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AMAÇ VE KAPSAM

Türkiye Parazitoloji Dergisi (Turkiye Parazitol Derg), Türk Parazitoloji Derneği'nin çift-kör hakemli, açık erişimli bilimsel yayın organıdır. Dergi Mart, Haziran, Eylül ve Aralık aylarında olmak üzere üç ayda bir yayınlanır ve dört sayıda bir cildi tamamlanır. Yayın dili Türkçe ve İngilizce'dir.

Türkiye Parazitoloji Dergisi; tıp, veterinerlik ve biyoloji alanlarında parazitoloji konulu klinik ve deneysel araştırma makaleleri, olgu sunumları, derleme ve editöre mektup türünde yayınladığı yüksek bilimsel standartlara sahip makalelerle uluslararası literatüre katkı sunmaktadır.

Derginin hedef kitlesi, tıbbi ve veteriner parazitoloji alanlarında ve biyoloji bilim dalının ilgili birimlerinde çalışan tüm bilim insanları ve bu alanlardaki yüksek lisans öğrencileridir.

Derginin editöryel ve yayın süreçleri International "Committee of Medical Journal Editors (ICMJE)", "World Association of Medical Editors (WAME)", "Council of Science Editors (CSE)", "Committee on Publication Ethics (COPE)", "European Association of Science Editors (EASE)" ve "National Information Standards Organization (NISO)" organizasyonlarının kılavuzlarına uygun olarak biçimlendirilir. Türkiye Parazitoloji Dergisi, "Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice)" ilkelerini benimsemiştir.

Türkiye Parazitoloji Dergisi, PubMed/MEDLINE, BIOSIS-Zoological Record, BIOSIS Previews Biological Abstracts, CABI Abstracts and Bibliographic Databases, SCOPUS, Embase ve TÜBITAK ULAKBİM TR Dizin tarafından indekslenmektedir.

Makale değerlendirme ve yayın işlemleri için yazarlardan ücret talep edilmemektedir. Tüm makaleler http://turkiyeparazitolderg.org/tr/Anasayfa sayfasındaki online makale değerlendirme sistemi kullanılarak dergiye gönderilmelidir. Derginin yazım kurallarına, gerekli formlara ve dergiyle ilgili diğer bilgilere web sayfasından erişilebilir.

Derginin tüm masrafları Türkiye Parazitoloji Derneği tarafından karşılanmaktadır. Basılı kopyalarda tıbbi ilaç, malzeme ve cihaz üreticilerinin reklamları yayınlanabilir. Reklam vermek isteyenlerin Editöryel Ofis ile iletişime geçmeleri gerekmektedir. Reklam görselleri sadece Baş Editör onayı ile yayınlanmaktadır.

Dergide yayınlanan makalelerde ifade edilen bilgi, fikir ve görüşler Türkiye Parazitoloji Derneği, Baş Editör, Editörler, Yayın Kurulu ve Yayıncı'nın değil, yazar(lar)ın bilgi ve görüşlerini yansıtır. Baş Editör, Editörler, Yayın Kurulu ve Yayıncı, bu gibi yazarlara ait bilgi ve görüşler için hiçbir sorumluluk ya da yükümlülük kabul etmemektedir.

Yayınlanan tüm içeriğe http://turkiyeparazitolderg.org/tr/Anasayfa adresinden ücretsiz olarak erişilebilir. Basılı kopyalar Türkiye Parazitoloji Derneği üyelerine ücretsiz olarak dağıtılır.

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Türkiye Parazitoloji Dergisi

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AIMS AND SCOPE

Turkish Journal of Parasitology (Turkiye Parazitol Derg) is the double-blind peer-reviewed, open access, international publication organ of Turkish Society for Parasitology. The journal is a quarterly publication, published on March, June, September and December and its publication languages are Turkish and English.

Turkish Journal of Parasitology aims to contribute to the international literature by publishing original clinical and experimental research articles, case reports, review articles, and letters to the editor biological, medical and veterinary parasitology.

The journal's target audience includes researchers, physicians and healthcare professionals who are interested or working on medical and veterinary parasitology, and relevant disciplines of biology, as well as PhD and MSc students studying on these topics.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

Turkish Journal of Parasitology is currently indexed in PubMed/MEDLINE, BIOSIS-Zoological Record, BIOSIS Previews Biological Abstracts, CABI Abstracts and Bibliographic Databases, SCOPUS, Embase, and TUBITAK ULAKBIM TR Index.

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system, which is available at http://turkiyeparazitolderg.org/eng/Anasayfa. The journal guidelines, technical information, and the required forms are available on the journal's web page.

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YAZARLARA BİLGİ

Türkiye Parazitoloji Dergisi (Turkiye Parazitol Derg), Türk Parazitoloji Derneği'nin çift-kör hakemli, açık erişimli bilimsel yayın organıdır. Dergi Mart, Haziran, Eylül ve Aralık aylarında olmak üzere üç ayda bir yayınlanır ve dört sayıda bir cildi tamamlanır. Yayın dili Türkçe ve İngilizce'dir.

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Özgünlük, yüksek bilimsel kalite ve atıf potansiyeli bir makalenin yayına kabulü için en önemli kriterlerdir. Gönderilen yazıların daha önce başka bir elektronik ya da basılı dergide, kitapta veya farklı bir ortamda sunulmamış ya da yayınlanmamış olması gerekir. Daha önce başka bir dergiye gönderilen ancak yayına kabul edilmeyen yazılar hakkında dergi önceden bilgilendirilmelidir. Bu yazıların eski hakem raporlarının Yayın Kuruluna gönderilmesi değerlendirme süresinin hızlanmasını sağlayacaktır. Toplantılarda sunulan çalışmalar için, sunum yapılan organizasyonun tam adı, tarihi, şehri ve ülkesi belirtilmelidir.

Türkiye Parazitoloji Dergisi'ne gönderilen tüm makaleler çift-kör hakem değerlendirme sürecinden geçmektedir. Tarafsız değerlendirme sürecini sağlamak için her makale alanlarında uzman en az iki dış-bağımsız hakem tarafından değerlendirilir. Dergi Yayın Kurulu üyeleri tarafından gönderilecek makalelerin değerlendirme süreçleri, davet edilecek dış bağımsız editörler tarafından yönetilecektir. Bütün makalelerin karar verme süreçlerinde nihai karar yetkisi Baş Editör'dedir.

Araştırmaların kabul edilen etik kurallar çerçevesinde yapıldığını temin etmek için yazarların etik uygunluk konusunda bilgi vermeleri gerekmektedir. İnsanlar üzerinde yapılan klinik ve deneysel çalışmalar, ilaç araştırmaları ve bazı olgu sunumları için "World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013, www.wma.net) çerçevesinde hazırlanmış Etik Komisyon raporu gerekmektedir. Gerekli görülmesi halinde Etik Komisyon raporu veya eşdeğeri olan resmi bir yazı yazarlardan talep edilebilir. İnsanlar üzerinde yapılmış deneysel çalışmaların sonuçlarını bildiren yazılarda, çalışmanın yapıldığı kişilere uygulanan prosedürlerin niteliği tümüyle açıklandıktan sonra, onaylarının alındığına ilişkin bir açıklama ile onay alınan etik kurul adı ve onay numarasına makalenin Yöntemler bölümünde yer verilmelidir. Hastaların kimliklerinin gizliliğini korumak yazarların sorumluluğundadır. Hastaların kimliğini açığa çıkarabilecek fotoğraflar için hastadan ya da yasal temsilcilerinden alınan imzalı izinlerin de gönderilmesi gereklidir. Hayvanlar üzerinde yapılan çalışmalar için de uluslararası etik kurallara uygunluğu gösteren komite onayı ilgili hayvan etik kurulundan alınmalıdır. Hayvanlar üzerinde yapılan çalışmalarda etik kurul onayının yanı sıra, hayvanlara ağrı, acı ve rahatsızlık verilmemesi için yapılmış olanlar açık olarak makalede belirtilmelidir.

Bütün makalelerin benzerlik tespiti denetimi, iThenticate yazılımı aracılığıyla yapılmaktadır.

Yayın Kurulu, dergimize gönderilen çalışmalar hakkındaki intihal, atıf manipülasyonu ve veri sahteciliği iddia ve şüpheleri karşısında COPE kurallarına uygun olarak hareket edecektir.

Yazar olarak listelenen herkesin ICMJE (www.icmje.org) tarafından önerilen yazarlık kriterlerini karşılaması gerekmektedir. ICMJE, yazarların aşağıdaki 4 kriteri karşılamasını önermektedir:

1. Çalışmanın konseptine/tasarımına; ya da çalışma için verilerin toplanmasına, analiz edilmesine ve yorumlanmasına önemli katkı sağlamış olmak; **VE**
2. Yazı taslağını hazırlamış ya da önemli fikirsel içeriğin eleştirel incelemelerini yapmış olmak; **VE**
3. Yazının yayından önceki son halini gözden geçirmiş ve onaylamış olmak; **VE**
4. Çalışmanın herhangi bir bölümünün geçerliliği ve doğruluğuna ilişkin soruların uygun şekilde soruşturulduğunun ve çözümlendiğinin garantisini vermek amacıyla çalışmanın her yönünden sorumlu olmayı kabul etmek.

Bir yazar, çalışmada katkı sağladığı kısımların sorumluluğunu almasına ek olarak, diğer yazarların çalışmanın hangi kısımlarından sorumlu olduğunu da teşhis edebilmelidir. Ayrıca, yazarlar birbirlerinin katkılarının bütünlüğüne güven duymalılardır.

Yazar olarak belirtilen her kişi yazarlığın dört kriterini karşılamalıdır ve bu dört kriteri karşılayan her kişi yazar olarak tanımlanmalıdır. Dört kriterin hepsini karşılamayan kişilere makalenin başlık sayfasında teşekkür edilmelidir.

Yazarlık haklarına uygun hareket etmek ve hayalet ya da lütuf yazarlığın önlenmesini sağlamak amacıyla sorumlu yazarlar makale yükleme sürecinde www.turkiyeparazitolderg.org adresinden erişilebilen Yazar Katkı Formu'nu imzalamalı ve taranmış versiyonunu yazıyla birlikte göndermelidir. Yayın Kurulu'nun gönderilen bir makalede "lütuf yazarlık" olduğundan şüphelenmesi durumunda söz konusu makale değerlendirme yapılmaksızın reddedilecektir. Makale gönderimi kapsamında; sorumlu yazar makale gönderim ve değerlendirme süreçleri boyunca yazarlık ile ilgili tüm sorumluluğu kabul ettiğini bildiren kısa bir ön yazı göndermelidir.

Türkiye Parazitoloji Dergisi; gönderilen makalelerin değerlendirme sürecine dahil olan yazarların ve bireylerin, potansiyel çıkar çatışmasına ya da önyargıya yol açabilecek finansal, kurumsal ve diğer ilişkiler dahil mevcut ya da potansiyel çıkar çatışmalarını beyan etmelerini talep ve teşvik eder.

Bir çalışma için bir birey ya da kurumdan alınan her türlü finansal destek ya da diğer destekler Yayın Kurulu'na beyan edilmeli ve potansiyel çıkar çatışmalarını beyan etmek amacıyla ICMJE Potansiyel Çıkar Çatışmaları Formu katkı sağlayan tüm yazarlar tarafından ayrı ayrı doldurulmalıdır. Editörler, yazarlar ve hakemler ile ilgili potansiyel çıkar çatışması vakaları derginin Yayın Kurulu tarafından COPE ve ICMJE rehberleri kapsamında çözülmektedir.

Derginin Yayın Kurulu, itiraz ve şikayet vakalarını, COPE rehberleri kapsamında işleme almaktadır. Yazarlar, itiraz ve şikayetleri için doğrudan Editöryel Ofis ile temasa geçebilirler. İhtiyaç duyulduğunda Yayın Kurulu'nun kendi içinde çözemediği konular için tarafsız bir temsilci atanmaktadır. İtiraz ve şikayetler için karar verme süreçlerinde nihai kararı Baş Editör verecektir.

Türkiye Parazitoloji Dergisi 'ne makale gönderen yazarlar makalelerinin telif haklarını Türkiye Parazitoloji Derneği'ne devretmeyi kabul ederler. Reddedilen makalelerin telif hakları yazarlarına geri iade edilir. Türkiye Parazitoloji Dergisi her makalenin www.turkiyeparazitolderg.org adresinden erişebileceğiniz Yayın Hakkı Devir Formu ile beraber gönderilmesini talep eder. Yazarlar, basılı ya da elektronik formatta yer alan resimler, tablolar ya da diğer her türlü içerik dahil daha önce yayınlanmış içeriği kullanırken telif hakkı sahibinden izin almalılardır. Bu konudaki yasal, mali ve cezai sorumluluk yazarlara aittir.

Dergide yayınlanan makalelerde ifade edilen görüşler ve fikirler Türkiye Parazitoloji Dergisi, Baş Editör, Editörler, Yayın Kurulu ve Yayıncı'nın değil, yazar(lar)ın bakış

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açılarını yansıtır. Baş Editör, Editörler, Yayın Kurulu ve Yayıncı bu gibi durumlar için hiçbir sorumluluk ya da yükümlülük kabul etmemektedir. Yayınlanan içerik ile ilgili tüm sorumluluk yazarlara aittir.

MAKALE HAZIRLAMA

Makaleler, ICMJE-Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (updated in December 2017 - http://www.icmje. org/icmje-recommendations.pdf) ile uyumlu olarak hazırlanmalıdır. Randomize çalışmalar CONSORT, gözlemsel çalışmalar STROBE, tanısal değerli çalışmalar STARD, sistematik derleme ve meta-analizler PRISMA, hayvan deneyli çalışmalar ARRIVE ve randomize olmayan davranış ve halk sağlığıyla ilgili çalışmalar TREND kılavuzlarına uyumlu olmalıdır.

Makaleler sadece www.turkiyeparazitolderg.org adresinde yer alan derginin online makale yükleme ve değerlendirme sistemi üzerinden gönderilebilir. Diğer ortamlardan gönderilen makaleler değerlendirilmeye alınmayacaktır.

Gönderilen makalelerin dergi yazım kurallarına uygunluğu ilk olarak Editöryel Ofis tarafından kontrol edilecek, dergi yazım kurallarına uygun hazırlanmamış makaleler teknik düzeltme talepleri ile birlikte yazarlarına geri gönderilecektir.

Yazarların; Yayın Hakkı Devir Formu, Yazar Katkı Formu ve ICMJE Potansiyel Çıkar Çatışmaları Formu'nu (bu form, tüm yazarlar tarafından doldurulmalıdır) ilk gönderim sırasında online makale sistemine yüklemeleri gerekmektedir. Bu formlara www.turkiyeparazitolderg.org adresinden erişilebilmektedir.

Başlık sayfası: Gönderilen tüm makalelerle birlikte ayrı bir başlık sayfası da gönderilmelidir. Bu sayfa;

- Makalenin Türkçe ve İngilizce başlıkları ile 50 karakteri geçmeyen kısa başlıklarını,
- Yazarların isimlerini, kurumlarını, eğitim derecelerini ve ORCID ID numaralarını,
- Finansal destek bilgisi ve diğer destek kaynakları hakkında detaylı bilgiyi,
- Sorumlu yazarın ismi, adresi, telefonu (cep telefonu dahil), faks numarası ve e-posta adresini,
- Makale hazırlama sürecine katkıda bulunan ama yazarlık kriterlerini karşılamayan bireylerle ilgili bilgileri içermelidir.

Özet: Editöre Mektup türündeki yazılar dışında kalan tüm makalelerin Türkçe ve İngilizce özetleri olmalıdır. Özgün Araştırma makalelerinin özetleri "Amaç", "Yöntemler", "Bulgular" ve "Sonuç" alt başlıklarını içerecek biçimde hazırlanmalıdır.

Anahtar Sözcükler: Tüm makaleler en az 3 en fazla 5 anahtar kelimeyle birlikte gönderilmeli, anahtar sözcükler özetin hemen altına yazılmalıdır. Kısaltmalar anahtar sözcük olarak kullanılmamalıdır. Anahtar sözcükler "National Library of Medicine (NLM)" tarafından hazırlanan "Medical Subject Headings (MeSH)" veritabanından seçilmelidir.

Makale Türleri

Özgün Araştırma: Ana metin "Giriş", "Yöntemler", "Bulgular", "Tartışma" ve Sonuç" alt başlıklarını içermelidir. Özgün *Araştırmalarla ilgili kısıtlamalar için lütfen Tablo 1'i inceleyiniz.*

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

Birimler, uluslararası birim sistemi olan International System of Units (SI)'a uygun olarak hazırlanmadır.

Editöryel Yorum: Dergide yayınlanan bir araştırmanın, o konunun uzmanı olan veya üst düzeyde değerlendirme yapan bir hakemi tarafından kısaca yorumlanması amacını taşımaktadır. Yazarları, dergi tarafından seçilip davet edilir. Özet, anahtar sözcük, tablo, **şekil**, resim ve diğer görseller kullanılmaz.

Derleme: Yazının konusunda birikimi olan ve bu birikimleri uluslararası literatüre yayın ve atıf sayısı olarak yansımış uzmanlar tarafından hazırlanmış yazılar değerlendirmeye alınır. Yazarları dergi tarafından da davet edilebilir. Bir bilgi ya da konunun klinikte kullanılması için vardığı son düzeyi anlatan, tartışan, değerlendiren ve gelecekte yapılacak olan çalışmalara yön veren bir formatta hazırlanmalıdır. Ana metin "Giriş", "Klinik ve Araştırma Etkileri" ve "Sonuç" **bölümlerini içermelidir.** *Derleme* **türündeki yazılarla** *ilgili kısıtlamalar için lütfen Tablo 1'i inceleyiniz.*

Olgu Sunumu: Olgu sunumları için sınırlı sayıda yer ayrılmakta ve sadece ender görülen, tanı ve tedavisi güç olan hastalıklarla ilgili, yeni bir yöntem öneren, kitaplarda yer verilmeyen bilgileri yansıtan, ilgi çekici ve öğretici özelliği olan olgular yayına kabul edilmektedir. Ana metin; "Giriş", "Olgu Sunumu", "Tartışma" ve Sonuç" alt başlıklarını içermelidir. *Olgu Sunumlarıyla ilgili kısıtlamalar için lütfen Tablo 1'i inceleyiniz.*

Editöre Mektup: Dergide daha önce yayınlanan bir yazının önemini, gözden kaçan bir ayrıntısını ya da eksik kısımlarını tartışabilir. Ayrıca derginin kapsamına giren alanlarda okurların ilgisini çekebilecek konular ve özellikle eğitici olgular hakkında da Editöre Mektup formatında yazılar yayınlanabilir. Okuyucular da yayınlanan yazılar hakkında yorum içeren Editöre Mektup formatında yazılarını sunabilirler. Özet, anahtar sözcük, tablo, **şekil**, resim ve diğer görseller kullanılmaz. Ana metin alt başlıksız olmalıdır. Hakkında mektup yazılan yayına ait cilt, yıl, sayı, sayfa numaraları, yazı başlığı ve yazarların adları açık bir şekilde belirtilmeli, kaynak listesinde yazılmalı ve metin içinde atıfta bulunulmalıdır.

Tablo 1: Makale türleri **için kısıtlamalar**

Makale türü	Sözcük limiti	Özet sözcük limiti	Kaynak limiti	Tablo limiti	Resim limiti
Özgün Araştırma	3500	250 (Alt başlıklı)	30	6	7 ya da toplamda 15 resim
Derleme	5000	250	50	6	10 ya da toplamda 20 resim
Olgu Sunumu	1000	200	15	Tablo yok	10 ya da toplamda 20 resim
Editöre Mektup	500	Uygulanamaz	5	Tablo yok	Resim yok

Tablolar

Tablolar ana dosyaya eklenmeli, kaynak listesi sonrasında sunulmalı, ana metin içerisindeki geçiş sıralarına uygun olarak numaralandırılmadır. Tabloların üzerinde tanımlayıcı bir başlık yer almalı ve tablo içerisinde geçen kısaltmaların açılımları tablo altına tanımlanmalıdır. Tablolar Microsoft Office Word dosyası içinde "Tablo Ekle" komutu kullanılarak hazırlanmalı ve kolay okunabilir şekilde düzenlenmelidir. Tablolarda sunulan veriler ana metinde sunulan verilerin tekrarı olmamalı; ana metindeki verileri destekleyici nitelikte olmalılardır.

Resim ve Resim Altyazıları

Resimler, grafikler ve fotoğraflar (TIFF ya da JPEG formatında) ayrı dosyalar halinde sisteme yüklenmelidir. Görseller bir Word dosyası dokümanı ya da ana

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doküman **içerisin**de sunulmamalıdır. Alt birimlere ayrılan görseller olduğunda, alt birimler tek bir görsel içerisinde verilmemelidir. Her bir alt birim sisteme ayrı bir dosya olarak yüklenmelidir. Resimler alt birimleri belli etme amacıyla etiketlenmemelidir (a, b, c vb.). Resimlerde altyazıları desteklemek için kalın ve ince oklar, ok başları, yıldızlar, asteriksler ve benzer işaretler kullanılabilir. Makalenin geri kalanında olduğu gibi resimler de kör olmalıdır. Bu sebeple, resimlerde yer alan kişi ve kurum bilgileri de körleştirilmelidir. Görsellerin minimum çözünürlüğü 300DPI olmalıdır. Değerlendirme sürecindeki aksaklıkları önlemek için gönderilen bütün görsellerin çözünürlüğü net ve boyutu büyük (minimum boyutlar 100x100 mm) olmalıdır. Resim altyazıları ana metnin sonunda yer almalıdır.

Makale içerisinde geçen tüm kısaltmalar, ana metin ve özette **ayrı ayrı** olmak üzere ilk kez kullanıldıkları yerde tanımlanarak, **kısaltma tanımın ardından parantez içerisinde** verilmelidir.

Makale içinde ve kaynaklarda geçen parazitlerin cins ve tür isimleri italik ve sadece cins isminin ilk harfi büyük olarak yazılmalıdır.

Ana metin içerisinde cihaz, yazılım, ilaç vb. ürünlerden bahsedildiğinde ürünün ismi, üreticisi, üretildiği şehir ve ülke bilgisini içeren ürün bilgisi parantez içinde verilmelidir; "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)".

Tüm kaynaklar, tablolar ve resimlere ana metin içinde uygun olan yerlerde **sırayla** numara verilerek atıf yapılmalıdır.

Özgün araştırmaların kısıtlamaları, engelleri ve yetersizliklerinden Sonuç paragrafı öncesi "Tartışma" bölümünde bahsedilmelidir.

Kaynaklar

Atıf yapılırken en son ve en güncel yayınlar tercih edilmelidir. Atıf yapılan erken çevrimiçi makalelerin DOI numaraları mutlaka sağlanmalıdır. Kaynakların doğruluğundan yazarlar sorumludur. Dergi isimleri Index Medicus/Medline/PubMed'de yer alan dergi kısaltmaları ile uyumlu olarak kısaltılmalıdır. Altı ya da daha az yazar olduğunda tüm yazar isimleri listelenmelidir. Eğer 7 ya da daha fazla yazar varsa ilk 6 yazar yazıldıktan sonra "et al" konulmalıdır. Ana metinde kaynaklara atıf yapılırken parantez içinde Arabik numaralar kullanılmalıdır. Farklı yayın türleri için kaynak stilleri aşağıdaki örneklerde sunulmuştur:

Dergi makalesi: Blasco V, Colavolpe JC, Antonini F, Zieleskiewicz L, Nafati C, Albanèse J, et al. Long-term outcome in kidney recipients from donors treated with hydroxyethylstarch 130/0.4 and hydroxyethylstarch 200/0.6. Br J Anaesth 2015; 115: 797-8.

Kitap bölümü: Sherry S. Detection of thrombi. In: Strauss HE, Pitt B, James AE, editors. Cardiovascular Medicine. St Louis: Mosby; 1974.p.273-85.

Tek yazarlı kitap: Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993.

Yazar olarak editör(ler): Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

Toplantıda sunulan yazı: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992.p.1561-5.

Bilimsel veya teknik rapor: Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

Tez: Kaplan SI. Post-hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Univ. 1995.

Yayına kabul edilmiş ancak henüz basılmamış yazılar: Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med In press 1997.

Erken Çevrimiçi Yayın: Aksu HU, Ertürk M, Gül M, Uslu N. Successful treatment of a patient with pulmonary embolism and biatrial thrombus. Anadolu Kardiyol Derg 2012 Dec 26. doi: 10.5152/akd.2013.062. [Epub ahead of print]

Elektronik formatta yayınlanan yazı: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

REVİZYONLAR

Yazarlar makalelerinin revizyon dosyalarını gönderirken, ana metin üzerinde yaptıkları değişiklikleri işaretlemeli, ek olarak, hakemler tarafından öne sürülen **öneriler**le ilgili notlarını "Hakemlere Cevap" dosyasında göndermelidir. Hakemlere Cevap dosyasında her hakemin yorumunun ardından yazarın cevabı gelmeli ve değişikliklerin yapıldığı satır numaraları da ayrıca belirtilmelidir. Revize makaleler karar mektubunu takip eden 30 gün içerisinde dergiye gönderilmelidir. Makalenin revize versiyonu belirtilen süre içerisinde yüklenmezse, revizyon seçeneği iptal olabilir. Yazarların revizyon için ek süreye ihtiyaç duymaları durumunda uzatma taleplerini ilk 30 gün sona ermeden dergiye iletmeleri gerekmektedir.

Yayına kabul edilen makaleler dil bilgisi, noktalama ve biçim açısından kontrol edilir. Yayın süreci tamamlanan makaleler, yayın planına dahil edildikleri sayıyla birlikte yayınlanmadan önce erken çevrimiçi formatında dergi web sitesinde yayına alınır. Kabul edilen makalelerin baskıya hazır PDF dosyaları sorumlu yazarlara iletilir ve yayın onaylarının 2 gün içerisinde dergiye iletilmesi istenir.

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Turkish Journal of Parasitology (Turkiye Parazitol Derg) is the double-blind peer-reviewed, open access, international publication organ of Turkish Society for Parasitology. The journal is a quarterly publication, published on March, June, September and December and its publication languages are Turkish and English.

Turkish Journal of Parasitology aims to contribute to the international literature by publishing original clinical and experimental research articles, case reports, review articles, and letters to the editor biological, medical and veterinary parasitology.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

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To ensure that the research has been conducted according to accepted ethical principles, authors should declare information on ethical compliance. For studies involving human participants, an approval of research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, www.wma.net) is required for experimental, clinical, and drug studies and for some case reports. Information on patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Methods section of the manuscript. For manuscripts concerning experimental research on animals, an approval of research protocols by an Animal Ethics Committee in accordance with international principles is required. If required, ethics committee reports or an equivalent official document will be requested from the authors. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly.

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Title page: A separate title page should be submitted with all submissions and this page should include:

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- Name(s), affiliations, highest academic degree(s) and ORCID ID's of the author(s),
- Grant information and detailed information on the other sources of support,
- Name, address, telephone (including the mobile phone number) and fax numbers, and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria.

