16(2):65-68.
7. Dai DF, Thajeb P, Tu CF, Chiang FT, Chen CH, Yang RB, et al. Plasma concentration of SCUBE1, a novel platelet protein, is elevated in patients with acute coronary syndrome and ischemic stroke. J Am Coll Cardiol. 2008 Jun 3;51(22):2173-80.
8. Turkmen S, Eryigit U, Karaca Y, Mentese A, Sumer UA, Yulug E, et al. Diagnostic value of plasma signal peptide-Cub-Egf domain-containing protein-1 (SCUBE-1) in an experimental model of acute ischemic stroke. Am J Emerg Med. 2015 Feb;33(2):262-5.
9. Bolayır A, Gökçe ŞF, Çiğdem B, Bolayır HA, Gülünay A, Çelik VK, et al. Can SCUBE1 be used to predict the early diagnosis, lesion volume and prognosis of acute ischemic stroke? Turk J Biochem. 2018;44:16-24.

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LETTER TO EDITOR

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Karbonmonoksit Zehirlenmesi İlişkili Hiperlaktatemi

Carbon Monoxide Poisoning Associated Hyperlactatemia

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Derginizin 2023 yılı ilk sayısında yayınlanan Acar ve Ertekin tarafından hazırlanan "Acil Serviste SII ve SIRI değerlerinin CO Zehirlenmesinin Şiddetini Tahmin Etmedeki Rolü" isimli yazıyı büyük bir ilgi ile okuduk (1). Yazarlara ve editoryal kurula, karbonmonoksit (CO) zehirlenmelerinde literatürde son dekatta tanımlanmış olan sistemik immün inflamasyon indeksi, sistemik inflamatuar cevap indeksi ve sistemik inflamasyon toplam indeksi gibi kombine hematolojik indekslerin, CO zehirlenmesi şiddeti ile ilişkisini tartışan yazıdan dolayı teşekkür ederiz. Bununla birlikte yazarların şiddetli zehirlenmeyi tanımlamak için kullandıkları hiperlaktateminin patogenezi ve CO zehirlenmesinde hemodinamik etkilenme ile ilgili, yazının tartışmasına katkı sunacak birkaç noktayı da belirtmek isteriz.

Acar ve Ertekin'in çalışmasında laktat düzeyi yüksek olan hastalarda artmış inflamasyon belirteç düzeyleri gösterilmişti (1). Literatürde artan serum laktatı, CO zehirlenmesinin neden olduğu doku hipoksisine bağlı anaerobik glikoliz ile ilişkilendirilmiştir. CO, hemoglobine yarışmalı bağlanarak hemoglobinin oksijen taşıma kapasitesini düşürür. İlk olarak bu etki sonucunda oksihemoglobin ayrışma eğrisi sola kayar ve dokuya oksijen sunumu azalır. CO'in diğer bir etkisi ise, periferik oksijen kullanımını da etkilemesidir (2). CO'in yaklaşık %10-15'i ekstravasküler alana dağılır ve bu alanda NADPH redüktaz, sitokromlar ve miyoglobin gibi biyomoleküllere bağlı olarak bulunur. Bu ikinci mekanizma ile de CO, mitokondriyal seviyede oksidatif fosforilasyonda bozulmaya neden olur ve glikolizin anaerobik yolağa kaymasına neden olur (3). Bununla birlikte laktat, CO zehirlenmesinde doku hipoksisi sonucu oluşmakla birlikte, hücre aracılı enflamasyon veya aerobik glikoliz aracılı bir ürün de olabilir. Bir diğer mekanizma ise CO, nöbet, hiperventilasyon ve kardiyak disfonksiyonun dahil olduğu karmaşık bir mekanizmanın etkilerinden kaynaklanabilir. Tonik klonik nöbetlerde metabolik faaliyet artma ve beraberinde solunum eforunun gerçekleştirilememesine bağlı anaerobik glikoliz ve hiperlaktatemi bildirilmiştir (4). CO zehirlenmesine sekonder nöbet geçiren hastalarda, hiperlaktatemiye nöbetin katkısı olabileceği söylenebilir. Hemodinamin etkilenmesi üzerinden hiperlaktatemiyi açıklayacak bir mekanizma ise CO'nun kardiyotoksik etkileridir. CO, sitokrom C üzerinden kardiyak fonksiyonları olumsuz etkiler. Artmış tromboza meyil ile koroner arterlerde tıkanıklık ve/veya koroner vazospazm ile miyokart kanlanmasını ve kalbin pompa fonksiyonunu da baskıladığı gösterilmiştir (5). Tüm kardiyak etkiler düşünüldüğünde hiperlaktatemiye miyokart fonksiyon bozukluğunun neden olması ile birlikte doku perfüzyon bozukluğu komponetinin de katkısı olabileceği söylenebilir.

KAYNAKLAR

1. Acar T, Ertekin B. Acil Serviste SII ve SIRI değerlerinin CO Zehirlenmesinin Şiddetini Tahmin Etmedeki Rolü. Phnx Med J. 2023;5(1):23-31.
2. Sert ET, Kokulu K, Mutlu H. Clinical predictors of delayed neurological sequelae in charcoal-burning carbon monoxide poisoning. Am J Emerg Med. 2021 Oct;48:12-17.
3. Özdemir S, Altunok İ, Eroğlu SE. Karbon monoksit zehirlenmesi laktat ve kardiyak belirteç ilişkisi. Van Tıp Derg. 2019; 26(3): 285-8.
4. Diler Y, Ozdemir S, Altunok I, Eroglu SE. Relationship between seizures and metabolic acidosis: a prospective observational study. Front Emerg Med. 2022;6(2):e20.
5. Ozdemir S, Alper B, Alp H, Aksel G, Doğanay F. Carbon Monoxide Poisoning and Sequels of Cardiac Function. Phnx Med J. 2022; 4(2): 94-95.

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