Abstract: A Turkish and an English abstract should be submitted with all submissions except for Letters to the Editor. Submitting a Turkish abstract is not compulsory for international authors. The abstract of Original Articles should be structured with subheadings (Objective, Methods, Results, and Conclusion). Please check Table 1 below for word count specifications.

Keywords: Each submission must be accompanied by a minimum of three to a maximum of five keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html).

Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Methods, Results, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Original Articles.

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

Units should be prepared in accordance with the International System of Units (SI).

Editorial Comments: Editorial comments aim to provide a brief critical commentary by reviewers with expertise or with high reputation in the topic of the research article published in the journal. Authors are selected and invited by the journal to provide such comments. Abstract, Keywords, and Tables, Figures, Images, and other media are not included.

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Case Reports: There is limited space for case reports in the journal and reports on rare cases or conditions that constitute challenges in diagnosis and treatment, those offering new therapies or revealing knowledge not included in the literature, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Report, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Case Reports.

Letters to the Editor: This type of manuscript discusses important parts, overlooked aspects, or lacking parts of a previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a "Letter to the Editor." Readers can also present their comments on the published manuscripts in the form of a "Letter to the Editor." Abstract, Keywords, and Tables, Figures, Images, and other media should not be included. The text should be unstructured. The manuscript that is being commented on must be properly cited within this manuscript.

Table 1. Limitations for each manuscript type

Type of manuscript	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	3500	250 (Structured)	30	6	7 or total of 15 images
Review Article	5000	250	50	6	10 or total of 20 images
Case Report	1000	200	15	No tables	10 or total of 20 images
Technical Note	1500	No abstract	15	No tables	10 or total of 20 images
Letter to the Editor	500	No abstract	5	No tables	No media

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Tables

Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When mentioning parasites in the main text and references, the genus and species names must be italicized and the genus name must be written with an initial capital letter.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

References

While citing publications, preference should be given to the latest, most up-to-date publications. If an ahead-of-print publication is cited, the DOI number should be provided. Authors are responsible for the accuracy of references. Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/ MEDLINE/PubMed. When there are six or fewer authors, all authors should be listed. If there are seven or more authors, the first six authors should be listed followed by "et al." In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. The reference styles for different types of publications are presented in the following examples.

Journal Article: Rankovic A, Rancic N, Jovanovic M, Ivanović M, Gajović O, Lazić Z, et al. Impact of imaging diagnostics on the budget – Are we spending too much? Vojnosanit Pregl 2013; 70: 709-11.

Book Section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.

Books with a Single Author: Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as Author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki Öğrencilerin Beslenme Durumları, Fiziksel Aktiviteleri ve Beden Kitle İndeksleri Kan Lipidleri Arasındaki Ilişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

Manuscripts Accepted for Publication, Not Published Yet: Slots J. The microflora of black stain on human primary teeth. Scand J Dent Res. 1974.

Epub Ahead of Print Articles: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol. 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Manuscripts Published in Electronic Format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

REVISIONS

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Türkiye Parazitoloji Dergisi

TURKISH JOURNAL OF PARASITOLOGY

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Türkiye Parazitoloji Dergisi

TURKISH JOURNAL OF PARASITOLOGY

EDİTÖRDEN

2018 yılının ilk sayısını 6 özgün araştırma makalesi, 3 olgu sunumu ve 2 derleme yazısı olmak üzere 11 makale ile çıkarmaktayız.

Özgün araştırmalarda, altı yıllık bir süreçte saptanan *P. falciparum* olguları ile ilgili bir analiz, *T. vaginalis*'in genotiplendirilmesi ve *L. tropica*'nın sebep olduğu enfeksiyonlarda kullanılabilecek bir ilaç adayına ait denemeler ile balık parazitleri ve piton yılanlarındaki kan parazitlerinin durumunu belirten birer makale yer almaktadır. Olgu sunumlarında da ilginç bulacağınız üç farklı olguya detaylı olarak yer verilmiştir. Derlemelerde ise ülkemizdeki zoonotik hastalıklar irdelenmiş ve kaynaklar açısından çok zengin bir özet yapılmıştır.

Makalelerin sisteme yüklenmesi sırasında, makale materyalleri ile birlikte yüklenmesi gereken formlarla ilgili olarak sıkıntılar yaşandığı görülmektedir. Bu formların tamamı dergimizin web sayfasında "Yazım Kuralları" sekmesinde yer almaktadır. Makale yüklenirken bu formlarında eksiksiz olarak yüklenmesi makalenin işlem sürecini kısaltacağından bu konuya dikkat edilmesini belirtmek isterim.

SCI Expanded kapsamında olan dergilerde yapacağınız yayınlarda dergimizde yer alan makalelere atıf yapılmasının, dergimizin bu endekse başvuru sürecinde büyük önem taşıdığını yeniden belirtmek isterim. Bilim alanımızın en önemli unsurlarından ve bizleri güçlendiren araçlarından biri olan "Türkiye Parazitoloji Dergisi"nin bu sayısının da bilimsel çalışmalarınıza ve birikimlerinize yararlı olmasını umuyorum.

2018 yılının sağlık ve çalışkanlıkla geçmesini, dergimizin de "SCI Expanded" sürecinde önemli bir yol almasını dilerim.

Prof. Dr. Yusuf Özbel
Baş Editör

Türkiye Parazitoloji Dergisi

TURKISH JOURNAL OF PARASITOLOGY

EDITORIAL

We present you the first issue of 2018 with a total of 11 studies including 6 original research articles, 3 case reports, and 2 review.

Original research articles include studies on an analysis related to *P. falciparum* cases detected in a 6-year period, on genotyping of *T. vaginalis*, on experiments for a candidate drug that can be used for infections caused by *L. tropica*, and on the state of fish parasites and blood flukes in pythons. In case reports, three different cases, which you will find to be interesting, are presented in detail.

It has been noticed that while loading the articles on the system, some problems related to the forms that must be submitted with the article materials are encountered. All of these forms can be reached in the tab of "Instructions for Authors" on the website of our journal. I would like to emphasize on this point because complete submission of these forms while loading an article will shorten the process.

Moreover, I would like to restate that making citations from the articles in our journal for the studies that will be published in the journals included in the SCI Expanded is very important during the application process of our journal to this index. I hope that this issue of the "Turkish Parasitology Journal", which is one of the most important components of our scientific field and one of tools that strengthen us, will contribute to your scientific works and knowledge.

I wish 2018 to bring healthy and fruitful days and our journal to take a great step in the process of "SCI Expanded".

Prof. Dr. Yusuf Özbel
Chief Editor

Fırat Üniversitesi Hastanesinde Takip Edilen *P.falciparum* Sıtmalı Olguların Epidemiyolojik, Klinik ve Laboratuvar Bulgularının Değerlendirilmesi: Altı Yıllık Retrospektif Analiz

Epidemiological, Clinical, and Laboratory Evaluation of *Plasmodium falciparum* Malaria Cases Followed in Firat University Hospital: A 6-Year Retrospective Analysis

Ayşe Sağmak Tartar, Ayhan Akbulut

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ÖZ

Amaç: Sıtma, Plasmodium cinsi parazitlerin neden olduğu bir enfeksiyon hastalığıdır. Bölgemizde 2010 yılından bu yana sporadik olgu görülmemesine rağmen seyahatler ve göçler nedeniyle import sıtma olguları görülmeye devam etmektedir. Bu çalışmada Elazığ'da bir üniversite hastanesinde izlenen *Plasmodium falciparum* (*P. falciparum*)'a bağlı sıtma olguları irdelenmiştir.

Yöntemler: Ocak 2011-Ocak 2017 tarihleri arasında kliniğimizde *P. falciparum*'a bağlı sıtma tanısı ile izlenen 15 erişkin hasta epidemiyolojik, klinik, laboratuvar bulguları, tedavi ve prognoz açısından retrospektif olarak değerlendirildi. Hastaların tümüne kalın damla ve ince yayma preparatı hazırlanarak tanı konuldu.

Bulgular: On beş olgunun 14'ü (%93,3) erkek, 1'i (%6,7) kadındı. Yaş ortalaması 35,6±9,6 saptandı. Bütün hastaların endemik bölgelere seyahat öyküsü vardı. Hiçbirine düzenli kemoproflaksi uygulanmamıştı. Hastaların klinik ve laboratuar bulgularında ateş (%100), splenomegali (%86,7), hepatomegali (%26,7), lökopeni (%13,3), trombositopeni (%80), karaciğer fonksiyon testlerinde yükselme (%40), serum kreatininde artış (%13,3) saptandı.

Sonuç: Seyahat, göçler ve sıtma eradikasyon programındaki aksaklıklar nedeniyle son yıllarda import vaka sayıları artış göstermektedir. *P. falciparum*'un neden olduğu sıtma olguları ise import vakalardır. Endemik bölgelere seyahat anamnezi veren her ateşli olguda sıtma ayırıcı tanıda mutlaka düşünülmelidir. Riskli bölgelere seyahat edecek bireylere kemoproflaksi uygulanması ve kişisel korunma önlemlerinin sağlanması için seyahat öncesi eğitim programları oluşturulmalıdır.

Anahtar sözcükler: Sıtma, *P. falciparum*, seyahat ilişkili enfeksiyonlar

Geliş Tarihi: 19.06.2017 **Kabul Tarihi:** 13.12.2017

ABSTRACT

Objective: Malaria is an infectious disease caused by *Plasmodium* parasite. Sporadic cases have not been observed in Turkey since 2010, but imported malaria cases are still prevalent owing to migration. The present study aimed to evaluate *Plasmodium falciparum* malaria in patients hospitalized in our hospital.

Methods: A total of 15 adult patients (14 males and 1 female) who were diagnosed with malaria and who were managed at our clinic between January 2011 and 2017 were evaluated retrospectively for their epidemiological, clinical, and laboratory findings; treatment; and prognosis.

Results: Of the 15 cases, 14 (93.3%) were male and (6.7%), female. All patients had a history of travelling to endemic areas, and none of them undertook regular chemoprophylaxis. Fever (100%), splenomegaly (86.7%), hepatomegaly (26.7%), leukopenia (13.3%), thrombocytopenia (80%), elevated liver function tests (40%), and increased serum creatinine levels (13.3%) were found in the patients.

Conclusions: The number of import cases is increasing owing to tourism, migration, and deficiency in eradication programs. Malaria caused by *P. falciparum* is an import case in Turkey. The current study emphasizes on the necessity of providing proper education to Turkish individuals traveling to endemic areas for the purpose of work or travel and on the necessity of initiating chemoprophylaxis.

Keywords: Malaria, *P. falciparum*, travel-related infections

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GİRİŞ

Sıtma, dünyada tropikal ve subtropikal bölgelerde, Türkiye'de ise daha çok Güneydoğu Anadolu ve Doğu Akdeniz Bölgesi'nde endemik olarak görülen paraziter bir hastalıktır. Dünya Sağlık Örgütü'nün 2015 yılı verilerine göre her yıl 300-500 milyon sıtma olgusu görülmekte ve 1,5-2,7 milyon insan bu hastalıktan kaybedilmektedir (1).

Sıtma insana infekte dişi anofel cinsi sivrisineğin ısırmasıyla bulaşır. *P. vivax*, *P. ovale*, *P. malariae, P. falciparum* ve *P. knowlesi* insanda hastalık oluşturan türleridir. *P. falciparum* ve *P. vivax* en büyük tehdidi oluşturmaktadır. *P. falciparum*, Afrika kıtasında en yaygın sıtma parazitidir. Sıtma ile ilişkili ölümlerin çoğundan küresel olarak sorumludur. *P. vivax*, Sahra altı Afrika dışındaki ülkelerde baskın sıtma parazitidir (2). Türkiye'de en sık *P. vivax* görülür, ancak son yıllarda importe *P. falciparum* sıtması olguları da artmıştır (3-5). *P. falciparum*'a bağlı sıtma olgularında titreme, ateş, terleme nöbetleri 36-48 saatte bir meydana gelir (2). *P. falciparum* sıtmasında komplikasyon oranları diğer sıtma etkenlerine göre daha yüksektir ve bu durum mortaliteyi de etkiler. Serebral sıtma, akut böbrek yetmezliği, hipoglisemi, ağır anemi, splenomegali ve akciğer ödemi daha sık olarak saptanır (2).

Bu çalışmada Fırat Üniversitesi Hastanesi'nde 2011-2017 yılları arasında *P. falciparum* sıtması tanısı alıp, tedavi verilen olguların, epidemiyolojik, klinik, laboratuvar bulguları ve prognozları retrospektif olarak incelenmiştir.

YÖNTEMLER

Ocak 2011-Mart 2017 tarihleri arasında Fırat Üniversitesi Hastanesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği'nde, *P. falciparum* sıtması tanısı ile izlenen 15 erişkin hasta retrospektif olarak değerlendirilmiştir. Epidemiyolojik özellikleri, klinik, laboratuvar bulguları, tanı, tedavi ve prognozları incelenmiştir. Tanı, hastalardan ateşli dönemde yapılan kalın damla ve ince yayma preparatlarında parazitin görülmesiyle konulmuştur. Çalışma için hastaların demografik bilgileri, klinik ve laboratuvar değerlerinin yer alacağı bir form oluşturulmuştur. Hastalara ait bilgilere dosya ve epikrizler incelenerek ulaşılmıştır.

İstatistiksel Analiz

Çalışmanın istatistiksel analizleri, Statistical Package for Social Science for Windows (SPSS) sürüm 15,0 (SPSS Inc. Chicago, IL, USA) ile yapıldı. Ölçülebilir değişkenlerin dağılımı, ortalama ve standart sapma olarak, sınıflandırılmış veriler sıklık ve yüzde olarak verildi. Çalışma için Fırat Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan onay alındı.

BULGULAR

Altı yıllık süreçte kliniğimizde total 17 hasta sıtma tanısıyla takip edilmiştir ve hepsi yurtdışı kaynaklı sıtmadır. Bu olguların 15'i (%88) *P. falciparum*, 2'si (%12) ise *P. vivax* kaynaklı sıtma olgularıdır. İki hasta *P. vivax* kaynaklı olması nedeniyle çalışma dışı bırakılmıştır. Hastaların yaş ortalaması 35,6±9,6 olarak bulundu. Bir (%6,7) hasta bayan, 14 (%93,3) hasta erkekti. İki (%13) hasta eğitim amaçlı, 13 hasta mevsimlik işçi olarak yurt dışına seyahat etmişti. Hastaların 1'i (%6,7) Etiyopya'ya, 1'i (%6,7) Pakistan'a, 2'si (%13,3) Nijerya'ya, 2'si (%13,3) Afganistan'a, 3'ü (%20) Ekvator Ginesi'ne, 6'sı (%40) Sudan'a seyahat etmişti. Şikayetlerinin başladıktan sonra hekime başvurma süresine bakıldığında ortanca değer 4 (min:2, max:20 gün) olarak saptandı.

Beş (%33,3) hastaya seyahat öncesi danışmanlık hizmeti verilip sıtma profilaksisi başlanmıştı. Ancak hastalar profilaksiyi erken bırakmışlardı. On (%67,7) hasta ise hiç sıtma profilaksisi almamıştı. Hastalara ait belirti ve bulgular Tablo 1'de verilmiştir.

Hastaların 8'i (%53,3) daha önce seyahat ettikleri bölgede sıtma tanısı almış ve bu sebeple tedavi görmüştü. Hipoglisemi ve hiperpotasemi yönünden takip edilen hastalarda, her iki durumla da karşılaşılmadı. Hastaların 1'inde (%6) lökositoz, 2'sinde (%13,3) lökopeni saptandı. On iki (%80) hastada trombositopeni vardı. Hastaların 1'inde (%6,7) sadece aspartat aminotrasferaz (AST), 6'sında (%40) AST/ alanin aminotransferaz (ALT) birlikte yüksek saptandı. On (%66,6) hastada total bilüribin, 9 (%60)'unda direkt bilüribin yüksek saptandı. İki (%13,3) hastanın kreatin değerleri yüksekti. On dört (%93,3) hastada CRP yüksek bulunurken, eritrosit sedimentasyon hızı 4 (%26,7) hastada artmıştı. Hastaların başvurusunda saptanan çeşitli laboratuvar parametreleri Tablo 2'de verilmiştir.

Hastaların tümüne kalın damla ve ince yayma preparatı hazırlanarak tanı konuldu (Resim 1, 2).

Hastalardan 14'üne (%93,3) artemether+lumefantrine (Coartem, Novartis, Basel, Switzerland), 1'ine (%6,7) ise artemether+ lumefantrine+ doksisiklin (Monodoks, Deva İlaç, İstanbul, Türkiye) tedavisi başlandı.

Takiplerde 1 (%6,7) hastada komplikasyon gelişti. Platelet değerleri takibinin 3. gününde 13.000'e kadar düştü ve subkonjunktival kanama gelişti, sekel kalmadan iyileşti. Sadece bu hastaya trombositopeni nedeniyle trombosit süspansiyonu ve taze donmuş plazma replasmanı yapıldı. Üç (%20) hastanın idrar tetkikinde albuminüri saptandı.

Hastalar ortalama 6,6±3,1 gün hastanede yatırılarak takip edildi. Tüm hastalar şifa ile taburcu oldu.

TARTIŞMA

Sıtma tedavi edilmezse ölümcül seyredebilen bir hastalıktır. Dünya Sağlık Örgütü'nün 2015 yılı raporuna göre sıtma enfeksiyon hastalıkları kaynaklı ölümlerde dünyada beşinci, Afrika'da ise

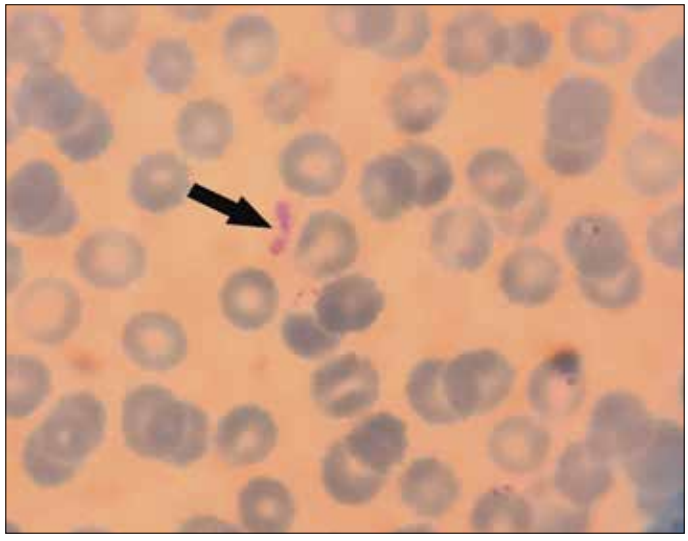
Tablo 1. Hastaların belirti ve bulguları

Belirti ve bulgular	Hasta sayısı, n (%)
Ateş	15 (100)
Üşüme-titreme	14 (93,3)
Terleme	13 (86,7)
Bulantı- kusma	8 (53,3)
İshal	5 (33,3)
Kabızlık	0 (0)
Periyodik ateş	5 (33,3)
Öksürük- balgam	2 (13,3)
Hepatomegali	4 (26,7)
Splenomegali	13 (86,7)

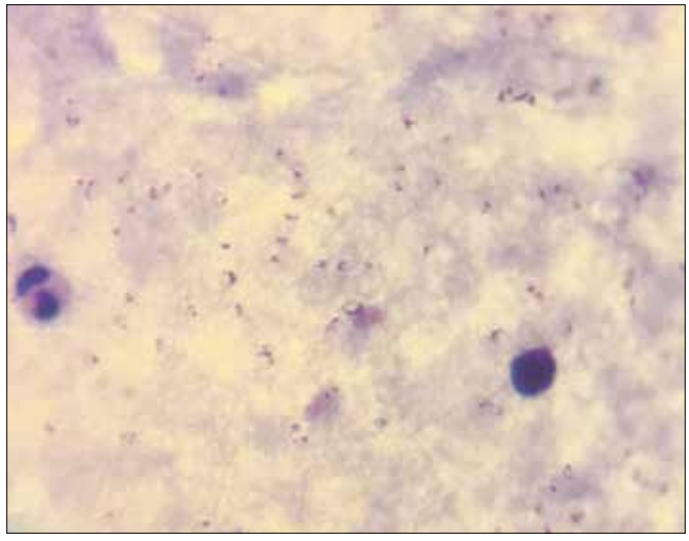
Tablo 2. Başvuru anında saptanan çeşitli laboratuvar değerleri

Laboratuvar testi	Ortalama değer*	Minimum-maksimum değer	Referans aralığı
Lökosit (/mm^3)	5266,66±1986,25	2080-10060	3800-8600
Hemoglobin (gr/dL)	13,22±2,85	8,6- 17	11,1-17,1
Trombosit (/mm^3)	113000±83743,65	32000- 372000	140000-360000
Sedimentasyon (mm/saat)	27,8±31,3	4-106	0-20
CRP (normal<5 mg/L)	55,93±54,09	4-157	0-5
AST (U/lt)	51,60±36,31	18-145	5-40
ALT(U/lt)	57,26±53,52	13-205	5-40
Total bilüribin (mg/dL)	1,59±1,03	0,28-4,3	0-1,10
Direkt bilüribin (mg/dL)	0,64±0,49	0,1-2	0-0,35
Üre (mg/dL)	28,8±6,44	17-37	10-50
Kreatinin (mg/dL)	0,88±0,33	0,1-1,5	0,6-1,2
Potasyum (meq/L)	4,01±0,5	3,4-5,0	3,5-5,5

*Ortalama±standart sapma. CRP: C-reaktif protein; AST: aspartat aminotransferaz; ALT: alanin



Resim 1. İnce yayma preparatında *P. falciparum* taşlı yüzük formları* (Ok: gametosit)
*Enfeksiyon hastalıkları laboratuvar arşivinden



Resim 2. Kalın damla preparatında görülen plasmodiumlar*
*Enfeksiyon hastalıkları laboratuvar arşivinden

ikinci sırada yer almaktadır (1). 2010 ile 2015 yılları arasında risk altındaki nüfuslardaki sıtma insidansı küresel olarak %21 düşmüştür. Aynı dönemde, risk altındaki popülasyonlardaki sıtma mortalite oranları, tüm yaş gruplarında küresel olarak %29 düşmüştür. Afrika Bölgesi, küresel sıtma yükünde orantısız olarak yüksek bir paya sahiptir. 2015 yılında bölge sıtma vakalarının %90'ı, sıtma ölümünün %92'si Afrika kıtasındadır.

Sıtma geçmişte ülkemizin en önemli enfeksiyonlarından biri iken, 1926 yılında başlatılan mücadele sonucunda olumlu gelişmeler yaşanmıştır. Dünya Sağlık Örgütü'nün 1955 yılında başlattığı sıtma eradikasyon programı kapsamında faaliyetler daha da yoğunlaştırılmıştır. Türkiye'de 2000 yılında 11381 vaka saptanmışken, 2010 yılında olgu sayısı dokuza düşmüştür. Bu mücadeleler sayesinde sıtma olgularında %99 azalma sağlanmış ve Dünya Sağlık Örgütü tarafından eliminasyon fazında kategorize edilmiştir (6). Yerli sıtma vakalarındaki dramatik bir düşüşe rağmen, 2010 yılında 78, 2011 yılında 128, 2013 yılında ise 285 yurt dışı kaynaklı sıtma olgusu bildirilmiştir. Kocaeli'nde yapılan bir çalışmada 2008-2010 yılları arasında sadece dört sıtma vakasına rastlanırken, 2011-2013 yılları arasında 23 hastaya sıtma tanısı konmuş, bu olguların %70'inin yurt dışı seyahatinin olduğu tespit edilmiştir (7). Seyahatlerin artışı, ülkeler arası iş gücü hareketliliğindeki artış, Suriye'den ülkemize göç nedeniyle sıtma ülkemizde hala önemini korumaktadır. Elazığ'da 1996-2004 yılları arasında yapılan çalışmaya göre toplam 200 sıtma vakası tanımlanmıştır. 200 vakanın biri hariç hepsi *P. vivax*'a bağlı sıtma olgusudur ve bu olgularda yurt içi riskli bölgelere seyahat öyküsü vardır. Bir hastada ise *P. malaria* saptanmış olup, bu hastanın Afrika'ya seyahat öyküsü vardır (8). 2005-2008 yılları arasında yapılan çalışmada ise 9 sıtma vakası saptanmıştır. Bir önceki çalışmayla uyumlu olarak Elazığ kaynaklı sıtma olgusu saptanmamış olup, 9 olguda da etken *P. vivax*'tır ve bu olgularında yurt içi riskli bölgelere seyahat

öyküsü vardır (9). Bizim çalışmamızda da ilimizde daha önce yapılan çalışmalarla uyumlu olarak Elazığ kaynaklı sıtma olgusu saptanmamıştır. Ancak önceki olgular yurt içi kaynaklıyken, son 6 yılda saptanan olguların tamamı import olgulardır. İmport olgularda saptanan tür 15 (%88) olguda *P. falciparum*, 2 olgu ise yine yurt dışı kaynaklı *P. vivax*'tır. Yıllar içinde yerli olgularımızın azalıp, rastlanmaması sıtma eradikasyon çalışmalarının başarısını göstermektedir. İmport sıtma olgularımızın artışı ise iş ve seyahat imkanlarının artması, mevsimlik işçiler ve eğitim faaliyetlerinin uluslararası boyut kazanmış olması ile açıklanabilir. Bizim olgularımızın 13 tanesi mevsimlik işçi olarak, 2 tanesi ise eğitim amaçlı seyahat etmişti.

Sıtma her iki cinste de görülen bir enfeksiyon hastalığı olmasına rağmen bizim olgularımızın 14'ü (%93,3) erkekti. Bu durum erkeklerde seyahat ve uluslararası işgücü hareketliliğinin daha fazla olması ile açıklanabilir.

Sıtma olguları her yaş grubunda görülebilir, ancak çalışmalarda vakaların çoğu 15 yaş üzeri hastalardır (5, 10, 11). Bu durum yetişkinlerin eğitim, turistik ya da iş amaçlı daha fazla seyahat etmeleri nedeniyle olabilir. Kliniğimizde takip edilen vakaların yaş ortalaması 35,6±9,6'dır.

Ateş sıtmanın en temel klinik bulgusudur. Klasik olarak *P. falciparum* enfeksiyonların da 36-48 saatte bir ateş nöbetleri olmaktadır (2). Çalışmamızda olguların tümünde (%100) ateş saptandı ve büyük oranda üşüme, titreme ve terleme de eşlik etmekteydi. Periyodik ateş ise 5 (%33,3) hastada vardı.

Bazı olgularda sıtmanın tipik periyodik nöbetleri görülmemiştir. Bu durum olguların immünitesinin zayıf olmasına veya parazitle birden fazla inoküle olmasına bağlı olabilir. *P. falciparum* olgularının ilk ataklarında da bu durumun görülebileceği bildirilmiştir (2).

Hastaların fizik muayenesinde splenomegali, hepatomegali, ikter, abdominal hassasiyet saptanabilir. Splenomegali, eritrosit yıkımının artması nedeniyle olup, hastalığın süresini gösteren bir ölçüdür. Ülkemizde yapılan çalışmalarda Mert ve arkadaşları hastaların %91'inde splenomegali, %55'inde hepatomegali, İnan ve arkadaşları %72'sinde splenomegali, Gül ve arkadaşları %67 splenomegali, %46 hepatomegali saptamışlardır (3, 4, 11). Bizim çalışmamızda ise %86,7 splenomegali, %26,7 hepatomegali saptanmıştır.

Sıtmada laboratuvar bulgusu olarak anemi, lökopeni ve trombositopeni görülebilir. Yapılan çalışmalarda, sıtma olgularının %67-70'inde anemiye, %32-40'ında lökopeniye ve %48-70'inde trombositopeniye rastlanıldığı bildirilmiştir (3). Bizim çalışmamızda anemi %26,7, lökopeni %13,3, trombositopeni %80 saptandı. Sıtma serilerinde AST/ALT yüksekliği %30-62 oranında saptanmıştır (12). Bizim hastalarımızda %40 AST/ALT yüksekliği saptandı.

Sıtmada standart tanı yöntemi, ışık mikroskobunda yapılan incelemede hazırlanan ince yayma ve kalın damla preparatlarında parazitin gösterilmesidir. İlk yayma negatif olarak değerlendirilse bile, klinik olarak sıtma şüphesi varsa, 12 saat arayla hazırlanan preparatlarda parazit aranmalıdır (2). Günümüzde geliştirilmiş hızlı testlerde olup, kullanım oranları giderek artmaktadır. Bizim hastalarımızın hepsinde tanı kalın damla ve ince yayma preparatı hazırlanarak tanı konmuştur.

Sıtma tedavisinde, parazit türü ve bölgenin olası direnç durumu göz önüne alınarak hızlı bir şekilde tedavi başlanmalıdır. Komplike olmayan *P. falciparum* sıtması tedavisinde seçilecek ilaç artemeter+lumefantrin, artesunat+amodiaquine, artesunat+meflokin, dihidroartemisinin+ piperaquin, artesunat+sulfadoxin/primetamin'dir (13). Bizim olgularımızın 14'üne (%93,3) artemeter+lumefantrin, 1 (%6,7) hastaya ise artemeter+lumefantrin+doksisiklin tedavisi başlandı. Tüm hastalar şifa ile taburcu edildi.

Dünya Sağlık Örgütü tarafından hazırlanan malaria tedavi kılavuzunda ciddi/ağır falciparum sıtması için kriterler bilinç bulanıklığı veya koma, yardımsız ayağa kalkamama, 24 saatte ikiden fazla konvüzyon gecirme, asidoz, hipoglisemi (kan şekeri <40 mg/dL), ciddi malarial anemi, renal yetmezlik, sarılık, pulmoner ödem, anormal spontan kanama, şok ve hiperparazitemi bulguları olarak bildirilmiştir (13). Bizim olgularımız komplike olmayan *P. falciparum* sıtmalı olgulardı. Özellikle ciddi/ ağır olgularda erken tanı ve etkili tedavi hayati öneme sahiptir.

Sıtmanın endemik olarak görüldüğü bölgelere seyahat edecek kişilere uygulanan kemoprofilaksi, morbidite ve mortaliteyi azaltır (14). Sıtmada kemoprofilaksisinin yeterliliği ilaç direncine bağlı olarak değişmektedir. Kişilerin kemoprofilaksinin önemi ve süresi hakkında aydınlatılması gerekir. Olgularımızın %33,3'üne profilaksi başlanmış ancak süre hakkında bilgi verilmemişti ve yetersiz profilaksi almışlardı.

SONUÇ

Son yıllarda seyahat imkanlarının gelişmesiyle birlikte ülkemizde yurt dışı kaynaklı sıtma olgularında artış görülmektedir. Son 20 yılın verilerine göre ilimiz kaynaklı sıtma olgusu saptanmamıştır. 1996-2010 yılları arası ilimizde 212 hastada sıtma tespit edilmiş, hastaların birinin yurt dışı, 211'inin ise yurt içi seyahat öyküsü saptanmıştır. Yurt dışından gelen olguda *P. malaria* saptanmışken, diğer olguların hepsinde etken *P. vivax* olarak tespit edilmiştir. Çalışmamızda olguların hepsinin yurt dışı kaynaklı olduğu göz önüne alındığında son 6 yılda bu verilerin dağılımının değiştiği söylenebilir. İmport *P. falciparum* sıtmasına ilimizde ilk kez rastlanmıştır. Seyahat sonrası erken dönemde saptanan ateşin en sık nedeni sıtmadır. Özellikle sıtmanın endemik görüldüğü bölgelere seyahat öyküsü olan ateşli hastalarda sıtma düşünülmelidir. Yurt dışına seyahat planı olan kişilere mutlaka seyahat öncesi danışmanlık hizmeti verilmeli, aşı ve profilaksi uygulamalarının doğru şekilde yapılması sağlanmalıdır. *P. falciparum* sıtmasında tanıdaki gecikme ölümcül komplikasyonlara neden olabilir. Dolayısıyla bu olguların acil tedavi edilmeleri gerekir. Riskli bölgelere seyahat edecek bireylere kemoproflaksi başlanması ve kişisel korunma önlemleri hakkında aydınlatmak için seyahat öncesi eğitim programları oluşturulmalıdır.

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Use of Internal Transcribed Spacer Sequence Polymorphisms as a Method for *Trichomonas vaginalis* Genotyping

Internal Transcribed Spacer (ITS) Sekans Polimorfizmlerinin *Trichomonas vaginalis* Genotiplendirmesinde Yöntem Olarak Kullanılması

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ABSTRACT

Objective: *Trichomonas vaginalis* is the most common non-viral, sexually transmitted pathogen with a worldwide distribution. The aim of the present study was to design a new genotyping tool for *T. vaginalis* isolates using internal transcribed spacer (ITS) sequences.
Methods: First, a total of 20 cryopreserved *T. vaginalis* isolates were thawed and genomic DNA was isolated from fresh cultures. A polymerase chain reaction (PCR) was performed to amplify the ITS regions and the amplicons were sequenced. These sequences were aligned with others from Genbank and polymorphisms were detected. At last, each ITS sequence was given a different sequence type.
Results: More than 99% homology was observed among sequences. Of 20 isolates, five had identical ITS sequence to reference (L29561) defined as ITST1. Moreover, 13 had A58 deletion (ITST10), one had C203T mutation (ITST2), and one had both A58 deletion and C203T mutation (ITST11). ITS typing of *T. vaginalis* sequences on Genbank revealed a total of 11 ITS types with the predominance of ITST1 (44.4%) globally.
Conclusions: ITS typing seems to be an applicable and useful tool for a better understanding of molecular epidemiology as well as for the dissemination of *T. vaginalis* clones.
Keywords: ITS, *Trichomonas vaginalis*, genotypes
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ÖZ

Amaç: *Trichomonas vaginalis* (*T. vaginalis*) cinsel yolla bulaşan hastalık etkenleri arasında viral patojenlerden sonra en sık görülen tür olup küresel bir dağılım göstermektedir. Bu çalışmanın amacı *T. vaginalis* internal transcribed spacer (ITS) dizilerini kullanarak parazitin genotiplendirilmesinde yeni bir yöntemin ortaya konulmasıdır.
Yöntemler: Çalışmamızda öncelikle farklı olgulardan izole edilen ve kriyoprezervasyon yapılarak saklanan 20 *T. vaginalis* izolatı canlandırılarak DNA izolasyonları yapılmıştır. Bu örneklerin ITS bölgeleri polimeraz zincir reaksiyonu (PZR) ile çoğaltılmış ve sekanslanmıştır. Genbank'da yer alan diğer ITS sekansları ile bu çalışmada elde edilenler sıralanarak polimorfizmler belirlenmiştir. Son olarak her bir farklı sekans için sekans tipi tanımlanmıştır.
Bulgular: *Trichomonas vaginalis* ITS sekansları arasında %99'a varan bir homoloji saptanmış olup bunlardan beşinin (n=20,%40), referans olarak seçilen L29561 Genbank numaralı ITST1 tipi *T. vaginalis* sekansı ile aynı olduğu görülmüştür. Bunun yanı sıra, izolatların 13'ünde A58 delesyonu (ITST10) ve birinde C203T mutasyonu (ITST2), birinde A58 delesyonu ve C203T mutasyonu (ITST11) tespit edilmiştir. Diğer ülkelerden izole edilen T. vaginalis izolatlarının ITS sekansları bizim çalışmamızdakilerle birlikte değerlendirildiğinde 11 farklı ITS sekans tipi tanımlanmış olup en sık ITST1 (%44,4) saptanmıştır.
Sonuç: Çalışmamızda ITS sekanslarına göre geliştirilen bu genotiplendirme yaklaşımının *T. vaginalis*'in moleküler epidemiyolojisinin daha iyi anlaşılmasına ve izolatların birbirinden genetik olarak ayırt edilmesinde faydalı olduğu düşünülmektedir.
Anahtar sözcükler: ITS, *Trichomonas vaginalis*, genotip
Geliş Tarihi: 15.08.2017 **Kabul Tarihi:** 12.12.2017

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INTRODUCTION

Trichomoniasis is the most common non-viral sexually transmitted infection (STI) worldwide and is caused by *Trichomonas vaginalis*, a flagellated, unicellular protozoon parasite of humans. However, very little public health attention has been provided to the disease (1). The World Health Organization reported an increase of 11.3% in global new cases of *T. vaginalis* infections from 248 to 276 million from 2005 to 2008 (2). It was reported that the frequency of infection in the USA was 1.3% among white Americans, 13.3% among African Americans, and 1.8% among Mexicans. Additionally, 2%-50% of people in Africa were thought to be infected with *T. vaginalis* (3, 4).

T. vaginalis infection is usually characterized by vaginitis, urethritis, and prostatitis; however, it may increase the risk of pelvic inflammatory disease and tubal infertility (5, 6). Recent reports have supported the idea that *T. vaginalis* may facilitate the transmission of HIV, particularly Type I (7-9). Trichomoniasis may cause profound health consequences, such as low birth weight infant, and preterm birth, in pregnancy (10, 11). Metronidazole, a 5-nitro imidazole derivative, is the primary drug of choice for trichomoniosis treatment; however, resistant cases to this drug have been reported in the USA, Russia, Africa, and Europe (12-15).

Although most studies have mainly focused on the prevalence of *T. vaginalis* and clinical characteristics of infection, little is known about the genetic diversity of *T. vaginalis* to date. Currently, a number of methods have been developed to discriminate *T. vaginalis* isolates; these methods include multisequence typing, microsatellite genotyping, and analyzing internal transcribed spacer (ITS) sequences (16, 17). It was reported that sequence analysis of ITS regions flanking the 5.8S subunit of the ribosomal DNA gene was a powerful tool for discriminating different genotypes (18).

The aim of the present study was to determine the genetic diversity of *T. vaginalis* isolates from a routine laboratory technique based on ITS sequences and also on a global scale.

METHODS

Isolates and Culture

In the study, we used cryopreserved *T. vaginalis* isolates that were isolated from 20 patients at Adnan Menderes University, Research and Training Hospital, Parasitology Laboratory between 2010 and 2014. The isolates were thawed, inoculated in trypticase yeast extract maltose medium, and incubated at 37°C. The cultures were observed after 48 h with direct microscopic examination, and positive cultures were utilized for DNA isolation.

PCR Amplification and Sequencing

The parasites in the logarithmic phase were pelleted by centrifugation for 5 min at 1500g. Genomic DNA was extracted from pellets using the High Pure PCR Template Preparation (Roche Applied Science, Berlin, Germany) according to the manufacturer's instructions and stored at −20°C.

The ITS region was amplified using primers as previously described by Snipes et al. (18): TVITSF (5'-ACCGCCCGTCGCTCCTACCGA-3') and TVITSR (5'-CTCCGCTTAATGAG ATGCTTC-3'). The reaction was set in a 50-µL volume containing 0.4 pmol of each of the primers, 1.5 U of Taq DNA polymerase, 0.2 mM of each dexynucleotide triphosphate (dNTP), 2 mM magnesium chloride ($MgCl_2$), and 1× Taq buffer with ammonium sulfate $(NH_4)_2SO_4$. The amplification was performed using a thermal cycler (TC-312, Techne, Minneapolis, USA) following the following protocol: initial denaturation step at 94°C for 5 min and 35 cycles (30 s at 94°C, 30 s at 54°C, and 60 s at 72°C) with a final extension step at 72°C for 5 min. A 5-8 µL of PCR product was run on a 2% agarose gel using SYBR Safe (Invitrogen, California, USA) and 50-base pair ladder marker (Thermo Scientific, Bartlesville, USA). The gels were visualized using a gel documentation system (VilberLourmat, Basel, Switzerland). PCR amplifications were purified and sequenced by a commercial facility (Macrogen Inc., South Korea). The sequences were aligned with references using CLUSTAL X (19).

ITS Sequences of *T. vaginalis* from Genbank

In total, 36 ITS sequences were found at Genbank. The accession numbers of these sequences were as follows: L29561, TVU86613, AY957955, AY871048, AY871047, AY871046, AY871045, AY871044, FJ813603, FJ813602, FJ813601, FJ813600, FJ813599, FJ813598, JN007004, AY245136, FJ376711, EU816897, AY349186, AY349185, AY349184, AY349183, KC513779, KC513778, KC513777, KC513776, KC513775, KC513774, JQ768335, JQ768334, JQ768333, JQ768332, JQ768331, JQ768330, KP221674, and KF164606. However, 2 of these sequences, AY957955, and KP221674, were excluded from the study. The sequence AY957955 had many undefined nucleotides, (symbolized as N) and the beginning as well as the end of the sequence KP221674 had multiple mismatches with the remaining sequences.

RESULTS

In total, 20 *T. vaginalis* isolates from patients at Adnan Menderes University, Research and Training Hospital were included in the present study. The ages of patients varied from 26 to 42 years (mean±standard deviation: 33.3±4.1). Total DNA was extracted from samples, and *T. vaginalis* ITS region was amplified and sequenced in all of the 20 culture-positive samples. The ITS sequences of these 20 samples were aligned, which showed >99 similarity. Sequences were deposited to Genbank (Accession Numbers: KP861811, KP861812, KP987798, and KP987799). The longest *T. vaginalis* ITS sequence in Genbank (Accession Number: L29561) was accepted as the reference ITS sequence. The comparative analysis of our sequences against the reference revealed that 5 of them (40%) were identical to the reference, 13 isolates had an "Adenine" deletion at the 58th position, one isolate had a single substation (C203T), and one isolate had both a deletion at the 58th position and a single substation (C203T).

In addition to our sequences, other *T. vaginalis* ITS sequences from Genbank were downloaded and each different ITS sequence was numerated. In total, eleven ITS types were defined by comparing sequences. Among them, ITST10 and ITST11 were from the present study. These sequences were different from the existing sequences in Genbank (Table 1). Based on the nomenclature described in this study, ITST10 was the most common ITS type among our samples (13 isolates, 65%), followed by ITST1 (5 isolates, 25%), ITST2 (one isolate, 5%), and

Table 1. ITS Typing; Distinct ITS types of sequences in Genbank and ITS sequences of the isolates*

	Base number (accession no. L29561)															
ITS Type	**58**	**68**	**69**	**127**	**128**	**135**	**170**	**180**	**203**	**352**	**359**	**424**	**435**	**439**	**Reference**	**Origin of isolate**
ITST1	A	A	A	T	T	G	T	A	C			A	A	A	L29561	USA
ITST2									T						AY349186	Brazil
ITST3		T	C						T						AY871046	China
ITST4												T			FJ813603	Philippines
ITST5							C								FJ813602	Philippines
ITST6													C		FJ813600	Philippines
ITST7														T	FJ813599	Philippines
ITST8				A	A	T				#C	#C				FJ376711	Brazil
ITST9								C							AY349185	Brazil
ITST10	‡Del														KP987798	Turkey (Present Study)
ITST11	‡Del								T						KP987799	Turkey (Present Study)

*Starting points: ITST2 and 9 at 137, ITST3 at 61, ITST4-7 at 131, ITST8 at 126, ITST10 and 11 at 46. #Insertion, ‡Del: deletion.

Table 2. Dissemination of *T. vaginalis* ITS types by country of 25 ITS sequences in Genbank and isolates from Turkey

Origin of country	**ITS Types**											
	ITST1	**ITST2**	**ITST3**	**ITST4**	**ITST5**	**ITST6**	**ITST7**	**ITST8**	**ITST9**	**ITST10**	**ITST11**	**Total**
USA	1	-	-	-	-	-	-	-	-	-	-	1
Brazil	3	1	-	-	-	-	-	1	1	-	-	6
China	1	3	1	-	-	-	-	-	-	-	-	5
Czech	1	-	-	-	-	-	-	-	-	-	-	1
Iran	3	3	-	-	-	-	-	-	-	-	-	6
Mexico	1	-	-	-	-	-	-	-	-	-	-	1
Philippines	1	1	-	1	1	1	1	-	-	-	-	6
Spain	6	-	-	-	-	-	-	-	-	-	-	6
Switzerland	2	-	-	-	-	-	-	-	-	-	-	2
Turkey	5	1	-	-	-	-	-	-	-	13	1	20
Total	24	9	1	1	1	1	1	1	1	13	1	54

ITST11 (one isolate, 5%). *T. vaginalis* ITS types were disseminated by country for 34 ITS sequences in Genbank and 20 isolates from Turkey (Table 2).

DISCUSSION

T. vaginalis infection is among the most common STIs all over the world. A systematic understanding of the variation in genotypes and outcomes are still lacking because of the low number of molecular studies on *T. vaginalis*. In previous studies, Random Amplified Polymorphic DNA analyses and ribosomal gene sequences were used to determine the genetic polymorphism of *T. vaginalis* isolates. The studies primarily focused on the relation between genotypes and possible outcomes such as clinical picture, resistance to drugs, and host specificity (20, 21). Hampl et al. (20) suggested that the clinical picture and resistance to metronidazole are related to the virulence and biological characteristics of isolates. It was reported that the strains from asymptomatic and symptomatic cases were different in terms of zymodeme patterns (22, 23). Another genotyping method for *T. vaginalis* isolates is sequencing the ITS region. ITS sequences are non-functional, neutrally evolving phylogenetic markers that are found in all eukaryotic cells. They are located between ribosomal genes and are less conserved than active genes. Snipes et al. (18) amplified the ITS region in 109 *T. vaginalis* isolates and found a C66 mutation in 16 isolates. They also found a high resistance in this group and concluded that it might be a result of this mutation.

In our study, 5 of the 20 isolates had identical ITS sequence to the reference sequence (ITST1), 13 had only an "Adenine" deletion (ITST10), one had C203T point mutation (ITST2), and one had both deletion at the 58th position and C203T point mutation (ITST11). Additionally, ITST10 was the most common (13 out of 20, 65%) ITS type in our study population. Although 2 ITS types

(ITST10 and 11) have not been reported yet in other parts of the world, we think that it is because of the absence of the data and lack of genotyping studies of *T. vaginalis*. ITS typing of more isolates from different regions in Turkey and the world will help us better understand the molecular epidemiology of the parasite, the relations among genotypes, and the virulence as well as resistance. In accordance with our study, Ibanez-Escribano et al. (24) reported a stable mutation in 26% of isolates and 99.7% ITS nucleotide sequence identity.

The analysis of ITS sequences in Genbank showed that ITST1 was the most common ITS type (24 out of 54, 44.4%) on a global scale. These ITST1 isolates were reported from a variety of countries such as USA, Brazil, Philippines, Spain, China, Switzerland, Czech Republic, Iran, Mexico, and Turkey. The second most common genotype ITST2 (9 out of 54, 16.6%) was reported from Philippines, China, Brazil, Iran, and Turkey. ITST3 was reported from China. ITST4, 5, 6, and 7 were reported from Philippines. ITST8 and 9 were reported from Brazil. Finally, ITST10 and 11 were reported from Turkey. The only available sequence from the USA was ITST1. There were 6 sequences from Brazil, 3 of them were ITST1 (50%) and the remaining were singleton ITST2, ITST8, and ITST9. In total, 5 sequences were reported from China and 3 (60%) were ITST2 and one (20%) was ITST1 and ITST3 each. From Philippines, 6 sequences were reported, one from each ITS types 1, 2, 4, 5, 6, and 7. One sequence reported from Czech Republic was ITST1. All of the 6 sequences from Spain and 2 from Switzerland were ITST1. There were 6 sequences from Iran, 3 of them were ITST1 (50%), and the remaining sequences were ITST2.

CONCLUSION

In the present study, we have genotyped *T. vaginalis* isolates by ITS sequencing in Turkey as well as we contributed a new approach for sequence-based genotyping; thus, the current findings have a potential of being a base for future studies. Further studies should be performed to show a relation between genotype and clinical outcome, virulence, resistance, and pathogenicity.

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Leishmania tropica Üzerinde *In vitro* ve *In vivo* İlaç Etkinliğinin Değerlendirilmesi: Pilot Çalışma

Evaluation of *In vitro* and *In vivo* Drug Efficacy Over *Leishmania tropica*: A Pilot Study

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ÖZ

Amaç: Kutanöz leishmaniasis (KL) tedavisinde ülkemizde antimon bileşiklerinden meglumin antimonat (Glucantime®, Fransa) ve sodyum stiboglukonat (Pentostam®, İngiltere) kullanılmaktadır. Çalışmamız, bu konuda çalışmalar planlayan genç araştırmacılara rehber olacak şekilde, *in vitro* ve *in vivo* modellerde ilaç direnç testlerinin ve etken madde taramalarının yapılmasına temel ve kaynak oluşturması amacıyla planlanmıştır.
Yöntemler: Bir KL izolatı sıvı nitrojenden çıkarıldıktan sonra internal transcribed spacer 1 (ITS1) problu gerçek-zamanlı polimeraz zincirleme reaksiyonu (PZR) testi uygulanarak genotiplendirilmiştir. Meglumin antimonat ve sodyum stiboglukonat'a karşı ilaç direncini belirlemek için in vitro ve in vivo direnç testleri uygulanmıştır. *In vitro* ilaç direncini araştırmak için hemositometre ve XTT (sodium 3,39-[1-(phenylaminocarbonyl)-3,4-tetrazolium]-bis (4-methoxy-6-nitro) benzene sülfonik asit hidrat) yöntemleri, *in vivo* ilaç direncini araştırmak için ise farelerde KL modelleri kullanılmıştır.
Bulgular: Kullanılan izolatın PZR ile ITS1 bölgesine göre yapılan genotiplendirmeyle *Leishmania tropica* olduğu saptanmıştır. *In vitro* ilaç direnç testlerinde meglumin antimonat'a göre sodyum stiboglukonat'ın daha etkili olduğu görülmüş fakat istatistiksel olarak belirgin bir fark görülmemiştir (p>0,05). *In vivo* çalışmalarda ise meglumin antimonat ve sodyum stiboglukonat tedavisinin ayaktaki lezyonları enfeksiyonun 5. haftadan sonra küçültmeye başladığı ve 3 ay sonunda her iki ilacın uygulandığı gruplarda klinik ve parazitolojik iyileşme olduğu görülmüştür.
Sonuç: Çalışacak genç araştırmacılar için rehber niteliğinde olacak şekilde in vitro ve in vivo modelde ilaç direnç testleri ve etken madde tarama yöntemleri temel ve basit olarak verilmiştir.
Anahtar sözcükler: Leishmaniasis, *in vitro*, *in vivo*, ilaç direnç testleri, Türkiye
Geliş Tarihi: 15.09.2017 **Kabul Tarihi:** 05.01.2018

ABSTRACT

Objective: Two pentavalent antimonials, meglumine antimoniate (Glucantime®, France) and sodium stibogluconate (Pentostam®, England), are used to treat cutaneous leishmaniasis (CL) in Turkey. The present study, serving as a guidebook for young researchers, aims to provide basis for conducting drug resistance tests and active ingredient scanning in *in vitro* and *in vivo* models.
Methods: A CL isolate kept in liquid nitrogen was initially thawed and genotyped by real-time polymerase chain reaction (PCR) using ITS1 prob. *In vitro* and *in vivo* tests were conducted to determine drug resistance against meglumine antimoniate and sodium stibogluconate. Hemocytometry and XTT (sodium 3,39-[1-(phenylaminocarbonyl)-3,4-tetrazolium]-bis (4-methoxy-6-nitro) Benzenesulfonic acid hydrate) methods were used to investigate *in vitro* drug resistance. CL mouse models were used to analyze *in vivo* drug resistance.
Results: The isolate was determined as *Leishmania tropica* by genotyping by PCR on the internal transcribed spacer 1 (ITS1) gene region. In *in vitro* drug resistance tests, sodium stibogluconate was observed to be more effective than meglumine antimoniate, but there was no statistically significant difference between the two (p>0.05). It was observed that the footpad lesions of the animals started to shrink afterward the 5th week of infection following treatment with these agents, and parasitologic recovery was observed at the end of 3 months.
Conclusions: With an aim to be used as a guidebook for young researchers, active ingredient scanning and drug resistance tests in both in vitro and *in vivo* models were presented in the current study.
Keywords: Leishmaniasis, *in vitro*, *in vivo*, drug resistance tests, Turkey
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GİRİŞ

Leishmaniasis'in Dünya Sağlık Örgütü'nün verilerine göre, beş kıtada 98 ülkede yaklaşık 12 milyon insanı enfekte ettiği ve 350 milyon kişinin ise risk altında olduğu bilinmektedir. Her yıl bu rakamlara iki milyon yeni olgunun eklendiği, bu olguların yaklaşık bir buçuk milyonunun kutanöz leishmaniasis (KL), yarım milyonunun ise visseral leishmaniasis (VL) olduğu tahmin edilmektedir. Leishmaniasis'e bağlı yıllık ölüm sayısının 50.000 olduğu belirtilmektedir. Kutanöz leishmaniasis olgularının %90'ı Afganistan, Cezayir, Brezilya, İran, Peru, Suudi Arabistan ve Suriye'de bulunmaktadır. KL'nin son 10 yılda görülme sıklığında artış gözlenmekte, yaklaşık her 20 saniyede bir kişinin KL'ye yakalandığı hesaplanmaktadır (1).

Leishmaniasis olgularının artma nedenleri arasında kırsal bölgelerden kentlere göç, enfeksiyonun endemik olduğu bölgelerde iş sahalarının açılması, malnütrisyon, sosyoekonomik düzeyin düşüklüğü ve HIV/*Leishmania* koenfeksiyonunda artış sayılabilir. Leishmaniasis'in yol açtığı ekonomik kayıp tıbbi bakım ve tedaviler ile birlikte iş gücü bakımından değerlendirildiğinde oldukça büyüktür; bu nedenle gelişmekte olan ülkelerin ekonomileri için leishmaniasis ciddi bir sorundur. Gelişmiş ülkelerde ise HIV/*Leishmania* koenfeksiyonunda görülen artış nedeniyle leishmaniasis'e ilgi artmaktadır (2-4).

Ülkemizde resmi rakamlara göre 2005-2012 yılları arasında 14.587 KL olgusu ve 207 VL olgusu bildirilmiştir. Son yıllarda, başta Akdeniz ve Ege Bölgesi illerimizde olmak üzere toplam 39 ilimizden sporadik olgular bildirilmiş, ayrıca enfeksiyon odağı olarak bilinen yörelerdeki leishmaniasis olgularında önemli oranda artış görülmüştür. Kutanöz leishmaniasis başta Güney Doğu Anadolu Bölgesi olmak üzere Akdeniz, Orta Anadolu ve Ege bölgelerinden bildirilmektedir. Şimdiye dek yapılan çalışmalarla hastalığın etkeninin *Leishmania tropica*'nın farklı zimodemleri olduğu aynı zamanda *Leishmania infantum*'un da KL'ye sebep olabildiği gösterilmiştir (5).

Farklı türlere bağlı olarak oluşan KL'deki lezyonlar tedaviye yanıt verme açısından değişkenlik gösterebilmektedir. KL tedavisinde uzun yıllardır daha yüksek dozların kullanımına ve daha kısa süreli tedavilere olanak sağladığından dolayı 5 değerli antimon bileşiklerinin organik tuzları tercih edilmektedir. *Leishmania* parazitinin glikoliz ve diğer metabolik yollardaki enzimlerini inhibe ederek etki gösterdiği düşünülen antimoniyallerin ticari olarak iki farklı 5 değerli antimon bileşiği bulunmaktadır. Bunlar Sodyum stiboglukonat ve Meglumin antimonyattır. Türkiye'de sodyum stiboglukonatın "pentostam" markalı ticari formu bulunurken meglumin antimonatın ticari ürünü "glucantime" dir. Sodyum stiboglukonat %10 antimon içerirken meglumin antimonyat ise %8,5 antimon içermektedir. Eşit dozlarda kullanıldığında iki ilacında aynı etkiye sahip olduğu düşünülmektedir. KL hastalarında bulunan lezyonun tek ve papulonodüler olduğu ve intralezyoner tadaviye uygun lokalizasyonda yer alan lezyonlarda intralezyoner (IL) tedavi uygun görülmektedir. Tedavinin 1-2 ml pentavalan antimoniyollerin IL olarak haftada 3 kez uygulanarak 4 ya da 5 hafta devam edilerek uygulanması tavsiye edilmektedir. Bununla birlikte, lezyona uygulanan ilacın miktarı lezyonun durumuna göre farklılık arz edebilmektedir. Hastada birden fazla lezyon bulunduğu durumlarda, IL uygulamaya uygun olmayan lezyonlarda ve tedaviye cevap alınamayan kronik olgularda ise sistemik tedavi uygulanmaktadır. Bu durumda ise 20 mg Sb^v/kg 20 gün süre ile IM olarak kür uygulanması tavsiye edilmektedir. Birinci kürden sonuç alınamayan olgularda ikinci hatta üçüncü kürün uygulanması önerilmektedir (6, 7).

Leishmaniasis kontrolü tedaviye dirençli parazitlerin ortaya çıkmasıyla çok daha karmaşık bir hal almıştır. Klinikte 5 değerli antimon bileşiklerine direnç önem kazanmakta olup Güney Amerika (8-10), Avrupa (11, 12), Orta Doğu (13, 14) ve özellikle Hindistan'da (15-18) bu direnç görülmeye başlanmıştır. Hatta Hindistan'da endemik bir bölge olan Bihar'da 5 değerli antimon bileşikleri ile tedavinin %60 başarısız olduğu görülmekte ve dirençli parazitler ile enfekte olguların tedaviye yanıt vermediği bildirilmektedir. Alternatif olarak kullanılabilecek az sayıda ilaç vardır; bunlar arasında amphotericin B, pentamidine ve oral kullanılan, Hindistan'da VL için 4. faz, İran'da ise KL için 3. faz klinik çalışmaları yürütülmekte olan miltefosin yer almaktadır. Miltefosin'e karşı parazitlerin etkinliğinde azalma görüldüğü bildirilmiştir (10, 19, 20). Bu nedenle Leishmaniasis konusunda yeni ilaç araştırmalarına gereksinim vardır.

Yeni ilaçların geliştirilmesi ve değerlendirilmesi süreci iki ana değerlendirme basamağından oluşmaktadır. Klinik öncesi değerlendirmede; sentez edilen veya doğal kaynaklardan izole edilen kimyasal maddelerin, önce mutlaka *in vitro* ve *in vivo* olarak etkinliklerinin araştırılması gerekmektedir.

Mikroorganizmalara karşı geliştirilen yeni maddeler, genellikle toksisite deneylerine tabi tutulmadan önce tarama testlerine tabi tutulurlar. *In vitro* ortamlarda tarama testleri yapılabilmekte ancak öngörülen etkinin özelliği nedeniyle bazı tarama testlerinin sadece *in vitro* ortamda yapılması uygun olmamaktadır. Tarama testlerinde hastalığı temsil eden hayvan modelleri kullanılmaktadır. Çünkü etken maddenin biyokinetik özellikleri, metobolizma hızları ve organlar arası etkileşim özellikleri sadece oluşturulan bu modellerle saptanabilmektedir. Bu sayede geliştirilme amacını oluşturan ve sahip olması öngörülen etki ya da etkileri gösteren maddeler belirlenmektedir. Bu özelliği bulunmayan maddeler için deneme artık bu kademede bitmiş olarak kabul edilmektedir.

Deneyler sonrası yalnızca tarama testlerini başarı ile geçen bileşikler toksisite testlerine tabi tutulmaktadırlar. Bu aşamada fonksiyonel, biyokimyasal ve histopatolojik toksik etkiler incelenmektedir. Klinik değerlendirme basamağının ise Faz I, Faz II, Faz III ve Faz IV denemelerinden oluştuğu bildirilmektedir (21).

Bu çalışmada ülkemizde bir olgudan izole edilen ve sıvı azot içinde suş bankasında saklanan bir *Leishmania tropica* izolatı üzerine yine Türkiye'de KL tedavisinde ilk seçenek olarak kullanılan ilaçların (meglumin antimonat (Glucantime®, Fransa)'ve sodyum stiboglukonat (Pentostam®, İngiltere)' etkinlik ve direnç varlığı *in vitro* ve *in vivo* model üzerinde çalışılmış olup kullanılan yöntemin bu konuda çalışacak araştırmacılara yol göstermesi ve kaynak oluşturması amaçlanmıştır.

YÖNTEMLER

NNN Besiyerinin Hazırlanması

Katı faz: Agar 5 gr, pepton 2 gr, NaCl 1 gr ve 200 mL distile su bir balona konularak 121^{0}C'de 20 dk. otoklavlanmıştır. Aseptik

koşullarda tavşan kalbinden 30 mL kan alınmış ve defibrinize edilerek küçük steril bir balona aktarılmıştır. 1,3 mL (%1) gentamisin ve 2,3 mL penisilin/streptomisin (%1) solüsyonu eklenerek karıştırılmıştır. Agar yaklaşık 50^{0}C'ye kadar soğutulup kan agarın üzerine eklenerek karışması sağlanmış ve hemen steril tüplere 3-4 mL dağıtılmıştır. Tüplere belli bir eğim verilerek katılaşıncaya kadar oda ısısında tutulup ardından +4^{0}C'de saklanmıştır.

Sıvı faz: Katı faz üzerine 1 ml %10 FCS içeren RPMI besiyeri eklenmiş ve besiyeri ekim yapmaya uygun hale getirilmiştir.

Kutanöz Leishmaniasis'li Olgudan Örnek Alınması
Örnek alınırken lezyonun çevresindeki doku %70 alkol ile temizlenip kurumaya bırakılmıştır. Lezyon baş ve işaret parmağı arasında tutularak yara ile sağlam dokunun birleşme sınırından 1 mL'lik insülin enjektörü ile 0,2-0,5 mL serum fizyolojik verilip tekrar geri çekilerek aspirasyon sıvısı alınmıştır. Lezyondan elde edilen aspirasyon sıvısından NNN besiyerlerine ekim yapılmıştır. Besiyerleri 25^{0}C'de saklanmış ve promastigotların varlığı açısından bir ay süreyle gün aşırı kontrol edilmiştir. İlk üremenin gerçekleştiği besiyerlerinden örnekler alınmıştır. Alınan örnekler fazla miktarda üretmek amacıyla RPMI-1640 besiyerinde (%10 FCS + %1 penisilin/streptomisin + %1 gentamisin) kültüre alınmıştır. RPMI 1640 besiyerinde logaritmik faza ulaşan promastigotlara %15 oranında DMSO eklenerek kryoprezervasyon işlemi uygulanmış ve sıvı azotta saklanmıştır. Çalışmamızda sıvı azotta saklanan bu izolatlar kullanılmıştır.

***Leishmania* İzolatının Kültürü**
Sıvı azotta kriyoprezervasyon uygulanarak saklanan promastigotlar sıvı azottan çıkarılıp sıcak su banyosunda hızlı bir şekilde çözdürüldükten sonra NNN besiyerine ekilmiştir. İlk üreme gerçekleştikten sonra fazla miktarda üretmek amacıyla RPMI-1640 besiyerinde kültüre alınmıştır. Ticari olarak temin edilen besiyeri içerisine kullanmadan önce %10 FCS, %1 penisilin/streptomisin ve %1 gentamisin eklenmiştir. 25 mL'lik flasklere 5 mL olacak şekilde dağıtılmış ve üreyen promastigotlardan 50 µL üzerine ilave edilerek ekim yapılmıştır. Ekim yapılan flaskler 25°C'lik etüvde inkübe edilmiştir. Parazitlerin çoğalması takip edilerek 2-3 günde bir besiyerinin eklenmesiyle 10^8 promastigot/mL içeren besiyeri elde edilmiştir. Daha sonra promastigot sayısı 10^6 promastigot/mL olacak şekilde Thoma lamı ile sayılarak promastigot içeren süspansiyon hazırlanmıştır.

Leishmania Promastigotlarının PZR Yöntemi İle Genotiplendirilmesi
DNA izolasyonu: *Leishmania* izolatının genotiplendirilmesi için genetik materyalin elde edilmesinde uygulanmıştır. DNA izolasyonu High Pure PCR Template Preparation Kit ile yapılmıştır.

Genotiplendirme: Çalışmalarda, ITS1 problu gerçek zamanlı PZR testi uygulanmıştır (22, 23). *Leishmania* parazitlerinin ssu rRNA ve 5.8S rRNA'yı kodlayan genleri ayıran ribozomal internal transcribed spacer 1 (ITS1) bölgesi, Forward primer; 5'-CTGGATCATTTTCCGATG-3', Reverse Primer; 5'-GAAGCCAAGTCATCCATCGC-3' primerleri QuantiTect Probe PCR Kit Master karışımı ile birlikte aşağıda yazılı özgün problar kullanılarak çoğaltılmıştır.

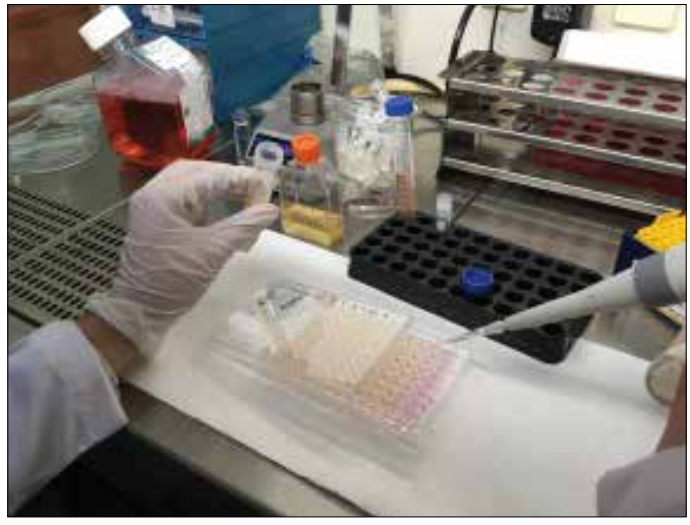
Probe 1: 5'- CCGTTTATACAAAAAATATACGGCGTTTCGGTTT-Fluo-3'

Probe 2: 5'-LCRed-640-GCGGGGTGGGTGCGTGTGTG-Pho-3'

Gerçek zamanlı PZR analizi için hazırlanan toplam 25 µL'lik reaksiyon karışımı; 1,5 µL H_20 (PCR grade water), 1 µL Forward Primer, 1 µL Reverse Primer, 0,5 µL Probe1, 0,5 µL Probe2, 12,5 µL QuantiTect Probe PCR Kit Master karışımı (Qiagen) ve 5 µL genomik DNA içermektedir. Rotor-Gene'de melting analizi yapılarak sonuçlar elde edilmiştir.

***In vitro* İlaç Direnç Testleri**
Çalışmamızda mikroplak dilüsyon yöntemi kullanılarak ilaçların *Leishmania* promastigotları üzerindeki antiparaziter etkinlikleri in vitro olarak test edilmiştir. Çalışmamızda sağaltımı tamamlanan hastalardan geriye kalan ilaçlar kullanılmıştır. Düz tabanlı 96'lık hücre kültürü plağı yatay olarak kullanılmış ve 12 sıranın 3'ü blank (Kör kuyucuk), 3'ü ilaçsız parazit kontrol, 3'ü meglumin antimonat (Glucantime®, Fransa) ve 3'ü sodyum stiboglukonat (Pentostam®, İngiltere) için olacak şekilde işaretlenmiştir. Her bir kuyucuğa RPMI 1640 besiyerinden (%10 FCS + %1 penisilin/streptomisin + %1 gentamisin) 100 µL dağıtılmıştır. Meglumin antimonat (Glucantime®, Fransa) ve sodyum stiboglukonat (Pentostam®, İngiltere) için ayrılmış olan 3 bölmenin her birinin ilk kuyucuğuna istenilen ilaç konsantrasyonunun iki katı olacak şekilde standart besiyerine ilaçlar eklenerek 100 µL hazırlanmıştır. (Bu çalışmamızda ilk doz 300 µg/mL bu nedenle 600 µg/mL olacak şekilde hazırlanmıştır) Hazırlanan bu ilaçlı besiyeri ilk kuyucuklara eklenmiştir. Çoklu pipet ile ilk kuyucuktan diğerlerine 100 µL aktarım yapılarak ilaç konsantrasyonları hazırlanmıştır (300, 200, 100, 50, 25 ve 12,5, 6,25 µg/mL) (Resim 1). Son kalan 100 µL atılmıştır. Daha sonra hazırlanan promastigot süspansiyonundan 100 µl olacak şekilde bütün kuyucuklara eklenmiştir. Blank bölmelerine parazit ilave edilmemiştir. Hücre kültürü plağının kapağı kapatılarak etrafı parafinle kaplanmıştır. Etüvde 25°C'de 48 saat inkübe edilmiştir (Resim 2). Bu işlemlerin ardından aşağıda tarif edilen iki yöntem kullanılarak *in vitro* etkinlik düzeyleri belirlenmiş ve çalışma grupları diskriminant analizi ile istatistiksel olarak değerlendirilmiştir (24).

Hemositometre yöntemi
Neubauer'in Thoma lamı üzerinde iki yanda bulunan çıkıntılar hafifçe ıslatılmıştır. Lamel bunların arasını kapatacak şekilde yer-



Resim 1. Hücre kültürü plağında ilaçların seri sulandırmalarının hazırlanması

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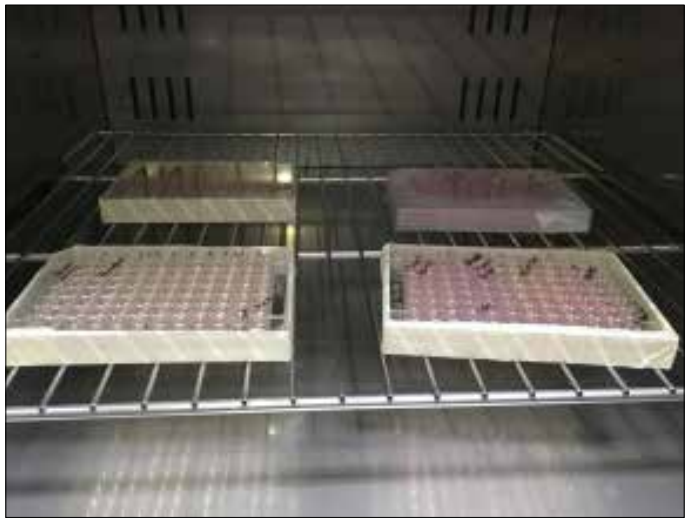
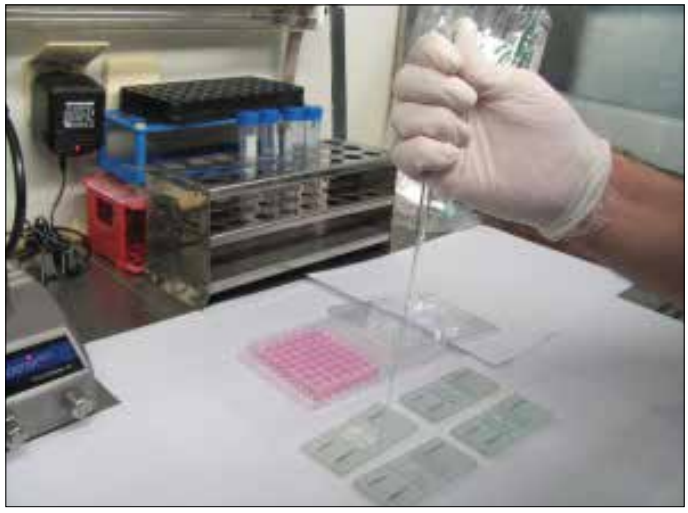


Resim 2. Hücre kültürü plağının 25°C'de 48 saat inkübe edilmesi



Resim 3. *In vitro* çalışma sonuçlarının hemositometre yöntemi ile değerlendirilmesi

leştirilmiştir. İki elin başparmakları ile konsantrik Newton halkaları belirinceye kadar bastırılmıştır. Daha sonra etüvden plak çıkarılıp her bir kuyucuktan ayrı ayrı örnek alınarak lam-lamel arasına sayım kamaralarının olduğu kenardan damlatılmıştır. Bu sıvı kapillarite nedeni ile lam üzerinde bulunan sayım alanına yayılmış ve aktarılan sıvının hareketsizleşmesi için 1-2 dakika beklenilmiştir. Önce mikroskobun diyaframı kapatılıp küçük büyütmesinde (10x) sayım yapılacak olan çizgili alan bulunmuş ardından karelere düşen *Leishmania* promastigotlarını saymak amacı ile büyük büyütme (40x) ile bakılmıştır. Thoma lamının her bir köşesinde bulunan toplam dört kare ve orta alandaki kare içerisinde bulunan promastigotlar sayılmıştır. Toplam promastigot sayısı 10.000 ile çarpılıp sayılan kareye bölünerek mL'deki promastigot sayısı bulunmuştur (Resim 3).

XTT (sodium 3,39-[1-(phenylaminocarbonyl)-3,4-tetrazolium]-bis(4-methoxy-6-nitro) benzene sülfonik asit hidrat) direnç testi

Yeni bir 96'lık düztabanlı hücre kültürü plağı alınıp süre sonunda plak etüvden çıkarılarak ve her bir kuyucukdan 100 µL alınarak yeni plağa aktarılmıştır. Ayrı bir yerde 5 mL reagent ve 0,1 mL

Resim 4. XTT testinde spektrofotometrede hücre kültürü plağının okutulması

"electron coupling" karıştırılmıştır. Yeni plağımızın her bir bölmesine 50 µL eklenerek 25°C'de 4 saat inkübe edilmiştir. İnkübasyon sonunda plak spektrofotometrede 450 nm'de okuma yapılmıştır (Resim 4). Okuma sonunda çıkan absorbans değerleri not edilerek canlılık hesaplaması için aşağıda belirtilen formüle göre hesaplama yapılmıştır.

$$\text{Canlılık yüzdesi (\%)} = \frac{\text{Çalışma örneği absorbansı – Blank absorbansı}}{\textit{Kontrol örneği absorbansı – Blank absorbansı}} \times 100$$

Çalışmalar üç kez tekrarlanmıştır (25).

***In vivo* İlaç Direnç Testleri**

Leishmaniasis modeli oluşturmak için kullanılan promastigotlar, 10 mL kültür sıvısının 1500 devirde 10 dakika santrifüjlenip, dipte kalan çökeltinin steril serum fizyolojik ile 3 kez yıkanması ile elde edilmiştir. Promastigot süspansiyonunun son konsantrasyonu 10^8 promastigot/mL olacak şekilde mikroskopta sayılarak ayarlanmıştır. Hayvan modellerinin geliştirilmesinde Balb/C cinsi fareler kullanılmıştır. Fareler dişi, 7-8 haftalık ve 20-25 gr ağırlığında olup, *ad libitum* olarak beslenmişlerdir. Deney hayvanlarının sağ ayak tabanlarına, derialtına 100 µL promastigot solüsyonu enjekte edilmiştir (Resim 5, 6). Enfeksiyonun oluşturulduğu tarihi takip eden 5. haftadan itibaren sağaltımı tamamlanan hastalardan geriye kalan ilaçlar kullanılarak aşağıdaki tedavi şeması uygulanmıştır;

1.Deney Hayvanı Grubu: Enfekte tedavi almayan grup.

2.Deney Hayvanı Grubu: Meglumin antimonat tedavisi alan (Beş değerlikli antimon olan meglumin antimonat 20 mg/kg/gün, 21 gün süreyle her gün intra-muskuler olarak verilmiştir).

3.Deney Hayvanı Grubu: Sodyum stiboglukonat tedavisi alan (Beş değerlikli antimon olan sodyum stiboglukonat 20 mg/kg/gün, 21 gün süreyle her gün intra-muskuler olarak verilmiştir).

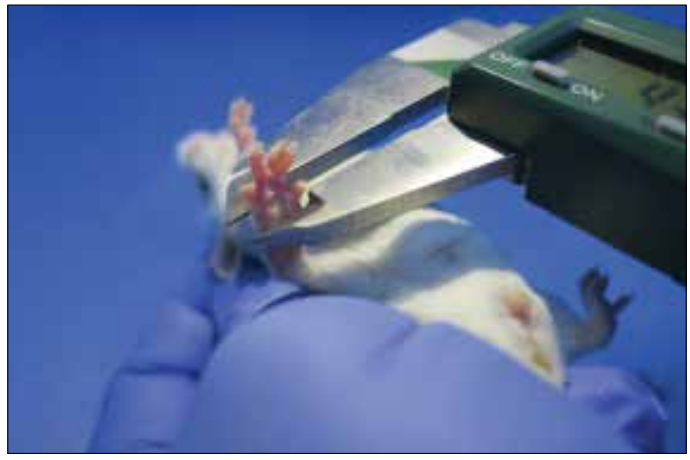
İnokülasyonun 2. haftasından sonra ayak tabanında kızarıklık ve şişme görülebilir (Resim 7). Farelerin lezyonlarının genişliği ve deriden yüksekliği milimetrik ölçüm aleti ile haftada bir ölçülmüştür (Resim 8). Ölçüme 3 ay boyunca devam edilmiştir. İnokülasyondan

Resim 5. Farelerin ayak tabanına intradermal enjeksiyon uygulaması

Resim 6. Farelerin ayak tabanından *L. tropica* promastigotlarının verilmesi

Resim 7. Farelerin ayak tabanında gelişen lezyonların görünümü

3 ay sonra hayvanlar sakrifiye edilmiş ve ayak tabanlarında oluşan lezyonlardan klinik örnek alınarak NNN besiyerlerine ekim yapılmış, yayma preparat hazırlanıp Giemsa ile boyanarak incelenmiş ve *Leishmania* amastigotlarının varlığı araştırılmıştır. *In vivo* ilaç etkinliği; ayak ölçümleri, yayma preparatlar ve besiyeri ekimlerinin sonuçları ile birlikte değerlendirilmiştir (26, 27).



Resim 8. Farelerin ayak tabanı çapının ölçülmesi

Tablo 1. Işık mikroskobunda hemositometre yöntemine göre 48 saatteki parazit sayısı (10^6/mL)

İzolatlar	Doz (µg/mL)					
	300	**200**	**100**	**50**	**25**	**12,5**
İlaçsız kontrol	81,00	81,00	79,00	81,00	80,00	82,00
Glucantime®	0,00	0,00	0,00	0,00	8,00	10,00
Pentostam®	0,00	0,00	0,00	0,00	0,00	0,00

Tablo 2. XTT yöntemi ile 48 saatteki parazitlerin canlılık yüzdeleri (10^6/mL)

İzolatlar	Doz (µg/mL)					
	300	**200**	**100**	**50**	**25**	**12,5**
İlaçsız kontrol	100	100	100	100	100	100
Glucantime®	0	0	0	0	10,8	15,9
Pentostam®	0	0	0	0	0	0

Bu çalışma, T.C. Manisa Celal Bayar Üniversitesi Hayvan Deneyleri Yerel Etik Kurulu'nun 26.04.2017 tarih ve 18931 sayılı kararı ile alınan Etik Kurul Onayı ile gerçekleştirilmiştir.

BULGULAR

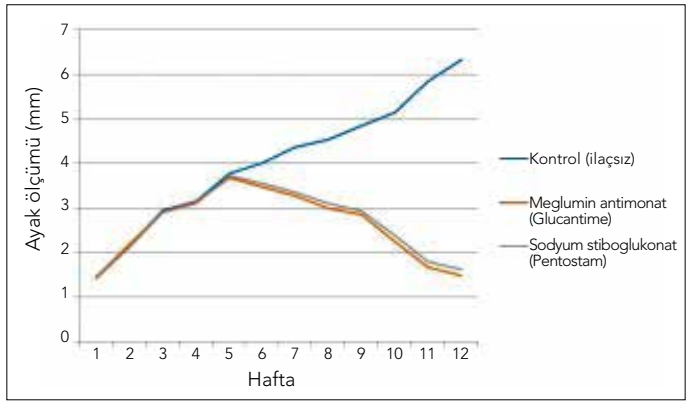
Uygulanan *in vitro* ilaç direnç testlerinin 48 saatteki sonuçları aşağıdaki tablolarda verilmiştir (Tablo 1, 2). Yapılan çalışmalarda ilaçsız kontrol grubundaki promastigotların sağlıklı ve üremelerine devam ettiği görülürken, meglumin antimonat (Glucantime®, Fransa)'ta 25 µg/mL ve 12,5 µg/mL dozda canlı parazitlere rastlandığı ancak sodyum stiboglukonat (Pentostam®, İngiltere)'ta ise hiç canlı parazitin görülmediği saptanmıştır (Tablo 1). Canlılık yüzdelerinin ise meglumin antimonat (Glucantime®, Fransa)'ta 25 µg/mL dozda 10,8 ve 12,5 µg/mL dozda 15,9 olduğu görülmüştür (Tablo 2).

Oluşturulan kutanöz leishmaniasis deney hayvanı modellerinde yapılan *in vivo* çalışmalar sonucunda meglumin antimonat (Glucantime®, Fransa) tedavisi alan ve sodyum stiboglukonat (Pentostam®, İngiltere) tedavisi alan deney hayvanı gruplarında enfeksiyonun verilmesinden sonraki 5. haftadan sonra ayak taba-

Tablo 3. Deney hayvanı gruplarında haftalık milimetrik ayak tabanı ölçümlerinin ortalamaları

	Haftalar											
Kod	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Kontrol (İlaçsız)	1,42	2,15	2,95	3,15	3,78	4,00	4,37	4,53	4,85	5,15	5,85	6,33
Meglumin antimonat (Glucantime®)	1,45	2,18	2,91	3,13	3,68	3,48	3,28	3,00	2,85	2,25	1,68	1,50
Sodyum stiboglukonat (Pentostam®)	1,43	2,13	2,90	3,10	3,72	3,55	3,35	3,10	2,94	2,39	1,79	1,59

nındaki lezyonların küçülmeye başladığı ve 3 aylık süreç sonunda başarılı bir şekilde iyileştiği görülmüştür (Şekil 1). Meglumin antimonat (Glucantime®, Fransa) tedavisi alan deney hayvanı grubunda ayak tabanı çapı 3,68 mm'den 1,50 mm'ye, sodyum stiboglukonat (Pentostam®, İngiltere) tedavisi alan deney hayvanı grubunda ise ayak tabanı çapı 3,72 mm'den 1,59 mm'ye gerilemiştir. Giemsa ile boyalı preparatlarda amastigotlar görülmemiştir. Klinik örneklerin ekildiği NNN besiyerlerinde promastigotlara rastlanmamıştır. İlaçsız kontrol grubunda ise lezyon gelişimi devam etmiş ve ayak tabanı çapı milimetrik ölçümlere göre düzenli olarak daima artmıştır (Tablo 3). Yayma preparatlarda amastigotlar görülmüş ve NNN besiyerinde promastigotlara rastlanmıştır.



Şekil 1. Deney hayvanı gruplarında haftalık ayak tabanı ölçümleri

TARTIŞMA

Leishmaniasis tedavisinde beş değerlikli antimon bileşikleri olan sodyum stiboglukonat (Pentostam®, İngiltere) ve meglumin antimonat (Glucantime®, Fransa) 50 yılı aşkın bir süredir ilk seçenek olarak kullanılmaktadır. Son yıllarda bu ilaçlara karşı tüm dünyada ve özellikle de Hindistan'ın kuzeyinde direncin arttığı bildirilmektedir (28).

Tedavide ikinci seçenek olan Amfoterisin B de damar yoluyla verilmektedir ve böbrekler üzerine belirgin toksisite göstermektedir. Hindistan'daki visseral leishmaniasis'e etkili olduğu gösterilen yeni ajanlar arasında yer alan lipozomal Amfoterisin B ise damar yoluyla kullanılmakta, ancak daha az sayıda enjeksiyon gerektirmekte ve daha iyi tolere edilmektedir, ancak tedavisi oldukça pahalıdır. Diğer yeni ajan olan Miltefosin ise oral yolla kullanılmaktadır, ancak teratojen etki gösterebilmektedir (29). Daha etkili ve sağlıklı ilaçlara ihtiyaç duyulduğundan leishmaniasis konusunda yeni ilaç araştırmalarına gereksinim vardır. Yukarıdaki nedenlerden dolayı, birçok makalede leishmaniasis tedavisinde kullanılma potansiyeli olan doğal bitki ekstrelerinin ve bileşenlerinin anti-leishmanial biyolojik aktivite yönünden tarama programlarının başlaması gerektiği ve yeni tedavi ürünlerinin bulunması gerektiği vurgulanmıştır (30-32).

Yapılan bir çalışmada endemik bir bitki olan *Haplophyllum myrtifolium'* un *in vitro* ve *in vivo* antileishmanial etkinliği değerlendirilmiştir. Bu çalışmada bulunan tüm ekstraktların ve saf bileşiklerin *L. tropica*'nın promastigotlarına karşı *in vitro* inhibitör aktivite gösterdiği bulunmuştur. Promastigotlara karşı γ-fagarin, asitlendirilmiş ekstrat, etanol ekstrat, skimmianin ve alkaloid ekstraktın *in vitro* %50 inhibisyon konsantrasyonları sırasıyla 8,7, 9,4, 10,9, 25,7 ve 25,8 µg/mL olarak bulunmuş ve *Haplophyllum myrtifolium'* un asitleştirilmiş ekstratının in vivo sonuçlarının ise bu bitkinin *Leishmania tropica* ile enfekte deney farelerinde bulunan lezyon boyutunu azaltmada sınırlı bir etkiye sahip olduğunu gösterilmiştir (33).

Yapılan başka bir çalışmada endemik bitkilerden *Centaurea calolepis, Phlomis lycia, Eryngium thorifolium, Origanum sipyleum* ve *Galium incanum ssp. centrale*'den elde edilen ekstraktların in vitro ve in vivo anti-leishmanial aktiviteleri üzerine bir araştırma yapılmış olup *Galium incanum ssp. centrale*'nin IC50 değeri 0,0316±0,005 ug/mL ile en yüksek sitoksisiteyi gösterdiği, *Eryngium thorifolium*'un metanol ekstraktının, 25 µg/mL'de %100 inhibisyon ile *L. tropica* promastigotları üzerinde en yüksek aktiviteye sahip olduğu, *C. calolepis*'in su ve kloroform ekstraktları ile *E. thorifolium*'un su ve metanol ekstraktlarının 100 mg/kg'lık bir dozda *L. tropica* ile enfekte olan farelerdeki parazitemiyi azalttığı saptanmıştır. Bu sonuçlara bağlı olarak parazit canlılığı, sitotoksik olmadığı düşünülen *Eryngium thorifolium*'un metanol ekstraktının *L. tropica* enfeksiyonunun tedavisinde umut verici bir aday ilaç olduğu kanısına varılmıştır (34).

Yapılan bir diğer bir çalışmada ise *Leishmania tropica* üzerine moksifloksasin ve linezolid ile kaspofunginin, potansiyel anti-leishmanial etkileri *in vitro* olarak araştırılmış olup moksifloksasin, linezolid ve kaspofunginin 4096 µg/mL-0,008 µg/mL arasındaki konsantrasyonlarda seri dilüsyonları yapılarak ajanların %50 inhibitör konsantrasyonları (IK50) kontrollerle karşılaştırılarak belirlenmiştir. Moksifloksasinin, *L. tropica* promastigotlarına karşı çalışılan diğer ajanlara göre daha düşük konsantrasyonlarda etkili olduğu sonucuna ulaşılmıştır (35).

Son yıllarda *Leishmania* türlerinin bilinen ilaçların kullanıldığı sağaltıma dirençli suşlarının ortaya çıkmaya başlaması yeni ilaçlar ve yeni ilaç kombinasyonlarının araştırılmasına ihtiyaç doğurmuştur. Dünya Sağlık Örgütü ve birçok araştırmacı, öncelikle halkın yöresel tedavide kullandığı bitkilerin araştırılması gerektiğini vurgulamış, bu sayede doğal bazı bileşiklerin sentetiklerinin de hızla yapılıp leishmaniasis'e karşı kullanılabileceğini belirtmişlerdir (36-38).

Yapılan birçok çalışmada, değişik bitkilerden elde edilen yeni etken madde taramalarında ve yeni ilaç çalışmalarında meglumin antimonat (Glucantime®, Fransa) ve sodyum stiboglukonat (Pentostam®, İngiltere) kontrol ilacı (pozitif kontrol) olarak kullanılıp etken maddenin veya ilacın etkinliğinin karşılaştırılmasında altın standart olarak baz alınmıştır.

In vitro bir çalışmada MTT testi uygulanarak kalsiyum kanal blokörü olan verapamil ve meglumine antimoniate kombinasyonunun meglumine antimonate'a göre promastigot ve amastigotlar üzerine daha etkili olduğu gösterilmiştir (39).

Sodyum stiboglukonat (Pentostam®, İngiltere)'ın *in vitro* ve *in vivo* ilaç direnci ile ilgili yapılan bir çalışmada ikisi sodyum stiboglukonat (Pentostam®, İngiltere) tedavisine yanıt vermeyen ve biri bu tedaviye yanıt veren 3 olgudan elde edilen klinik izolatların enfektivitesi ve kemoterapötik yanıtları *in vitro* olarak makrofaj-amastigot sisteminde ve *in vivo* olarak hamsterlerde değerlendirilmiştir. Sodyum stiboglukonat (Pentostam®, İngiltere) direncinin sürekliliği de tekrarlı pasajlarla *in vivo* ve *in vitro* olarak kontrol edilmiştir. Sodyum stiboglukonat (Pentostam®, İngiltere) tedavisine yanıt vermeyen izolatların Amfoterisin-B ve Miltefosin tedavisine makrofajlarda ve hamsterlerde yanıt verdiği bildirilmiştir (40).

Fare modellerinde yapılan bir çalışmada 100 mg/kg/gün intra-peritoneal olarak Glucantime® ve susam yağı içerisinde hazırlanan thalidomine 30 mg/kg/gün oral olarak 12 gün süreyle tedavi amacıyla verilmiş ve bu kombinasyonun hastalık sürecinde önemli oranda (üç ay) azalmaya neden olduğu saptanmıştır (41). Diğer bir çalışmada enfeksiyonun verilmesinden bir ay sonra 3 fare grubu oluşturulmuş, birinci gruba sodyum selenit (0,35 mg/kg 30 gün), ikinci gruba çinko sülfat (2 mg/kg 30 gün), üçüncü gruba kontrol amaçlı distile su (0,01 mL/gr vücut ağırlığı 30 gün) ve aynı zamanda tüm gruplara intra-peritoneal olarak (60 mg/kg) Glucantime® 14 gün boyunca tedavi amaçlı verilmiştir. Sodyum selenit *in vitro* çalışmalarda kutanöz leishmaniasis üzerine etkili olsa da *in vivo* modelde etkisiz olduğu bulunmuştur. Çinko sülfat ise düşük dozlarda uzun süre kullanıldığında etkisiz olduğu saptanmıştır (42). Bir başka çalışmada lipozomal antimon formulasyonlarının (günde 2 kez 4 hafta süreyle 50 mg topikal olarak) deri içerisindeki makrofajlara ilacın nüfus etmesinde başarılı olduğu, lipozomların meglumin antimonat gibi suda çözünen maddelerin tutulmasını sağladığı, uygun boyutlardaki formulasyonların geliştirilmesi ile ilacın etkili bir şekilde dermis ve epidermise ulaştığı ve lipozomların düşük toksisiteli güvenli bileşikler olduğu gösterilmiştir (43).

Yukarıdaki literatürlerde görüldüğü üzere tedavide altın standart olarak meglumin antimonat (Glucantime®, Fransa) ve sodyum stiboglukonat (Pentostam®, İngiltere)'ın baz alındığı görülmüştür. Bizim çalışmamızda da Türkiye'de KL hastasından elde edilen *L. tropica* suşu üzerine bu iki ilacın da *in vitro* olarak etkili olduğu görülmüştür. Meglumin antimonat (Glucantime®, Fransa)'ta parazitlerin canlılık yüzdelerinin 25 µg/mL dozda 10,8 ve 12,5 µg/mL dozda 15,9 olduğu görülürken, sodyum stiboglukonat (Pentostam®, İngiltere)'ta canlı parazite rastlanmamıştır. Bu nedenle *in vitro* çalışmada sodyum stiboglukonat (Pentostam®, İngiltere)'ın daha etkili olduğu görülmüş fakat istatistiksel olarak anlamlı bulunmamıştır ($p>0,05$). *In vivo* çalışmada ise her iki ilacın da verilmesinden sonra deney hayvanlarının ayak tabanındaki lezyonların küçülmeye başladığı, meglumin antimonat (Glucantime®, Fransa) tedavisi alan deney hayvanı grubunda ayak taban çapının 3,68 mm'den 1,50 mm'ye, sodyum stiboglukonat (Pentostam®, İngiltere) tedavisi alan deney hayvanı grubunda ise 3,72 mm'den 1,59 mm'ye gerilemiş olduğu ve 3 aylık süreç sonunda başarılı bir şekilde iyileştiği görülmüştür. Giemsa ile boyalı preparatlarda amastigotlar görülmemiştir. Klinik örneklerin ekildiği NNN besiyerlerinde promastigotlara rastlanmamıştır. Bu nedenle iki ilacın da Türkiye'de KL olgusundan izole edilen *L. tropica* promastigotları ile oluşturulan *in vivo* modellerde de etkili olduğu saptanmıştır.

SONUÇ

Bu çalışma, bu konularda araştırma yapmayı planlayan araştırmacılara rehber olacak şekilde kutanöz leishmaniasisin *in vitro* ve *in vivo* modelleri oluşturularak ilaç araştırmalarında ve etken madde taramalarında kullanımları ayrıntılarıyla sunularak araştırmacılara yardımcı olması için planlanmıştır. Aldığımız sonuçlar Türkiye'den elde edilecek izolatlarda bu iki ilacın hem *in vitro* hem de *in vivo* çalışmalarda altın standart olarak başarı ile kullanılabileceği görülmüştür.

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Mehmet Akif İnan Eğitim ve Araştırma Hastanesi Mikrobiyoloji Laboratuvarında Ekim 2015-Ekim 2016 Tarihleri Arasında İncelenen Dışkı Örneklerindeki Parazit Dağılımı

Distribution of Intestinal Parasites Detected in Şanlıurfa Mehmet Akif Inan Education and Research Hospital Between October 2015 and October 2016

Koray Öncel

Mehmet Akif İnan Eğitim ve Araştırma Hastanesi, Mikrobiyoloji Laboratuvarı, Şanlıurfa, Türkiye

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ÖZ

Amaç: Ekim 2015-Ekim 2016 arasındaki bir yıllık süreçte, Şanlıurfa Mehmet Akif İnan Eğitim ve Araştırma Hastanesi Mikrobiyoloji Laboratuvarına başvuran toplam 7.353 hasta bağırsak parazitleri açısından değerlendirilmiştir.
Yöntemler: Tüm dışkılara doğrudan bakı (nativ-lugol), formol etil asetat çöktürme ve trikrom boyama yöntemleri uygulanmıştır. Selofan bant tekniği, hastanemizde pediatri kliniği olmadığı için kısıtlı sayıda hastaya tatbik edilebilmiştir.
Bulgular: Toplam 7.353 hastanın 2.322'sinde (%31,6) bir veya daha fazla bağırsak paraziti tespit edilmiştir. Dışkı örneklerinde sıklık sırası ile *Blastocytis* spp. (n=1884; %63,6), *Entamoeba coli* (n=390; %13,2) ve *Giardia intestinalis* (n=169; %5,7) görülmüştür. Parazit görülen olguların 528'inde (%22,7) birden fazla parazit saptanmıştır. Kadınlardaki parazit oranı %30,3 iken erkeklerde %33,4 olarak tespit edilmiştir.
Sonuç: İl bazında bağırsak parazitozları toplum sağlığı açısından halen önemini korumaktadır.
Anahtar sözcükler: Parazit, dağılım, Şanlıurfa
Geliş Tarihi: 10.11.2017 **Kabul Tarihi:** 12.12.2017

ABSTRACT

Objective: A total of 7353 patients who referred to the Microbiology Laboratory of Mehmet Akif Inan Education and Research Hospital between October 2015 and October 2016 were evaluated for intestinal parasites.
Methods: All fecal samples were investigated using three methods: wet mount, formalin ethyl acetate concentration, and trichrome staining. The cellophane tape method could only be used in a limited number of patients owing to the absence of a pediatrics outpatient clinic in our hospital.
Result: One or more intestinal parasites were detected in 2,322 (31.6%) among the 7,353 patients. *Blastocystis* spp. (1,884, 63.6%), *Entamoeba coli* (390, 13.2%), and *Giardia intestinalis* (169, 5.7%) were the most frequently observed parasites in stool samples. Two or more parasites were detected in 528 (22.7%) of the positive cases. The positivity rate was 30.3% among women and 33.4% among men.
Conclusion: Intestinal parasitosis is still significant for community health care in the Şanlıurfa Province
Keywords: Parasite, dissociation, Şanlıurfa
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GİRİŞ

Birçok teknolojik alanda (endüstri, bilişim, yapı, biyomedikal, vb.) her geçen gün önemli ilerlemeler kaydedilmesine rağmen günümüz dünyasında paraziter hastalıklar, özellikle gelişmekte olan ülkelerde ve tüm dünyada yaklaşık 3,5 milyar kişiyi etkilemesi sebebiyle önemli bir sağlık sorunu olmaya devam etmektedir (1).

Genellikle intestinal parazitozların yayılışı; iklim ve çevre koşulları, rezervuar ve ara konakların sıklığı, toprağın ve suların dışkı ile kontaminasyonu, fiziksel alt yapı yetersizlikleri, eğitim düzeyi, ekonomik durum, temizlik ve beslenme alışkanlıkları gibi faktörler ile ilişkilendirilmektedir (2).

Bağırsak parazitlerinin sebep olduğu infeksiyonlarda; karın ağrısı, ishal, kabızlık, bulantı, kusma, kilo kaybı, anemi, alerjik

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reaksiyonlar bulunabildiği gibi özellikle çocuklarda beslenme ve emilim bozukluğunun neden olduğu zihinsel ve bedensel gelişim yetersizliğine yol açabilmektedirler (2).

Ülkemizin subtropikal iklim kuşağında bulunması, ekonomik koşullarının ve eğitim seviyesinin düşük olması, alt yapı eksikliğinin bulunması ve halkımızın paraziter hastalıklar hakkında yeteri kadar bilgi sahibi olmaması paraziter bağırsak infeksiyonlarının yaygınlığının başlıca sebepleri olarak sayılabilir (3, 4).

Bu çalışmada; Şanlıurfa Mehmet Akif İnan Eğitim ve Araştırma Hastanesi mikrobiyoloji laboratuvarına başvuran hastaların dışkı örnekleri bağırsak parazitleri açısından incelenmiş ve retrospektif olarak değerlendirilmiştir.

YÖNTEMLER

Mehmet Akif İnan Eğitim ve Araştırma Hastanesi Mikrobiyoloji Laboratuvarı'na 01.10.2015-27.10.2016 tarihleri arasında başvuran toplam 7.353 hastanın dışkı örnekleri bağırsak parazitleri yönünden incelenmiştir.

Bu çalışma için etik kurul onayı Harran Üniversitesi Tıp Fakültesi Etik Kurulu'ndan alınmıştır (08.06.2017 tarih, 06 no'lu oturum, 16 sayılı karar).

Tüm dışkı örnekleri makroskobik ve mikroskobik (nativ-lugol X400 büyütme) olarak değerlendirilmiş ek olarak yoğunlaştırma metodu (%10 formol-etil asetat X400 büyütme) uygulanmıştır. Şüpheli yapıların tanımlanması amacı ile de trikrom kalıcı boyama yöntemi de üçüncü yöntem olarak (X1000 büyütme) uygulanmıştır (5-7).

Çocuk hastalıkları polikliniği olmayan hastanemizde, klinisyen hekimler araştırma yöntemi olarak selofan bant yöntemini çok kısıtlı sayıda tercih etmişlerdir.

Blastocystis spp. için önemli bir patojenite kriteri olan; X400 büyütmede her mikroskop sahasında beş ve üstünde parazitin görülmesi halinde rapor edilmiş olup, patojen olmayan bağırsak parazitleri toplumun hijyen algısı hakkında fikir vermesi açısından değerlendirilmiştir (8).

İstatistiksel Analiz

Elde edilen verilerin istatistiksel analizi için Pearson Chi-Square testi kullanılmıştır. Tüm istatistiksel analizlerde $p<0,05$ anlamlılık değeri olarak kabul edilmiştir.

BULGULAR

Laboratuvarımıza başvuran 7353 hastanın 2322'sinde (%31,6) bağırsak parazitlerine rastlanmış olup, 528 hastada (%22,7) birden fazla parazit tespit edilmiştir. Parazitlerin yaş gruplarına göre dağılımı Tablo 1'de, cinsiyete göre dağılımı Tablo 2'de verilmiştir. Birden fazla parazit saptanan hastalardaki parazit kombinasyonları ve sayısal dağılımları Tablo 3'te verilmiştir.

Laboratuvara başvurmuş olan 7.353 hastanın 4.428'i (%60,2) kadın, 2.925'i (%39,8) erkek olup, parazit saptanan 2.322 hastanın ise 1.345'i (%57,9) kadın, 977'si (%42,1) erkektir. Tespit edilen 2.961 parazitin cinsiyete göre dağılımı ise; kadınlarda 1.717 (%58,0) erkeklerde 1.244 (%42,0) adet olmuştur. Parazit saptanan kadın ve erkeklerin kendi cinsleri içindeki oranları sırası ile %30,3 ve %33,4 olarak tespit edilmiştir. Parazit görülme sıklığı erkek hastalarda istatistiksel olarak anlamlı şekilde yüksek bulunmuştur ($p=0,006$).

Tespit edilen parazitler içinde protozoonlar 2.915 (%98,5), helmintler ise 46 (%1,5) adet bulunmuştur. Parazitlerin içerisinde en sık görüleni *Blastocystis* spp. olup; 1.306 adet non-patojen, 578

Tablo 1. Parazitlerin yaş aralıklarına göre dağılımı

Yaş	<20		20-30		30-40		40-50		50-60		>60		Toplam	
Parazit	**Sayı**	**%**	**Sayı**	**%**	**Sayı**	**%**	**Sayı**	**%**	**Sayı**	**%**	**Sayı**	**%**	**Sayı**	**%**
Blastocystis spp.(*)	186	6,3	334	11,3	220	7,4	193	6,5	204	6,9	169	5,7	1306	44,1
Blastocystis spp.	78	2,6	152	5,1	110	3,7	76	2,7	77	2,6	85	2,9	578	19,5
Giardia intestinalis	57	1,9	50	1,7	26	0,9	16	0,5	12	0,4	8	0,3	169	5,7
Dientamoeba fragilis	12	0,4	17	0,6	23	0,9	13	0,4	11	0,4	12	0,4	88	3,0
Entamoeba histolytica/dispar	1	0,0	1	0,0	1	0,0	-	-	2	0,1	2	0,1	7	0,2
Hymenolepis nana	11	0,4	10	0,3	1	0,0	-	-	-	-	-	-	22	0,7
Taenia spp.	1	0,0	6	0,2	3	0,1	3	0,1	1	0,0	2	0,1	16	0,5
Enterobius vermicularis	3	0,1	2	0,1	-	-	-	-	2	0,1	1	0,0	8	0,3
Entamoeba coli	42	1,4	81	2,7	89	3,0	56	1,9	65	2,2	57	1,9	390	13,2
Endolimax nana	13	0,4	28	0,9	15	0,5	14	0,5	8	0,3	15	0,5	93	3,1
Chilomastix mesnili	5	0,2	13	0,4	13	0,4	12	0,4	20	0,7	24	0,8	87	2,9
Iodomoeba bütschlii	5	0,2	13	0,4	12	0,4	7	0,2	10	0,3	5	0,2	52	1,8
Entamoeba hartmanni	10	0,3	15	0,5	11	0,4	14	0,5	14	0,5	11	0,4	75	2,5
Trichomonas hominis	2	0,1	2	0,1	2	0,1	3	0,1	2	0,1	1	0,0	12	0,4
Retortamonas intestinalis	2	0,1	1	0,0	3	0,1	-	-	2	0,1	4	0,1	12	0,4
Enteromonas hominis	5	0,2	8	0,3	4	0,1	11	0,4	9	0,3	9	0,3	46	1,6
Toplam	433	14,6	733	24,8	533	18,0	418	14,1	439	14,8	405	13,7	2961	100

Blastocystis spp. için önemli bir patojenite kriteri olan; X400 büyütmede her mikroskop sahasında beş ve üstünde parazitin görülmediği hasta sayısı

Tablo 2. Parazitlerin cinsiyete göre dağılımı

Parazit	Kadın		Erkek	
	Sayı	%	Sayı	%
Blastocystis spp.(*)	761	25,7	545	18,4
Blastocystis spp.	327	11,0	251	8,5
Giardia intestinalis	87	2,9	82	2,8
Dientamoeba fragilis	55	1,9	33	1,1
Entamoeba histolytica/dispar	2	0,0	5	0,2
Hymenolepis nana	6	0,2	16	0,5
Taenia spp.	13	0,4	3	0,1
Enterobius vermicularis	3	0,1	5	0,2
Entamoeba coli	245	8,3	145	4,9
Endolimax nana	50	1,7	43	1,5
Chilomastix mesnili	54	1,8	33	1,1
Iodomoeba bütschlii	26	0,9	26	0,9
Entamoeba hartmanni	47	1,6	28	0,9
Trichomonas hominis	3	0,1	9	0,3
Retortamonas intestinalis	8	0,3	4	0,1
Enteromonas hominis	30	1,0	16	0,5
Toplam	1717	58,0	1244	42,0

Blastocystis spp. için önemli bir patojenite kriteri olan; X400 büyütmede her mikroskop sahasında beş ve üstünde parazitin görülmediği hasta sayısı

Tablo 3. Birden fazla parazit saptanan hastalarda tür ve sayısal dağılım

Parazit	Olgu sayısı	Parazit sayısı
Blastocystis spp.+ Entamoeba coli	170	340
Blastocystis spp.+ Giardia intestinalis	40	80
Blastocystis spp.+ Endolimax nana	31	62
Blastocystis spp.+ Entamoeba hartmanni	27	54
Blastocystis spp.+ Trichomonas hominis	2	4
Blastocystis spp.+ Chilomastix mesnili	28	56
Blastocystis spp.+ Dientamoeba fragilis	39	78
Blastocystis spp.+ Iodomoeba bütschlii	17	34
Blastocystis spp.+ Hymenolepis nana	5	10
Blastocystis spp.+ Taenia spp.	2	4
Blastocystis spp.+ Entamoeba histolytica/dispar	3	6
Blastocystis spp.+ Retortamonas intestinalis	3	6
Blastocystis spp.+ Enteromonas hominis	9	18
Blastocystis spp.+ Enterobius vermicularis	1	2
Giardia intestinalis + Hymenolepis nana	3	6
Giardia intestinalis + Entamoeba coli	3	6
Giardia intestinalis + Trichomonas hominis	1	2
Giardia intestinalis + Iodomoeba bütschlii	2	4
Giardia intestinalis +Endolimax nana	2	4

Tablo 3. Birden fazla parazit saptanan hastalarda tür ve sayısal dağılım (devamı)

Parazit	Olgu sayısı	Parazit sayısı
Dientamoeba fragilis + Entamoeba coli	1	2
Dientamoeba fragilis + Chilomastix mesnili	2	4
Entamoeba coli + Endolimax nana	6	12
Entamoeba coli + Chilomastix mesnili	6	12
Entamoeba coli + Iodomoeba bütschlii	4	8
Entamoeba coli + Entamoeba hartmanni	1	2
Entamoeba coli + Retortamonas intestinalis	1	2
Entamoeba coli + Enteromonas hominis	6	12
Entamoeba coli + Taenia spp.	1	2
Endolimax nana + Iodomoeba bütschlii	1	2
Chilomastix mesnili + Endolimax nana	2	4
Iodomoeba bütschlii + Trichomonas hominis	1	2
Entamoeba hartmanni + Endolimax nana	1	2
Entamoeba hartmanni + Enterobius vermicularis	1	2
Entamoeba hartmanni + Iodomoeba bütschlii	1	2
Blastocystis spp.+ Entamoeba coli + Endolimax nana	13	39
Blastocystis spp.+ Entamoeba coli + Chilomastix mesnili	15	45
Blastocystis spp.+ Entamoeba coli + Entamoeba hartmanni	3	9
Blastocystis spp.+ Entamoeba coli + Trichomonas hominis	1	3
Blastocystis spp.+ Entamoeba coli + Iodomoeba bütschlii	4	12
Blastocystis spp.+ Entamoeba coli + Enteromonas hominis	3	9
Blastocystis spp.+ Entamoeba coli + Retortamonas intestinalis	1	3
Blastocystis spp.+ Giardia intestinalis + Endolimax nana	1	3
Blastocystis spp.+ Giardia intestinalis + Iodomoeba bütschlii	1	3
Blastocystis spp.+ Giardia intestinalis + Entamoeba coli	6	18
Blastocystis spp.+ Giardia intestinalis + Enteromonas hominis	1	3
Blastocystis spp.+ Giardia intestinalis + Entamoeba hartmanni	2	6
Blastocystis spp.+ Dientamoeba fragilis + Entamoeba coli	3	9
Blastocystis spp.+ Dientamoeba fragilis + Endolimax nana	4	12
Blastocystis spp.+ Dientamoeba fragilis + Chilomastix mesnili	3	9
Blastocystis spp.+ Dientamoeba fragilis + Iodomoeba bütschlii	1	3

Tablo 3. Birden fazla parazit saptanan hastalarda tür ve sayısal dağılım (devamı)

Parazit	Olgu sayısı	Parazit sayısı
Blastocystis spp.+ Dientamoeba fragilis + Taenia spp.	1	3
Blastocystis spp.+ Dientamoeba fragilis + Retortamonas intestinalis	2	6
Blastocystis spp.+ Dientamoeba fragilis + Trichomonas hominis	1	3
Blastocystis spp.+ Endolimax nana+ Entamoeba hartmanni	4	12
Blastocystis spp.+ Chilomastix mesnili + Endolimax nana	1	3
Blastocystis spp.+ Chilomastix mesnili + Retortamonas intestinalis	1	3
Blastocystis spp.+ Chilomastix mesnili+ Entamoeba hartmanni	2	6
Blastocystis spp.+ Iodomoeba bütschlii.+ Chilomastix mesnili	1	3
Blastocystis spp.+ Iodomoeba bütschlii.+ Entamoeba hartmanni	2	6
Blastocystis spp.+ Iodomoeba bütschlii.+ Enteromonas hominis	1	3
Blastocystis spp.+ Taenia spp. + Chilomastix mesnili	2	6
Blastocystis spp + Entamoeba histolytica/dispar+ Endolimax nana	2	6
Blastocystis spp + Entamoeba hartmanni+ Hymenolepis nana	1	3
Blastocystis spp.+ Enterobius vermicularis + Entamoeba coli	1	3
Giardia intestinalis + Dientamoeba fragilis+ Endolimax nana	1	3
Giardia intestinalis + Entamoeba coli + Endolimax nana	1	3
Dientamoeba fragilis + Chilomastix mesnili+ Endolimax nana	2	6
Entamoeba coli + Endolimax nana.+ Iodomoeba bütschlii	1	3
Entamoeba coli + Trichomonas hominis+ Retortamonas intestinalis	1	3
Blastocystis spp.+ Giardia intestinalis + Entamoeba coli+ Endolimax nana	1	4
Blastocystis spp.+ Giardia intestinalis + Entamoeba coli+ Enteromonas hominis	1	4
Blastocystis spp.+ Dientamoeba fragilis + Endolimax nana+ Chilomastix mesnili	1	4
Blastocystis spp.+ Entamoeba coli + Chilomastix mesnili + Entamoeba hartmanni	1	4
Blastocystis spp.+ Entamoeba coli + Enteromonas hominis+ Entamoeba hartmanni	1	4
Blastocystis spp.+ Entamoeba coli + Hymenolepis nana + Trichomonas hominis	1	4
Blastocystis spp.+ Entamoeba coli + Endolimax nana + Retortamonas intestinalis	1	4
Blastocystis spp.+ Entamoeba coli + Endolimax nana + Chilomastix mesnili	1	4
Blastocystis spp.+ Entamoeba coli + Iodomoeba bütschlii + Entamoeba hartmanni	4	16
Blastocystis spp.+ Endolimax nana+ Chilomastix mesnili+ Enteromonas hominis	1	4
Blastocystis spp.+ Iodomoeba bütschlii + Chilomastix mesnili + Retortamonas intestinalis	1	4
Blastocystis spp.+ Iodomoeba bütschlii + Entamoeba hartmanni+ Retortamonas intestinalis	1	4
Toplam	528	1176

adet patojen, toplamda 1.884 (%63,6) adet ile ilk sırada yer almıştır. İkinci sıklıkta görülen parazit 390 (%13,2) adet ile *Entamoeba coli*, üçüncü sıklıkta görülen parazit ise *Giardia intestinalis* 169 (%5,7) olmuştur (Resim 1).

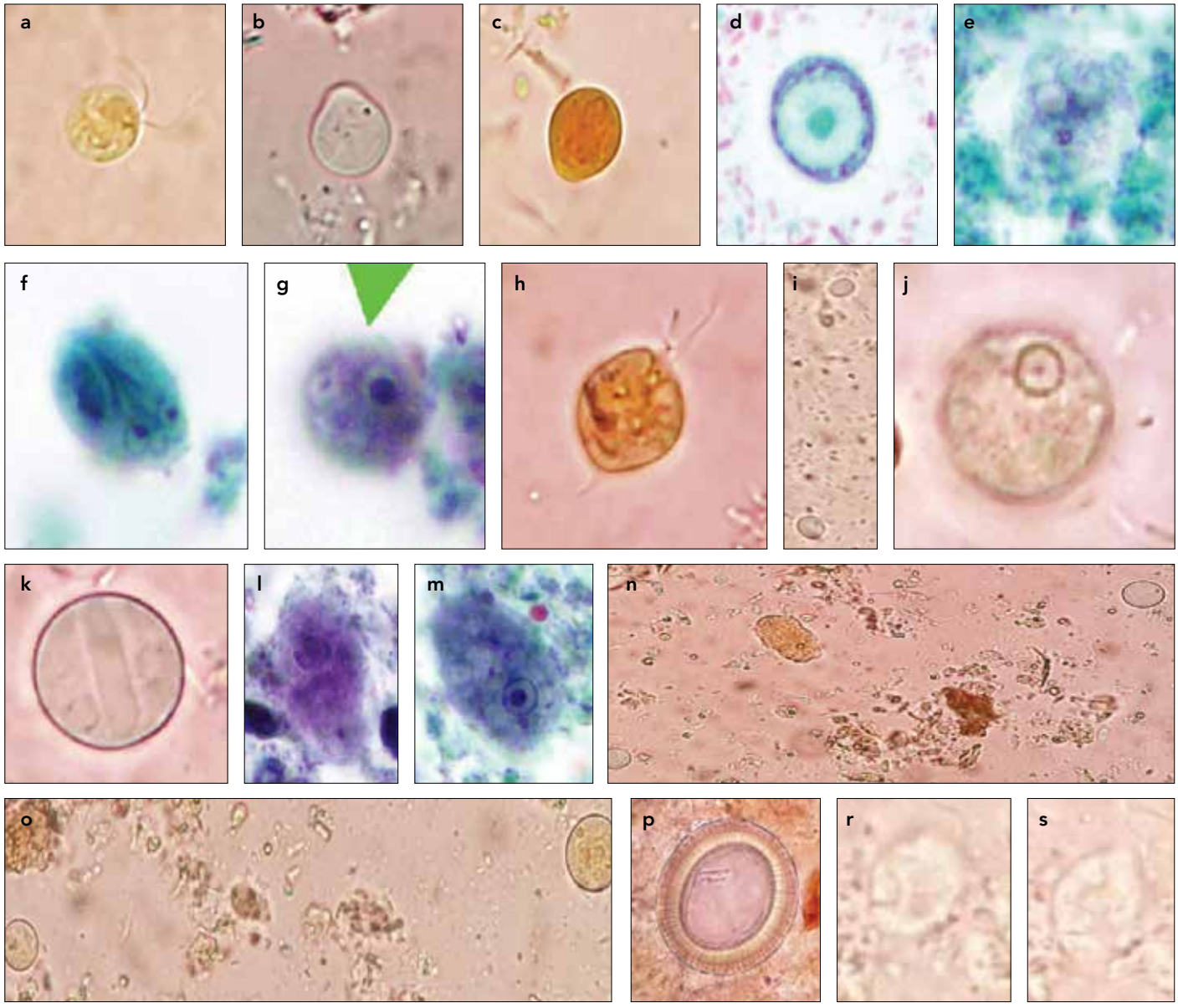
Birden fazla parazitin tespit edildiği 81 kombinasyon görülmüş olup, 528 hastada toplam 1.176 parazite karşılık gelmiştir. Genel toplam ile kıyaslandığında parazit saptanan hastaların %22,7'sini, tespit edilen parazit sayısının %39,7'sini oluşturmaktadır.

Parazit tespit edilen hastaların il içindeki demografik dağılımlarına bakıldığında; başvuru yapan hastalar Merkez İlçe (Karaköprü, Haliliye, Eyyübiye ve merkeze bağlı köyler), diğer ilçeler, il dışı gelenler ve yabancı uyruklular (Suriye ve Irak) olmak üzere sınıflandırılmıştır. Merkez İlçe'den başvuran 5346 hastanın 1594'ünde (%29,8) parazit saptanırken, çevre ilçelerden gelen 1494 hastanın 569'unda (%38,0) parazit saptanmıştır. Parazit görülme sıklığı çevre ilçelerden gelen hastalarda istatistiksel olarak anlamlı şekilde yüksek bulunmuştur (p=0,006). İl dışından gelen 267 hastanın 92 (%34,5)'sinde parazit tespit edilirken, 1'i Irak'lı-245'i Suriye'li olmak üzere 246 yabancı uyruklu hastanın 67'sinde (%27,2) parazit tespit edilmiştir. Demografik dağılıma ait ayrıntılı döküm Tablo 4'te verilmiştir. Şanlıurfa ilinin ilçelerini gösteren harita Resim-2'de verilmiştir.

TARTIŞMA

Birçok ülkede ve ülkemizde yapılan çok sayıdaki epidemiyolojik çalışmada; ülkeler arası, hatta aynı ülkenin farklı bölgelerinde parazit tür, sayı ve oranları farklılık gösterebilmektedir. Bu değişkenlik toplumun sosyo-ekonomik düzeyine, yaşam tarzına, hijyen algısına, çalışma gruplarının oluşturuluş biçimine ve seçilen inceleme yöntemlerine bağlı olabilmektedir (9-11).

Son 15 yıl içinde ülkemizde yapılan birçok çalışmada gastrointestinal sistem kaynaklı parazitozlarda en yüksek ve en düşük oranlar sırası ile %39 ve %4,2 olarak bildirilmiştir (11, 12). Çalışmamızda bu oran %31,6 olarak bulunmuş olup bağırsak parazitozlarının Şanlıurfa ilinde önemli bir sorun olmaya devam ettiğini göstermektedir.



Resim 1. a-s. *Retortamonas intestinalis* (a), *Chilomastix mesnili* (b), *C. mesnili* (c), *Blastocystis spp.* (d), *Dientamoeba fragilis* (e), *Giardia intestinalis* (f), *Endolimax nana* (g), *Enteromonas hominis* (h), *E. hominis* (i), *Entamoeba hartmanni* (j), *E. hartmanni* (k), *Entamoeba coli* (l), *Entamoeba histolytica/Entamoeba dispar* (m), *Entamoeba coli* ve *Entamoeba hartmanni* (n), *Entamoeba coli* ve *Entamoeba hartmanni* (o), *Taenia* spp. yumurta (p), *Trichomonas hominis* (r), *T. hominis* (s)

Bu süreç içerisinde ülkemizin muhtelif yerlerinde yapılan çalışmaların bir kısmında; *Blastocytis* spp. ve *Giardia intestinalis* birinci ve ikinci sıklıkta (1, 2, 13), bir kısmında *G. intestinalis* ve *Enterobius vermicularis* birinci ve ikinci sıklıkta (12, 14-16), bir kısmında da *Blastocytis* spp., *G. intestinalis*, *E. coli* ve *E. vermicularis* olmak üzere farklı kombinasyonlarda ilk iki sırayı almıştır (9-11, 17, 18). Diğerlerinden farklı olarak *Cryptosporidium* spp.'nin ilk sırada yer aldığı tek bir yayın bulunmaktadır (19). Yapmış olduğumuz çalışmada ilk iki sırayı %63,6 ile *Blastocytis* spp. ve %13,2 ile *E.coli* almıştır.

Bulunduğumuz ili kapsayan daha önceki bir çalışmada, Zeyrek ve ark. (20) 1998 ve 2001 yılının ilk altı ayı arasında sırası ile yıllara göre %38-%34,79-%34,89 ve 2001'in ilk altı ayında %30,68 oranında, yılların ortalaması alındığında ise %34,86 oranında dışkıda parazit tespit etmişlerdir. En sık görülen ilk iki parazit sırası ile %51,38 ile *Ascaris lumbricoides* ve %20,65 ile *G. intestinalis* olmuştur. Aynı ilde bizim çalışmamızdan yaklaşık yirmi yıl önce yapılan bu çalışmada da parazit görülme sıklığı hemen hemen aynı oranlarda iken, ilk çalışmada görülen yüksek oranlardaki helmintoz bulguları yapmış olduğumuz çalışmada yerini protozoonlara bırakmış görülmektedir. Parazit türlerindeki bu denli değişimi, ilk çalışmada Trikrom boyama yönteminin kullanılmamış olması, bizim çalışmamızda çok az sayıda çocuk hastanın incelenmesi, yaklaşık yirmi yıl öncesinde toplumun hijyen algısındaki eksikler ile yaşam standartlarına bağlı olarak insan dışkısı ile temasın büyük ölçüde önlenmiş olması bir dereceye kadar açıklamak mümkün görünmektedir.

Tablo 4. Parazit tespit edilen hastaların demografik dağılımı

Yerleşim yeri	Parazit tespit edilmeyen (sayısal)	Parazit tespit edilen (sayısal)	Toplam (sayısal)	Parazit tespit edilen (%) İlçe bazında
Merkeze bağlı köyler	476	945	1421	33,49
Merkez (Eyyübiye)	418	903	1321	31,64
Merkez (Haliliye)	569	1498	2067	27,52
Merkez (Karaköprü)	131	406	537	24,39
Suruç	57	89	146	39,0
Viranşehir	89	144	233	38,19
Harran	70	125	195	35,89
Siverek	101	163	264	38,25
Bozova	64	100	164	39,0
Birecik	5	12	17	29,4
Akçakale	78	142	220	35,45
Ceylanpınar	28	60	88	31,8
Hilvan	74	89	163	45,39
Halfeti	3	1	4	75,0
Diğer iller	92	175	267	34,45
Yabancı uyruklu	67	179	246	27,2
Toplam (sayısal)	2322	5031	7353	

Resim 2. Şanlıurfa il ve ilçeleri haritası

Çalışmamızda parazit saptanan kadın ve erkeklerin kendi cinslerindeki içindeki oranları sırası ile %30,3 ve %33,4'tür. Parazit görülme sıklığı erkek hastalarda istatistiksel olarak anlamlı şekilde yüksek bulunmuştur (p=0,006). Birçok çalışmada cinsiyet bazlı analizler yapılmış olup, yayınların çoğunluğunda erkeklerde bağırsak parazitozlarının daha sık görüldüğü (1, 2, 9, 11, 13-15, 19) tespit edilmiştir.

Hastanemizde çocuk hastalıkları polikliniği olmadığı için çocuk ve erişkin gibi yaşa bağlı bir kıyaslama yapma şansımız olmamıştır. Ancak, verilerimiz bağırsak parazitlerinin en sık 20-30 yaş aralığında (%24,8) olduğunu göstermektedir.

Çalışmamızda, bağırsak parazitozu saptanan olguların %77,3'ünde tek bir paraziter etken, %22,7'sinde ise birden fazla etken saptanmıştır. Yerli ve yabancı bazı çalışmalarda da bulgularımıza benzer bir şekilde paraziter etkenlerin çoğunlukla tek başına görüldüğü bildirilmiştir (21-23). Buna göre parazitozlara daha çok tek bir paraziter etkenin sebep olduğunu söylemek mümkündür. Bununla birlikte çalışmamızda olguların %22,7'si, total parazit sayısının %39,7'si gibi yüksek rakamlar, öncelikli olarak toplumun hijyen algısındaki eksiklikleri göstermekte, ayrıca inceleme esnasındaki yöntemlerin ve sürenin optimal düzeyde değerlendirilmesi gerektiği konusunda da fikir vermektedir.

Çalışmamızda, parazit tespit edilen hastaların il içindeki demografik dağılımlarına bakıldığında; Merkez İlçeler (Karaköprü, Haliliye, Eyyübiye ve merkeze bağlı köyler) olarak kabul ettiğimiz yerleşim birimlerinden başvuran 5346 hastanın 1594'ünde (%29,8) parazit saptanırken, çevre ilçelerden gelen 1494 hastanın 569'unda (%38,0) parazit saptanmıştır. Parazit görülme sıklığı çevre ilçelerden gelen hastalarda istatistiksel olarak anlamlı şekilde yüksek bulunmuştur (p=0,006). Büyükşehir olduktan sonra Merkeze bağlanan köylerden başvuran hastalarda parazit oranı %33,49 ile Merkez İlçelerdeki en yüksek oranı oluştururken, yaklaşık 10 sene içinde hızla büyüyen ve yapılaşan yeni yerleşim birimi Karaköprü İlçesinde ise bu oran %24,39 ile Merkezdeki en düşük oranı oluşturmuştur. Bu farklılıkta Merkeze bağlanmalarına rağmen köylerin altyapı sorunlarının tam olarak giderilememesi ve hijyen algısındaki eksiklikler/farklılıkların etki edebileceği düşünülmektedir. Çevre ilçelere baktığımızda Birecik ve Halfeti ilçeleri konum olarak Gaziantep'e yakınlığı nedeniyle toplamda 21 hasta ile en az hastanın geldiği ilçeler olup istatistiksel anlamda sağlıklı bir yorum yapılamamıştır. Diğer ilçelerde Hilvan %45,39 ile en yüksek oranı teşkil ederken, %31,8 ile %39 arasında değişen oranlarda parazitoz saptanmıştır. İl dışından gelen 267 hastanın 92'sinde (%34,5) parazit tespit edilirken, bu hastaların

belli bir süre aralığı (misafir, ziyaret veya gezi, vb.) için mi yoksa Şanlıurfa ilinde daimi ikamette olup olmadıkları ile net bir bilgiye sahip olunamamıştır. Eğer belli bir süre aralığı için gelmişler ise bağırsak parazitozlarının genel anlamda Türkiye'nin birçok bölgesinde halen önemli bir sağlık sorunu olduğuna dair fikir verdiğini söyleyebiliriz. 1'i Irak'lı-245'i Suriye'li olmak üzere 246 yabancı uyruklu hastanın 67'sinde (%27,2) parazit tespit edilmiştir. İlginç olan bir şekilde onca problem/badire atlatan bu hastalarda parazit oranlarının yerleşik halka oranla düşük çıkmasıdır. Belki başvuran Suriye'li hastaların büyük bir kısmı kamplardan değil de 3-5 senedir Şanlıurfa ilinde yerleşik hayata geçenlerden gelmiş olabilir. Hastane bilgi sisteminde sadece uyruk belirtilip adres bilgisi yer almadığından dolayı sağlıklı bir değerlendirme yapılamamıştır.

SONUÇ

Bilişim ve teknoloji çağında evrilmekte olan bir toplumda hala bağırsak parazitozlu olgu sayısı rakamsal olarak %31,6 düzeyinde ise o toplumun hijyen algısı ile ilgili olarak ciddi yanlışlar ve bilgi eksiklikleri bulunduğu düşünülebilir. Her ne kadar çocuk hastalar bu çalışma içinde yer almamış ya da minimal düzeyde dahil edilmişse de, bağırsak helmintozlarının çok düşük seviyelerde kalması hiç olmazsa epidemiyolojik olarak insan kaynaklı helmintozlarda önemli bulaş yollarından insan dışkısı ile temasın bir ölçüde engellendiğini göstermektedir. Belediyeler olarak katı ve sıvı atık projelerine önem verilmesi, alt yapı eksikliklerinin giderilmesi, tarımda eski yöntemlerin terk edilmesi ve insan dışkısının gübre olarak kullanılmıyor olması, ayrıca beslenme alışkanlıklarımızdaki yanlışlardan (çiğ et ve türevlerinin tüketilmesi) kaçınılması bağırsak helmintozlarındaki düşüşü anlamlı kılmaktadır. Bu konuda daha sağlıklı veriler edinilebilmesi amacıyla toprakla daha çok temas eden ve hijyen algısı tam oluşmamış çocuklarda bağırsak parazitleri değerlendirilmelidir.

Kurumsal bazda görülen olumlu değişikliklere paralel olarak hijyen algısı ile ilgili toplum bazında farkındalık yaratmak amacıyla verilecek eğitimlerin en ucuz ve etkili yöntemler olacağı açıktır.

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Haemogregarine Genetic Diversity in Captive African Rock Pythons from Nigeria Suggests a Geographical Pattern

Nijerya'daki Afrika Kaya Pitonlarındaki Hemogregarin Genetik Çeşitlilik Coğrafik Bir Paterni Göstermektedir

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ABSTRACT

Objective: Understanding the processes that drive parasite diversification, distribution, and abundance is central to disentangle the dynamics and evolution of diseases. In this study, we screened African rock pythons from Nigeria for the presence of blood parasites to assess their distribution, diversity, and phylogenetic relationships.
Methods: A total of 21 captive African rock pythons collected from across 11 locations in Nigeria were sampled between August 2016 and January 2017. Samples were microscopically and genetically analyzed.
Results: From the blood smears analyzed, 10 (47.6%) snakes were found to be infected with haemogregarines. Eight of the infected samples were genetically assessed and confirmed as haemogregarines of the recently described *Bartazoon* group. Two haplotypes were retrieved, of which one was distributed in the northern-central sampled localities and the other in the southern localities. The two haplotypes were clustered in a clade of haemogregarines from snake, gecko, and rodent hosts, and among them, the haemogregarine species *Hepatozoon ayorgbor* was described from the ball python *Python regius*.
Conclusions: Two haemogregarine haplotypes in Nigerian rock pythons, which appear to have a geographical pattern across the country, were detected in this study.
Keywords: Hemoparasites, apicomplexa, haemogregarines, snake, African rock python, phylogenetic analysis, Africa
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ÖZ

Amaç: Parazit diversifikasyonu, dağılımı ve bolluğunu yönlendiren süreçlerin anlaşılması hastalıkların dinamikleri ve evrimlerini çözmek için önemlidir. Bu çalışmada Nijerya'daki Afrika kaya pitonları dağılım, çeşitlilik ve filogenetik ilişkilerini değerlendirmek amacıyla kan parazitlerinin varlığı açısından incelendiler.
Yöntemler: Ağustos 2016 ile Ocak 2017 arasında Nijerya'daki 11 farklı bölgeden alınan 21 Afrika kaya pitonu örneklendirildiler. Örnekler mikroskopik ve genetik olarak analiz edildiler.
Bulgular: Kan yayma analizlerinde 10 pitonun (%47,6) hemogregarinler tarafından enfekte oldukları bulundu. Enfekte numunelerin sekizi genetik açıdan değerlendirildi ve son zamanlarda tanımlanan *Bartazoon* grubunun hemogregarinleri olarak konfirme edildiler. İki haplotip yeniden kazanıldı. Bunlardan birisi kuzey-merkez bölgelerde ve diğeri de güney bölgelerde dağılım gösterdi. İki haplotip yılan, geko ve kemirgen konaklardan alınan bir hemogregarin türünde kümelendiler. Bunlardan hemogregarin cinsi *Hepatozoon ayorgbor* top pitondan *(Python regius*) tanımlandı.
Sonuç: Bu çalışmada Nijerya kaya pitonlarında, tüm ülkede coğrafik bir paterninin olduğu görülen iki hemogregarin haplotipi tespit edildi.
Anahtar sözcükler: Hemoparazitler, apicomplexa, hemogregarinler, yılan, Afrika kaya pitonu, filogenetik analiz, Afrika
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INTRODUCTION

The phylum Apicomplexa is notable for its high medical and veterinary importance, particularly owing to the impacts of *Plasmodium*, *Babesia*, and *Toxoplasma* among others (1). Regardless of this, the knowledge on the taxonomical diversity of this phylum remains relatively limited. It has been estimated that only 0.1% of the Apicomplexan species have been described (2). Moreover, within this percentage, there is a bias in studies toward a few genera, being even less known regarding the parasites of wild hosts, including their identity, evolutionary relations, and ecology (3). Having this basic information could greatly improve the conservation efforts of hosts as well as increase the overall knowledge on Apicomplexa. Haemogregarines are geographically ubiquitous parasites that infect all groups of terrestrial vertebrates and an array of hematophagous arthropods (4). They present various life cycles, which usually involve an invertebrate vector as the definitive host and a vertebrate as the intermediate host but might also include other vertebrates as paratenic hosts upon whom the intermediate hosts prey. The use of prey–predator networks by these parasites has been shown by experimental transmission studies (5, 6) and supported by phylogenetic assessments (7). However, other factors, such as vertebrate host distribution, habits, and relatedness and their exposition to vectors have also been suggested to play a role in shaping the presence, frequency, and diversity of haemogregarines in host communities (7-9). Recent phylogenetic studies have also identified taxonomical incongruences, suggesting that the taxonomy of terrestrial haemogregarines should be rearranged and divided into four genera: *Hepatozoon*, *Hemolivia*, *Karyolysus*, and the newly created *Bartazoon* (10). Members from all these four genera have been found infecting reptiles; haemogregarines are one of the most commonly reported blood parasites, particularly in reptiles (1). Although haemogregarines are generally considered apathogenic in reptiles, the degree of the effect differs among studies, from no apparent effect to severe health effects (11). In this study, we screened African rock pythons from Nigeria for the presence of these parasites to assess their distribution, diversity, and phylogenetic relationships.

METHODS

Sampling

A total of 21 captive African rock pythons from 11 locations in the northern, central, and south-western parts of Nigeria across eight states were sampled between August 2016 and January 2017 (Figure 1a for the sampling map). Each snake was subjected to physical and clinical examinations, sexed, weighed, and measured. Blood was collected from the ventral coccygeal vein, as described by Lock (12), and stored in heparinized tubes for later use. Blood smears were examined for parasite detection using a light microscope. In ophidian hosts, haemogregarines are easily detected by observing their stages inside red blood cells (1). Photomicrographs were taken using a Magnus Fixed microscope adapter (FMA050 3MP) attached to a computer (MagnusPro 3.7 software). Blood from infected pythons was transferred to Whatman Flinders Technology Associates cards for molecular identification.

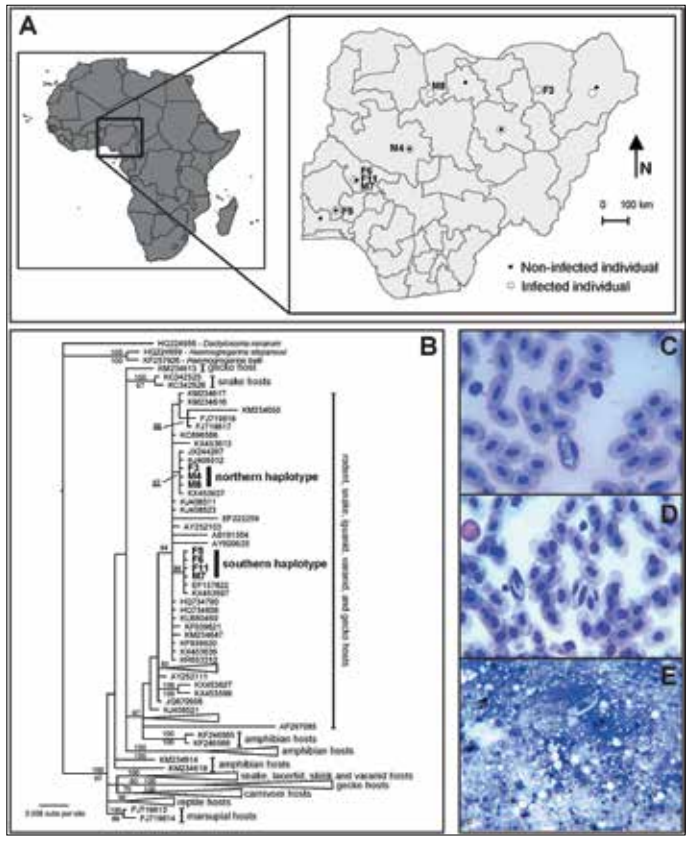

Figure 1. a-e. Sampling locations, phylogenetic tree of detected haemogregarine, and selected photographs of the parasites. (a) Map of the study area containing locations of the infected (white dots) and non-infected (black dots) individuals. Some location points overlap. (b) Estimates of the evolutionary relationships (pictured is the tree derived from the Bayesian phylogenetic analysis). Bayesian posterior probabilities are presented above nodes and bootstrap values for the maximum likelihood analyses are presented below them (only values >75 for the former and 70 for the latter are shown). (c) Haemogregarine photograph 1. (d) Haemogregarine photograph 2. (e) Haemogregarine gametocyte and possible sporocysts (black arrow) in the hemocoel of an Aponomma tick attached to one of the sampled snakes

DNA Extraction and Amplification

DNA was extracted using standard high-salt methods (13). Polymerase chain reaction (PCR) was performed using primers specific for a 600-bp long region of the 18S rRNA gene, HepF300, and HepR900 (14). PCR was performed as described by Harris (15). Amplified products were purified and thereafter sequenced by an external company (Beckman Coulter Genomics, UK). Sequences were blasted in the GenBank database to confirm the identity of the amplified products. Sequences were corrected and aligned in Geneious v5.6.7, Biomatters Limited, New Zealand (16) using the MUSCLE algorithm (17). For phylogenetic analyses, GenBank sequences of other haemogregarines were added to the dataset, which resulted in a final dataset that included 145 sequences and was 584-bp long. The substitution model of evolution was chosen according to the Bayesian information criterion selected by jModelTest 2 (model 012030+G+F) (18). Phylogenetic relationships were estimated using the maximum likelihood (performed in

PhyML 3.1, South of France bioinformatics platform, Montpellier, France) (19) and Bayesian inference (Mr. Bayes v.3.2.6 developed by Ronquist et al. (20) methods) (Figure 1b). For more details on parameters, see Tomé (21).

RESULTS

All pythons were apparently healthy at the time of blood collection based on physical examination. From the 21 blood smears analyzed under the microscope, 10 (47.6%) snakes were found to be infected, with haemogregarines being the suspected parasite in all cases (Figure 1c and d). Eight of the infected samples were genetically assessed; however, all attempts of PCR amplification failed in one of the samples. All the seven obtained sequences belong to the *Bartazoon* haemogregarine group, as identified by Karadjian (10), in a well-supported clade of haemogregarines from snake, gecko, and rodent hosts, but in two distinct lineages (Figure 1b). The haemogregarines infecting pythons from the southwestern region of Nigeria grouped with *Hepatozoon ayorgbor*, described from the ball python *Python regius* in Ghana, and a sequence retrieved from *Hemidactylus alkiyumii* and the Oman saw-scaled viper *Echis omanensis*, both from Oman. The remaining four positive samples were from pythons of the north and central parts of Nigeria. They were grouped with sequences from a white-lipped Herald snake *Crotaphopeltis hotamboeia* from Niger, a horseshoe whip snake *Hemorrhois hippocrepis* from Spain, the Arabian horned viper *Cerastes gasperettii*, and the diademed sand snake *Lytorhynchus diadema* from Oman.

DISCUSSION

Haemogregarines have been previously reported in two python species (14, 22-25) and other snakes from Africa (9, 24, 26, 27). For snakes of tropical Africa, prevalence appears to increase in captivity, with values of 47.6% (in the present study) and 78.2% in imported snakes from Ghana (22). In contrast, wild snakes were less commonly infected, presenting frequencies of approximately 14% (24, 26) and 16.7% (25). There is not yet a consensus on the effect of haemogregarines on their reptile hosts. While some authors have reported none or little effect, higher parasitemia levels have been reported to be associated with erythrocyte hemolysis, anemia, and mortality (11, 28-32). However, the patterns observed appear to suggest that captivity increases the predisposition to infection, and such information should be considered in captivity and conservation programs.

Several haemogregarine species have been described from python hosts [Smith (4) included a list of available species description from the bibliography, and more recently, Sloboda et al. (22) described *H. ayorgbor*]. Unfortunately, molecular data are only available for *H. ayorgbor*; therefore, it is not possible to determine whether the haemogregarine haplotypes detected here belong to any described species. However, because the haplotype infecting southern Nigerian rock pythons shares the same 18S rRNA sequence as that of *H. ayorgbor*, it can be suspected that it belongs to this species or at least to a very closely related species. Other haemogregarine haplotypes infecting pythons have also been reported. Rosado et al. (25) screened the samples of *Python sebae* from Mauritania, Senegal, and Mali and detected a distinct haemogregarine haplotype and Haklová-Kočíková et al. (24) sampled pythons (*Python natalensis* and *P. regius*) from Swaziland and found one to be infected. Unfortunately, the region of the 18S rRNA analyzed in this study did not overlap with the sequence retrieved by Haklová-Kočíková et al. (24), and, thus, it was not included in the present phylogenetic analysis. However, Haklova's haplotype belongs to the same clade of haemogregarine as that in our study and that of others identified from pythons. Thus, based on the information available to date, African pythons, specifically rock pythons, are infected by three (possibly four) haemogregarine haplotypes.

A striking pattern in our results is the geographical division in the distribution of the two detected haplotypes, with one haplotype occupying the northern and central parts of Nigeria and the other occupying the southern part. Notably, Nigeria presents a latitudinal climatic variation, with a dryer savannah north and a tropical south (33), which might correlate with the distribution pattern of the haemogregarines. This is also supported by the grouping of the northern haplotype with haemogregarines from snakes of Niger and Spain (both countries with dryer climates) and those of the southern haplotype with a haemogregarine species described from Ghana (a tropical country). In contrast, sequences of haemogregarines from snakes in Oman (9) also grouped with both haplotypes. This might happen for several reasons but contradicts the climatic explanation for the pattern (or at least as the only explanation). In this study, we did not seek to identify the definitive host of these haemogregarines. However, the tick *Aponomma latum* was found infecting some snakes, and a gamont and suspected sporocyst was observed in a slide preparation from one of these ectoparasites (but no developmental stages in the hemocoel) (Figure 1e). Conversely, Sloboda et al. (22) established the role of the mosquito *Culex quinquefasciatus* as a vector in the experimental transmission of *H. ayorgbor*. Because the haplotypes detected are closely related to this species, they might have the same type of definitive host. Only further experiments can confirm this, but additionally, the identity of the definitive host might offer clues to explain the geographical pattern in the distribution of these haemogregarines, along with other factors such as differences in diet and genetic structuration of the python hosts.

CONCLUSION

To our knowledge, this is the first study on the presence and molecular assessment of blood parasites infecting snakes from Nigeria. Two haemogregarine haplotypes infecting Nigerian rock pythons genetically identified as part of the *Bartazoon* group, which appear to be differently distributed across the country, were detected in this study. Further studies are required to identify the possible definitive hosts of the haemogregarine parasites and to expand the sampling to other hosts and localities to assess whether the uncovered geographical pattern is due to climatic differences, particular of the host group, or distorted by the captivity.

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Metazoan Parasite Faunas of Three Gobiid Species (Actinopterygii: Gobiidae) Inhabiting the Lower Kızılırmak Delta in Samsun: A Comparative Study

Samsun'da Aşağı Kızılırmak Deltasında Yaşayan Üç Kaya Balığının (Actinopterygii: Gobiidae) Karşılaştırmalı Metazoan Parazit Faunası

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ABSTRACT

Objective: The aim of the present study was to investigate and compare metazoan parasite faunas of three gobiid fishes, *Neogobius fluviatilis*, *Proterorhinus marmoratus*, and *Pomatoschistus marmoratus,* inhabiting the Lower Kızılırmak Delta.
Methods: Fish specimens were caught using fishing nets and electroshock device. The fishes were transferred to the laboratory and examined under a dissecting microscope for metazoan parasites using conventional methods. The isolated parasites were fixed with 70% ethyl alcohol. The Czekanowski–Sørensen Index (ICS) was used for comparing the metazoan faunas of the three gobiid fishes.
Results: Overall, 13 metazoan parasite species comprising 2 monogeneans (*Gyrodactylus proterorhini* and *Gyrodactylus* sp.), 6 digenean metacercariae (T*ylodelphys clavata, Diplostomum spathaceum, Apatemon gracilis, Posthodiplostomum* sp., *Ascocotyle* sp., and *Echinostoma* sp.), 1 cestoda (*Bothriocephalus acheilognathi*), 3 nematodes (*Spiroxys contortus, Eustrongylides excisus*, and *Contraceacum rudolphii*), and 1 arthropoda *Ergasilus* (sieboldin) were observed. The maximum parasite diversity was found in *N. fluviatilis*; *Po. marmoratus* had significantly fewer parasitic species (4). Total parasite abundance was significantly high in *Pr. marmoratus*, which was infected with 9 parasite species. A closer resemblance was observed in the parasite faunas of *N. fluviatilis* and *Pr. marmoratus* (ICS=80.0%).
Conclusions: To the best of our knowledge, this is the first study on metazoan parasite faunas of *N. fluviatilis*, *Pr. marmoratus*, and *Po. marmoratus* in Turkey.
Keywords: Black Sea, gobiid fishes, Lower Kızılırmak Delta, metazoan parasites, Turkey
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ÖZ

Amaç: Bu çalışmanın amacı, Aşağı Kızılırmak Deltasında yaşayan 3 kaya balığının, *Neogobius fluviatilis*, *Proterorhinus marmoratus* ve *Pomatoschistus* marmoratus metazoan parazit faunalarını araştırmak ve karşılaştırmaktır.
Yöntemler: Kaya balıkları, balık ağları ve elektroşok cihazıyla yakalandı. Balıklar laboratuvara nakledildi ve metazoan parazitleri için klasik yöntemlerle disseke mikroskop altında incelendi. İzole edilen parazitler %70 etil alkol ile tespit edildi. Üç kaya balığının metazoan faunalarını karşılaştırmak için Czekanowski-Sorensen indeksi (Ics) kullanıldı.
Bulgular: 2 monogenea *Gyrodactylus proterorhini* ve *Gyrodactylus* sp., 6 digenea (metaserker) *Tylodelphys clavata*, *Diplostomum spathaceum*, *Apatemon gracilis*, *Posthodiplostomum* sp., *Ascocotyle* sp., ve *Echinostoma* sp., bir sestod, B*othriocephalus acheilognathi*, üç nematod *Spiroxys contortus*, *Eustrongylides excisus*, *Contraceacum rudolphii* ve bir arthropod *Ergasilus sieboldii* olmak üzere toplamda 13 metazoan parazit türü belirlendi. Maksimum parazit tür çeşitliliği *N. fluviatilis*'de bulundu. *Pomatoschistus marmoratus*'un tür sayısı (4) daha azdı. Toplam parazit bolluğu 9 parazit türü ile infekte Proterorhinus marmoratus'da belirgin olarak daha yüksekti. *N. fluviatilis* ve *Pr. marmoratus*'un parazit faunalarında benzerlik gözlemlendi (Ics: %80,0).
Sonuç: Bu çalışma, *N. fluviatilis*, *Pr. marmoratus* ve *Po. marmoratus*'un metazoan parazit faunaları üzerine Türkiye'de ilk rapordur.
Anahtar sözcükler: Karadeniz, kaya balıkları, Aşağı Kızılırmak Deltası, metazoan parazit, Türkiye
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INTRODUCTION

The family Gobiidae is one of the largest taxons of fish and vertebrate animals. It comprises >2000 species with >200 genera. They are abundant worldwide in every kind of environment, including tropical to temperate marine, estuarine, and freshwater (1). A total of 5 out of 27 species of this family, which inhabited the Black Sea (2), *Neogobius*, *Proterorhinus*, and *Pomatoschistus* are the most common genera of the family. *Neogobius fluviatilis* and *Proterorhinus marmoratus* are native species in the Ponto–Caspian basin. Their native habitats include the coastal zones of the Black Sea, Caspian Sea, Azov Sea, and Marmara Sea (3-5). *Pomatoschistus marmoratus* is a species of the Mediterranean Basin and is widespread in the Eastern Atlantic, Mediterranean, Black Sea, Azov Sea, and Suez Canal (3, 6). The gobiid fishes play important roles in the ecosystem. Regarding food chains, the gobies are secondary consumers and are themselves prey for larger fish, sea birds, and seals. Their availability for predators implies that they are important transmitters of parasites, which complete their life cycle in several hosts (7). Gobiids may be definitive, intermediate, or paratenic hosts of parasites such as digeneans, cestodes, and nematodes. Owing to their ecological tolerance, small sizes, habitation, and diversity, gobiids are appropriate fishes to study the course of colonization by parasites (8).

Several studies are available about the helminths of lagoons and estuaries in the northwestern Black Sea (9-21). Although there is considerable information available on the parasite fauna of gobiids mainly from the northern coasts of the Black Sea, only few studies have reported on those of the gobiids that reside close to Turkish coasts (22-24). In Turkey, there is so far only one published study on the metazoan parasite fauna of *Neogobius melanostomus*, which is not a gobiid species investigated in the present study (23). Moreover, no published study has reported on the metazoan parasites of *N. fluviatilis*, *Pr. marmoratus*, and *Po. marmoratus* from the southern coast of the Black Sea so far. Thus, more studies are required to determine the metazoan parasite fauna of various gobiid species.

The aim of the present study was to investigate and compare the metazoan parasite faunas that occur on *N. fluviatilis*, *Pr. marmoratus*, and *Po. marmoratus* from the Lower Kızılırmak Delta located on the southern coastal zones of the Black Sea. The results are comparable with those of a few previous studies, which investigated in different coastal zones from the Black Sea. The results of the present study present new data about parasite–host relationship.

METHODS

The three gobiid species were fished from the Lower Kızılırmak Delta, which is located on the border of Samsun city (41°38'38.84" N and 36°04'09.89" E) and lies at the sea level. The specimens of these fishes were caught using fishing nets and electroshock device. Sampling was conducted over a 1-year period. A total of 221 specimens of the three gobiid species, *N. fluviatilis* (160), *Pr. marmoratus* (45), and *Po. marmoratus* (16), were investigated for the presence of helminths. The fishes were measured and weighed, and their external and internal organs were carefully examined.

Parasitological Indices and Statistical Analysis

The prevalence, mean intensity, and abundance for metazoan parasites from monkey goby *N. fluviatilis*, tubenose goby *Pr. mar-*

Table 1. Component community of parasites of three gobiid fishes from the Lower Kızılırmak Delta (bold data for homogeneity)

	***Neogobius fluviatilis* (n=160)**			***Proterorhinus marmoratus* (n=45)**			***Pomatoschistus marmoratus* (n=16)**		
Host species	**P**	**MI±SE**	**A**	**P**	**MI±SE**	**A**	**P**	**MI±SE**	**A**
Gyrodactylus proterorhini	9.4	2.7±0.6	0.25	28.9	15.2±3.9	**4.40**	12.5	2.5±05	0.31
Gyrodactylus sp.	–	–	–	–	–	–	6.25	26.0±0.0	1.63
Ascocotyle sp. met.	4.4	1.3±0.2	0.06	–	–	–	–	–	–
Echinostoma sp. met.	60.0	16.7±2.1	**10.03**	37.8	15.4±5.3	**5.82**	25	1.3±0.3	0.31
Tylodelphys clavata met.	15.0	3.5±1.8	1.19	28.9	4.8±1.4	1.38	18.8	1.0±0.0	0.19
Diplostomum spathaceum met.	18.8	6.6±1.4	1.24	13.3	2.0±0.6	0.27	–	–	–
Apatemon gracilis met.	3.8	5.0±2.1	0.19	46.7	63.9±16.2	**29.84**	–	–	–
Posthodiplostomum sp. met.	6.3	5.7±2.3	0.36	17.8	38.9±12.6	**6.91**	–	–	–
Bothriocephalus acheilognathi pl.	5.0	1.4±0.3	0.07	17.8	1.3±0.2	0.22	–	–	–
Spiroxys contortus L3	2.5	1.4±0.4	0.04	–	–	–	–	–	–
Eustrongylides excisus L3	2.5	1.6±0.6	0.05	–	–	–	–	–	–
Contraceacum rudolphii L3	–	–	–	8.9	1.8±0.5	0.16	–	–	–
Ergasilus sieboldi	8.8	1.3±1.2	0.31	2.2	1.0±0.00	0.02	–	–	–
Total	75	18.4±2.1[ab]	13.78	77.8	63.0±15.4[b]	49.02	43.8	6.0±4.0[a]	2.63

n: number of examined fish; P: prevalence (%); MI: mean intensity; SE: standard error; A: abundance; met.: metacercaria; pl.: plerocercoid; L3: L3 stage

Table 2. Infracommunity index

	Neogobius fluviatilis	*Proterorhinus marmoratus*	*Pomatoschistus marmoratus*
Gyrodactylus proterorhini	0.07	0.14	0.30
Gyrodactylus sp.			0.09
Ascocotyle sp. met.	0.03		
Echinostoma sp. met.	0.44	0.24	0.40
Tylodelphys clavata met.	0.11	0.14	0.30
Diplostomum spathaceum met.	0.14	0.07	
Apatemon gracilis met.	0.03	0.23	
Posthodiplostomum sp. met.	0.05	0.09	
Bothriocephalus acheilognathi pl.	0.04	0.09	
Spiroxys contortus L3	0.02		
Eustrongylides excisus L3	0.02		
Contraceacum rudolphii L3		0.04	
Ergasilus sieboldi	0.06	0.01	
Mean infracommunity	1.82	2.02	1.43
Species richness	11	9	4
Shannon Index	1.06	1.30	0.99
Species evenness	0.44	0.56	0.72

(ICI>0.30). met.: metacercaria; pl.: plerocercoid, L3: L3 stage; ICI: infracommunity index

moratus, and marbled goby *Po. Marmoratus* were determined according to Bush et al. (25). The standard error for mean intensity is provided. The Czekanowski–Sørensen Index (ICS, %) was used to compare the helminth faunas (26). The significance of the host–parasite relationship was determined according to the abundance values. The scales used for species were >2 for core species, 0.6-2 for secondary species, 0.2-0.6 for satellite species, and 0.2 for rare species (27). The tendency to participate in the infracommunity was evaluated in terms of the infracommunity index with >0.30 as the highest value. The mean infracommunity was characterized as the mean number of parasite species per host individual (28). The species evenness was calculated according to the formula provided by Zander et al. (7). The evenness values > 0.6 represented a greater part of the homogeneity with >0.7 being a high homogeneity. All statistical tests were carried out using GraphPad Instat 3.0 for Windows 2000 (Software, San Diego, CA, USA) software ($p<0.05$: statistically significant).

RESULTS

In total, the following 13 metazoan parasite species were found: 2 monogenea (*Gyrodactylus proterorhini* and *Gyrodactylus* sp.) 6 digenean metacercariae (*Tylodelphys clavata*, *Diplostomum spathaceum*, *Apatemon gracilis*, *Posthodiplostomum* sp., *Ascocotyle* sp., and *Echinostoma* sp.), 1 cestoda (*Bothriocephalus acheilognathi*), 3 nematodes (*Spiroxys contortus*, *Eustrongylides excisus*, and *Contraceacum rudolphii*), and 1 arthropoda *Ergasilus* (*sieboldi*). The monkey goby has the richest parasite fauna with 11 parasite species. Although the monkey goby was infected with 11 parasite species has the richest parasite fauna, the marbled goby was infected with only 4 parasite species. The highest prevalence and abundance values (77.8% and 49.02) were found in tubenose goby infected with 9 parasite species (Table 1).

Table 3. Czekanowski-Sørensen Index (%) in helminth fauna of various gobiid species in the study area

	Nf	Pr	Po
Neogobius fluviatilis (Nf)	100.0	-	-
Proterorhinus marmoratus (Pr)	80.0	100	-
Pomatoschistus marmoratus (Po)	40.0	46.0	100

The monogenean *Gyrodactylus proterorhini* and the digenean metacercariae *Tylodelphys clavata* and *Echinostoma* sp. were determined in three gobiid fishes. *Contraceacum rudolphii* occurred only in tubenose goby; *Spiroxys contortus* and *Eustrongylides excisus* were found only in monkey goby, and *Gyrodactylus* sp. occurred only in marbled goby (Table 1). Four species, *G. proterorhini*, *Apatemon gracilis*, *Posthodiplostomum* sp., and *Echinostoma* sp., played core roles in the metazoan parasite faunas of gobies from the Lower Kızılırmak Delta. *G. proterorhini*, *A. gracilis*, and *Posthodiplostomum* sp. were essential in the tubenose goby parasite fauna and *Echinostoma* sp. in the monkey and tubenose goby parasite faunas. Moreover, *Echinostoma* sp. was core in all cases except in marbled goby (Table 1).

The species composition of metazoan faunas of the three gobiid species differed, and the parasite species richness was variable among the gobiid fishes. The metazoan parasite fauna of the marbled goby, which is of Mediterranean origin, differed markedly from those of the monkey and tubenose gobies (Table 1). The homogeneity of the parasite component faunas was low in monkey and tubenose gobies, but it was high in marbled goby (Table 2). The mean infracommunity index (ICI) of the monkey goby was higher than that of the marbled goby. The ICI of the tubenose goby differed from that of the monkey and marbled gobies (Table 2). A high Czekanowski–Sorensen index, indicating a close similarity, was observed in the metazoan parasite fauna of the monkey and tubenose gobies (*Ics*=80.0%) (Table 3).

DISCUSSION

Data on parasites of various gobiid fishes found in the Black Sea coast are previously reported (12-17, 20, 21, 29-31). These studies include the parasites of the three gobiid species (*N. fluviatilis*, *Pr. marmoratus*, and *Po. marmoratus*) and 34 metazoan parasite species (Table 4). We found 13 parasite species; 6 species were reported on in a previous study, but 7 species, including *Gyrodactylus* sp., *Bothriocephalus acheilognathi*, *Echinostoma*

Table 4. List of the metazoan parasites reported from three gobiid fishes in different geographical localities in the Black Sea region

	Neogobius fluviatilis	***Proterorhinus marmoratus***	***Pomatoschistus marmoratus***
Gyrodactylus proterorhini	[43], Present study	[43], [20], [21], Present study	Present study
Gyrodactylus leopardinus			[30]
Gyrodactylus sp.			Present study
Ascocotyle sp. met.	Present study		
Echinostoma sp. met.	Present study	Present study	Present study
Tylodelphys clavata met.	[31] Present study,	Present study	Present study
Diplostomum spathaceum	[21], [31] Present study	Present study	
Apatemon gracilis met.	[31] Present study	Present study	
Posthodiplostomum sp. met.	Present study	Present study	
Cryptocotyle concavum met.	[12], [13], [14], [16], [21], [32], [43]	[10], [15], [16], [17], [20], [21]	[10], [15], [16], [29], [21]
Cryptocotyle lingua met.	[12], [13], [16], [21], [43],	[16], [17], [20], [21]	[15], [16], [21], [29]
Pygidiopsis genata met.	[12], [13], [16], [21], [31]	[20], [21]	[21], [29]
Acanthostomum imbutiformis	[10], [21], [31], [43],	[20], [21]	[15], [16], [21], [29]
Stephanostomum bicoranatum		[43]	
Monascus filiformis	[43]	[43]	
Pronopyrmna ventricosa	[43]	[43]	[31]
Pronopyrmna petrowi	[43]	[43]	
Magnibursatus skrjabini		[20], [21]	
Asymphylodora imitans	[31]		
Asymphylodora pontica	[21]		[15], [16], [21], [29]
Aphalloides coelomicola			[15], [16], [21], [29]
Galactosomum lacteum	[43]		
Paratimonia gobii			[15], [16], [21], [29]
Nicolla skrjabini	[16], [31]		
Holostephaluscobitis met.	[31]		
Ichthyocotylurus variegatus	[31]		
Rhipidocotyle companula met.	[31]		
Maritrema subdolum met.	[10]		
Proteocephalus gobiorum	[12], [16], [31]	[20]	
Proteocephalus torulosus	[31]		
Ligula pavlovskii	[13], [14], [16]		
Bothriocephalus gregarius			[16], [29]
Bothriocephalus acheilognathi pl.	Present study	Present study	
Agamonema sp. L3	[31]		
Contraceacum rudolphii L3	[21]	[21], Present study	
Contraceacum microcephalum			[29]
Eustrongylides excisus L3	[14], [16], [31],		
Present study			
Dichelyne minutus	[12], [14], [16], [21], [31]	[15], [16], [17], [20], [21]	[15], [16], [29], [21]
Cucullanus heterochrous	[43]		
Streptocara crassicauda	[31]	[20]	
Raphidascaris acus	[14], [16], [31]		
Pseudocapillaria tomentosa	[13]		
Spiroxys contortus	Present study		
Acanthocephaloides propinquus	[12], [13], [16], [31]	[12], [16], [17], [20]	[16], [29]
Telosentis exiguus	[10], [12], [16]	[20]	[16]
Ergasilus sieboldi	Present study		
Thersitina gasterostei	[43]		

met.: metacercaria; pl.: plerocercoid; L3: L3 stage

sp., *Posthodiplostomum* sp., *Ascocotyle* sp., *S. contortus*, and *Ergasilus sieboldi*, were mentioned from the three examined gobiids for the first time in the Black Sea (Table 4). Parasites such as the trematodes *Pygidiopsis genata* (metacercaria), *Cryptocotyle concavum* met., *Cryptocotyle lingua* met., and *Timoniella imbutiforme* met., nematode *Dichelyne minutus*, and acanthocephalan *Acanthocephaloides propinquus* were previously observed in the three gobiids in various sites of the northwestern Black Sea and Crimean coasts. Overall, these parasite species are typical for the resident gobiids in the Black Sea, but we did not find them during our study. *C. concavum*, *C. lingua*, *P. genata*, *T. imbutiforme*, *D. minutus*, and *A. propinquus* are brackish water and marine parasite species. Moreover, the first intermediate hosts of these parasites are also absent in fresh waters (7, 14). The absence of parasites mentioned in the present study could be explained by low salinity in our study area (approximately 1%).

According to previous studies, five of the listed species, *G. proterorhini*, *A. gracilis*, *T. clavata*, *Diplostomum spathaceum*, and *E. excisus*, have been reported in the monkey goby from different localities of the Black Sea (14, 16, 21, 31, present study) (Table 4). Similarly, *G. proterorhini* and *C. rudolphii* have been previously reported in the tubenose goby (20, 21). *G. proterorhini* is a specific species for gobiids inhabiting the Black and Azov Seas and their estuaries (32). Additionally, *it* is reported in various rivers belonging to the Black Sea drainage within the natural living area of the Ponto–Caspian gobiids (20, 29, 33). To date, *Zosterisessor ophiocephalus*, *Gobius cobitis*, *Gobius niger*, *N. melanostomus*, *N. fluviatilis*, *Neogobius platyrostris*, *Mesogobius batrachocephalus*, and *Neogobius kessleri* have been reported as host of *G. proterorhini* (19, 23, 34-40). To the best of our knowledge, the occurrence of *G. proterorhini* in *Po. marmoratus* is reported for the first time in this study. A new host has been added to the host list of *G. proterorhini*. Until today, three *Gyrodactylus* species that are known to parasitize *Po. Marmoratus* include *G. branchialis* and *G. ostendicus* that are reported from the western Mediterranean Sea (41) and *G. leopardinus* that is reported from the Azov Sea (30, 42).

To date, 47 metazoan parasite species have been mentioned in the Black Sea basin according to data from different authors (Table 4). We found 13 parasite species; 7 of these had already been mentioned in published studies, but 6 species, *Ascocotyle* sp., *Posthodiplostomum* sp., *Echinostoma* sp., *B. acheilognathi*, *S. contortus*, and *E. sieboldi*, were mentioned from three gobiid fishes for the first time. Particularly, tendency to join the infracommunity of *Echinostoma* sp., which is a limnetic parasite species, differs from other parasites in the present study (Table 2). The species composition of the metazoan fauna of gobiid fishes from the Lower Kızılırmak Delta located on the southern coastal zones of the Black Sea differed from those reported from various sites of the northern coastal zone of the Black Sea. The results of the present study indicated that the euryhaline and limnetic species are prevalent in this basin, but the marine and brackish water species are prevalent in its northern part. The gobiid parasite fauna does not show homogeneity in the Black Sea (34). It consists of Ponto–Caspian, Mediterranean, Boreal–Atlantic, and limnetic parasite species that are attributed to the different ranges of euryhalinity of the hosts. Thus, the species composition of the gobiid metazoan fauna in the present study is formed according to the ecology of the host species.

CONCLUSION

The present study comprises current data regarding the metazoan parasite fauna of gobiids in the Lower Kızılırmak Delta from the Black Sea. The data presented in this paper contribute to the list of parasite species that inhabit this basin. In general, the metazoan parasite communities of the three gobiid fishes from the Lower Kızılırmak Delta comprised limnetic species and differed from the other regions of the Black Sea.

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Overview of Zoonotic Diseases in Turkey: The One Health Concept and Future Threats

Türkiye'de Zoonotik Hastalıklara Genel Bakış: Tek Sağlık Konsepti ve Gelecek Tehditler

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ABSTRACT

Zoonotic infections are globally important diseases and lead to huge economic losses in both low- and middle-income and high-income countries. Global warming, environmental and ecological changes, illegal movement of animals and humans, regional civil wars, and poverty are predisposing factors for the emergence of zoonotic infections and their distribution worldwide; they are also a big threat for the future. In addition, environmental pollution and antimicrobial resistance are immense serious threats and dangers to prevent and control zoonotic infections. The natural location of Turkey allows many emerged or re-emerged infections with zoonotic characteristics by animal movements, such as bird immigrations, and by human movements due to civil wars as seen with regional refugees. Numerous zoonotic diseases, including 37 bacterial, 13 fungal, 29 viral, 28 parasitic (3 trematodes, 7 cestodes, 10 nematodes, and 8 protozoan), and totally 107 infections, have been reported from Turkey to date. Additionally, many ectoparasitic zoonoses within 15 different arthropod groups and one leech infestation have been reported from Turkey to date. The "One Health" initiative is particularly relevant for developing strategies to combat zoonotic diseases. In this article, we review the occurrence of zoonotic diseases in man and animals in Turkey in the light of the "One Health" perspective.
Keywords: Zoonotic diseases, Turkey, one health concept, future threats
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ÖZ

Zoonotik enfeksiyonlar global öneme sahip olup gerek düşük ve orta gelirli ülkelerde gerekse geliri yüksek ülkelerde büyük ekonomik kayıplara neden olmaktadır. Küresel ısınma, çevresel ve ekolojik değişiklikler, yasadışı insan ve hayvan hareketleri, bölgesel sivil savaşlar ile fakirlik zoonotik enfeksiyonların ortaya çıkması ve dünya genelinde yayılmasında predispoze faktörler olup ayrıca gelecek için büyük tehdit oluşturmaktadırlar. Bununla birlikte, çevre kirliliği ve antimikrobiyel direnç zoonotik enfeksiyonların kontrolü ve önlenmesinde çok ciddi tehdit oluşturmaktadır. Doğal lokasyonu, sivil savaşlara bağlı bölgesel mülteci göçleri ve göçmen kuşlar gibi hayvan hareketleri dolayısıyla Türkiye birçok yeni ve tekraren ortaya çıkan zoonotik enfeksiyonlar açısından risk taşımaktadır. Türkiye'de bugüne kadar 37 bakteriyel, 13 mantar, 29 viral, 28 parazitik (3 trematod, 7 cestod, 10 nematod ve 8 protozoon) olmak üzere toplam 107 farklı zoonotik enfeksiyon bildirilmiştir. Buna ilaveten 15 farklı artropod grubu ve 1 sülük enfestasyonu olmak üzere birçok ektoparazitik zoonozlar da günümüze kadar Türkiye'den bildirilmiştir. "Tek Sağlık" konsepti, özellikle zoonotik enfeksiyonlarla mücadele stratejilerinin geliştirilmesinde uygun bir yaklaşımdır. Bu derlemede "Tek Sağlık" perspektifi ışığında Türkiye'de insan ve hayvanlarda görülen zoonotik hastalıklar hakkında bilgi verilmiştir.
Anahtar sözcükler: Zoonotik hastalıklar, Türkiye, tek sağlık konsepti, gelecek tehditler
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INTRODUCTION

Zoonotic diseases are contagious or non-contagious infections with emerging and/or re-emerging characteristics and naturally transmissible from vertebrate animals to humans and vice-versa via contact, food, water, and by vectors in the human and animal ecosystems; their increasing risks affect global health security (1-3). These infections are caused by all types of pathogens, including bacteria, fungi, parasites, viruses, and unconventional agents such as prions. Prior to the 20th century, the best known zoonoses were rabies, anthrax, glanders, tuberculosis, plague, yellow fever, influenza, and certain zoonotic parasitic diseases (4). Sixty percent of 300 infectious agents identified between 1940 and 2004 have been classified as zoonoses, and most of these infections belong to the neglected diseases (5, 6). More than 200 zoonoses have previously been described to date, and their epidemiological appearance and distributions occur in sporadic, endemic, epidemic, and pandemic forms in the world causing deaths among humans, livestock, as well as wildlife. Zoonotic infections also result in great economic losses (5, 7) and could be one of the major reasons of poverty (6-8). The public health impact and financial consequences of these diseases can devastate the already overburdened economic conditions in developing countries as well as in Turkey (9, 10). Over the last decade, the global economic impact of zoonotic diseases has been estimated as more than $220 billion ($20 billion from direct costs and $200 billion from indirect losses) (11, 12). In the second-half of the last century, the control and/or elimination of zoonotic diseases has been successful in several industrialized countries through expensive infrastructural investments and meticulous coordinated interventions, including "test and cull of animals," feed bans, mass vaccination of domestic animals and wildlife, health education, and milk pasteurization. Naturally, these highly effective methods for elimination of zoonotic diseases involve legal and financial collaterals. However, in most developing countries, livestock practices have primarily focused on implementing prevention and eradication measures with much less emphasis on the effect of mitigation (transmission control) strategies, considering the economic and development impacts at the macro (national economy and environment) or micro (health, livelihoods, and food security of smallholder farmers) levels. Thus, in most developing countries, the surveillance of zoonotic diseases is not recognized in the One Health context between veterinary medicine and human medicine. In addition, many countries lack diagnostic capacity and health infrastructure (7). Meanwhile, the global increase in zoonotic diseases was reported as 22% in 1990–2000 and 21% in 2000–2010 (13). The zoonotic infections that have emerged or re-emerged globally are Severe Acute Respiratory Syndrome (SARS) in 2003, Influenza A H1N5 (avian influenza) in 2003, Influenza A H1N1 (pandemic influenza or swine flu) in 2009–2010, Middle East Respiratory Syndrome (MERS) in 2012, Influenza A H7N9 in 2013, Ebola in 2014, and Zika virus in 2015–2016. To combat of zoonoses, the One Health concept has been defined by the World Health Organization (WHO) as a worldwide strategy that would expand interdisciplinary collaborations and communications in all aspects of health care for humans, animals, and environment (14).

Turkey is geographically located in Eurasia and represents a natural bridge for the transmission of many zoonotic infections that involve the movement of animals (particularly bird immigrations) and humans (illegal transport of humans or mass immigrations of populations) among the continents of Europe, Asia, and Africa. Turkey has a population of over 80 million and a livestock population of over 50 million, and its economic structure currently depends on a mix of industrial and agricultural products (10). Currently, Turkey has been affected from illegal animal and human movements. In particular, regional conflicts in the countries neighboring Turkey has led to massive refugee and illegal human movements during the past 30 years (15-17). In addition, Turkey has highly variable climatic conditions, vegetation structures, wildlife, and particularly many sanctuaries for immigrant birds. The geographic structure of Turkey also allows suitable habitats for various vector arthropods, such as bloodfeeding insects and ticks, throughout the four seasons of the year (10, 18-21). Thus, several zoonotic diseases are endemic throughout the country and affect humans and animals (22-24) with economic losses (25-30). In this review, an overview of the zoonotic diseases (Figure 1) in Turkey are described in the One Health concept and future threats perspectives.

ZOONOTIC DISEASES IN TURKEY

The dynamic interactions of zoonoses among humans, animals, and pathogens in the same environment could be evaluated within the "One World-One Health" concept with a holistic perspective. Actually, this approach dates back to the ancient periods of humankind (31). Prior to the discovery and application of sanitation and hygiene, particularly sterilization and antibiotics, bacterial zoonotic diseases, such as bovine tuberculosis, bubonic plague, and glanders, caused millions of human deaths in the world as well in Turkey (32). The discovery and application of insecticides and acaricides, and entomopathogens led to the reduction of vector-borne infections in the last century in Turkey as well globally (33). Effectively implemented control measures have resulted in a decrease in many community-acquired infections, including bacterial and parasitic diseases, such as tuberculosis and malaria, which constituted major public health problems until a few decades ago. Meanwhile, the frequent use of antibiotics in human medicine and veterinary purposes have led to the emergence of antimicrobial resistance in various nosocomial isolates of gram-positive and gram-negative bacteria. However, recent guidelines limiting antibiotic applications have been promising (34).

In addition, over 50 vector-borne infections (19 tick-borne diseases [TBDs]) caused by different pathogens have been reported in farm animals and humans (20, 21) and in cats and dogs (35). A total of 47 tick species (38 ixodid and 9 argasid) have also been reported in the last century in Turkey (10), and these zoonotic diseases have a significant impact on the livestock industry of the country (26, 29, 30).

Modes of transmission for zoonotic diseases between animals and humans involve several routes: (i) via blood-feeding arthropods, such as ticks, mites, fleas, biting midges, mosquitoes, and sand flies; (ii) via contaminated food (food-borne) and/or contaminated water (water-borne); (iii) via direct contact (ie, farmers,

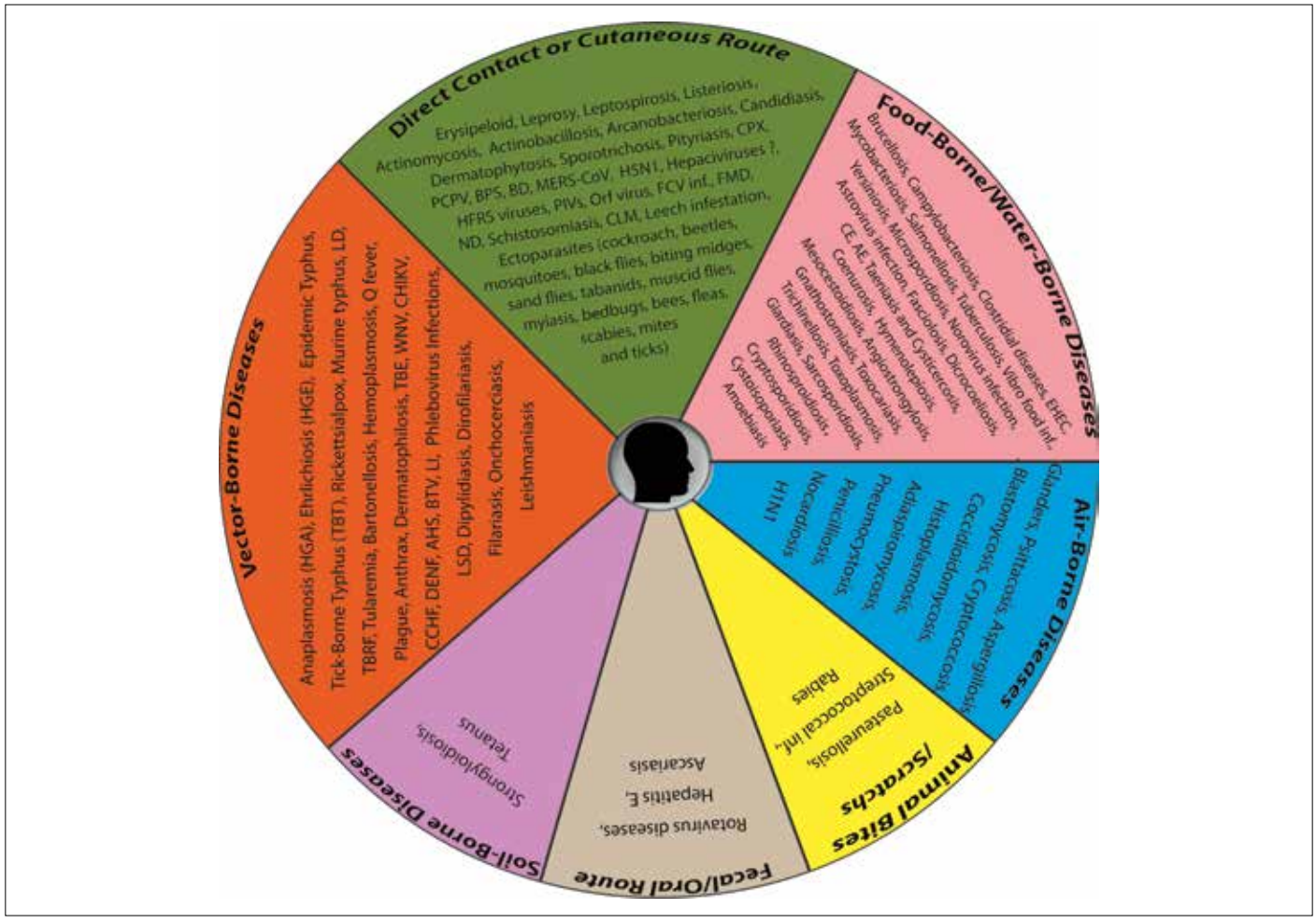

Figure 1. Overview of zoonotic diseases found in Turkey

workers, and veterinarians at increased risk to exposure with zoonotic agents); (iv) via soil contaminated with manure; (v) via animal bites and/or animal scratches; and (vi) invasion with active penetration (36). In addition, some zoonotic diseases can be transmitted from patients to health care workers and health professionals (physicians, nurses, and other health staffs) (37).

Bacterial Zoonotic Diseases in Turkey

Bacterial zoonoses are grouped based on the infection routes described above. Most of the vector-borne bacterial zoonotic diseases are classified depending on the biological vector involved in its transmission, such as tick-, mite-, flea-, and insect-borne. In addition, mechanical transmission of some bacterial zoonoses are also possible by iatrogenic or by insects, whereas a few zoonotic bacterial pathogens can be transmitted by the ingestion of trematodes and caddishflies as well. Particularly, tick-borne bacterial zoonoses are complex and have been grouped as rickettsial (38) and non-rickettsial (39). The reported bacterial zoonotic diseases in Turkey are shown in Table 1.

Anaplasmosis is an opportunistic rickettsial vector-borne disease of humans and animals, caused by *Anaplasma* species including *A. marginale*, *A. centrale*, *A. bovis*, and *A. ovis* for ruminants; *A. platys* for canines; and *A. pagacytophilum* for human and domestic animals such as horses. The infection is widespread and transmitted iatrogenically and mainly intrastadially by male ticks; the disease is called Human Granulocytic Anaplasmosis or Human Granulocytic Ehrlichiosis (HGE) in man. The etiologic agent of HGE *A. phagocytophilum* is transmitted by *Am. americanum* ticks in endemic areas (40). *A. phagocytophilum* was determined in farm animals (41, 42) and in humans (43, 44) in Turkey. Additionally, *A. phagocytophilum* was detected in *Ixodes ricinus* ticks isolated from humans (45). A few bovine anaplasmosis outbreaks were also reported in cattle from some areas (35, 46-49) and one *A. platys* infection was reported in a dog in Turkey (50).

Ehrlichiosis is caused by *A. phagocytophilum*, *Ehrlichia chaffeesis*, and *E. ewingii* in humans and is called Human Monocytotropic Ehrlichiosis and by *A. phagocytophilum* and *E. canis* in dogs and is called Canine Monocytotropic Ehrlichiosis (CME). The diseases are transmitted by ixodid ticks and are of public health and veterinary importance (38). In Turkey, the studies on CME are very limited but few reports have documented seropositivity (51), clinical cases, treatment (52), and molecular prevalence (53, 54).

Typhus (Epidemic Typhus) is an arthropod-transmitted infection in humans and animals caused by *Rickettsia prowazekii*. At least

Table 1. Reports on zoonotic diseases in Turkey

Diseases	Causative Agent	Known Distribution	Principal Animals Involved	Zoonotic Transmission	References
Bacterial zoonotic diseases					
Anaplasmosis (HGA)	*Anaplasma phagacytophilum*		Ruminants, canines, horses	Tick-borne	(464)
Ehrlichiosis (HME)	*A. phagocytophilum*, *E. chaffeesis*, and *E. ewingii*		Dogs	Tick-borne	(53, 54)
Typhus	*Rickettsia prowazekii*	Worldwide	Flying squirrels	Lice-transmitted infection	(57)
Tick-borne Typhus (TBT)	*R. conorii*		Tortoises	Tick-borne	(61, 63)
Rickettsialpox	*Rickettsia akari*		Mice, humans	Mite-transmitted	(69)
Murine typhus	*Rickettsia typhi*	Worldwide	Rats, cats, and humans	Flea borne	(71)
Lyme Disease (LD)	*Borrellia burgdorferi*	Northern temperate zone	Humans, domesticated animals	Tick-borne	(78, 90)
Tick-borne Relapsing Fever (TBRF)	*Borrelia* spp.	Africa, Asia, Europe, Eurasia and America		Tick-borne	(93, 94)
Tularemia	*F. tularensis*	Northern hemisphere		Arthropod-transmitted	(18, 96)
Bartonellonsis (Cat Scratch Disease)	*Bartonella* spp.	Northern hemisphere	Cats	Sand flies, human body louse, cats, cat flea	(101)
Hemoplasmosis	*Mycoplasma* spp.		Humans, and animals	Blood-feeding arthropods-transmitted	(110)
Q Fever	*Coxiella burnetii*		Cows, sheep, goats, and dogs	Tick-borne	(116)
Plague (Black Death)	*Yersinia pestis*	Worldwide	Rat	Flea borne	(15)
Anthrax	*Bacillus anthracis*	Worldwide	Mammals	Tabanid, mosquito species, stable flies	(119, 120)
Brucellosis	*Brucella* spp.	Worldwide		Food-borne	(23, 122)
Campylobacteriosis	*Campylobacter jejuni*		Poultry, livestock, or household pets	Food-borne	(126)
Clostridial diseases	*Clostridium* spp.		Domestic and wild animals	Food-borne	(128)
Enterohemorrhagic Escherichia coli (EHEC) infection	*Escherichia coli*	Worldwide	Cattle or sheep	Water-borne	(135, 136)
Erysipeloid	*Erysipelothrix* spp.		Farmed animals	Contact with infected animals	(141)
Glanders (Malleus)	*Burkholderia mallei*	Some Asian, African and South American countries	Horses, mules, and donkeys	Contact with infected animals	(148-150, 465)
Leprosy	*Mycobacterium leprae*		Armadillos	By close contact	(152)
Leptospirosis	*Leptospira interrogans*	Worldwide		Close contact with infected animals	(155)
Listeriosis	*Listeria monocytogenes*		A wide range of animals	By close contact, food-borne	(156, 159)
Mycobacteriosis	*Mycobacterium* spp.	Worldwide	Aquarium and culture fish	Contact with contaminated water sources or infected fish	(162, 164)
Pasteurellosis	*Pasteurella* spp.			Animal bites or contact with nasal secretions	(167, 168)
Psittacosis	*Chlamydophila psittaci*		Birds	Airborne	(169, 170)

Salmonellosis		*Salmonella enterica*	Worldwide	Domestic and wild animals	Food-borne	(172, 175)
Streptococcal infections		*Streptococcus* spp.		Dog and cat, wild predatory animal	Dog and cat bites	(181, 182)
Tetanus (lockjaw)		*Clostridium tetani*	Many developing countries		Soil borne	(131)
Tuberculosis		*Mycobacterium tuberculosis*	Worldwide		By close conctact	(124)
Vibrio Food Infection		*Vibrio* spp.			Food-borne, water-borne	(188)
Yersiniosis		*Yersinia* spp.			Food-borne	(189, 191)
Actinomycosis		Actinomyces spp.		Cattle	By contact with infected animals	(194, 195)
Actinobacillosis		*Actinobacillus lignieresii*		Sheep and cattle	Cutaneous route	(194)
Arcanobacteriosis		*Arcanobacterium* spp.		Cattle and sheep	By close contact	(200, 201)
Dermatophilosis		*Dermatophilus congolensis*		Horses, dogs, cats, and ruminants	Vector-borne	(202, 203)
Nocardiosis		*Nocardia asteriodes*		Dog	Ways such as inhalation, traumatic inoculation	(206, 207)
Fungal Zoonotic Diseases						
Aspergillosis		*Aspergillus* spp.		Birds, dogs, and horses	Airborne	(213, 214)
Blastomycosis		*Blastomyces dermatitis*	North America	Humans and animals	Airborne	(216)
Candidiasis		*Candida albicans*		Humans and birds	Direct contact	(217)
Coccidioidomycosis		*Coccidioides* spp.	Western Hemisphere	Cattle, cats, horses, dogs, and wildlife	Airborne	(219)
Cryptococcosis		*Cryptococcus neoformans*	Worldwide	Livestock animals, dogs, cats, birds, and wild life	Airborne	(221)
Histoplasmosis		*Histoplasma capsulatum*	Worldwide	Dogs, cats, farm animals, and other wild mammalians	By inhalation of the spores	(223)
Dermatophytosis		*Trichophyton* spp.		Humans and animals	By direct contact	(225)
Sporotrichosis		*Sporothrix schenckii*	Worldwide	Horses and cats	Contaminated environment	(228)
Penicilliosis		*Penicillium* spp.	South Asia countries	Human	Still not known	(229)
Pneumocystosis		*Pneumocytis* spp.		Rodents, rabbits, and humans	Airborne	(238)
Malassezia Infection or Pityriasis		*Malassezia pachydermatis*		Humans and animals	Mechanically via hands	(235)
Adiaspiromycosis		*Emmonsia* spp.	Worldwide	Humans and animals	Airborne	(237)
Microsporidiosis		*Encephalitozoon* spp. and *En. bieneusi*	Worldwide	Humans and animals	By ingestion or inhalation of the spores	(244)
Viral Zoonotic Diseases						
1	Encephalitis group	Rabies	*Lyssavirus*		Carnivores	Dog bites	(252)
2	Encephalitis group	Tick-Borne Encephalitis (TBE)	*Flavivirus*	Asia and Europe		Tick-borne	(20)
3	Encephalitis group	West Nile Virus (WNV)	*Flavivirus*	Worldwide	Domestic animals	Mosquito-borne	(21)
4	Rashes and arthralgia group	Chikungunya virus (CHIKV)	*Alphavirus*	Africa and Asia		Mosquito-borne	(254, 255)

6	Hemorrhagic fever group	CCHF	*Nairovirus*	Sub-Saharan Africa, Eastern Europe, Russia, the Middle East, West China	Wild and livestock animals	Tick-borne	(20)
7		Dengue fever (DENF)	*Flavivirus*	Worldwide		Mosquito-borne	(258)
8	Emerging group	Middle East Respiratory Syndrome Coronavirus	*Coronavirus*	Middle East countries	Bats, dromedary camel	By close contact	(263)
9		*Avian Influenza* (H5N1)	*Influenza A*	Worldwide	Birds	By direct contact	(265)
10		*Swine Influenza* (H1N1)	*Influenza A*	Worldwide	Swine	Airborne	
11	Hemorrhagic fever with renal syndrome	Hepatitis E	*Hepatitis E virus*	Worldwide		Fecal/oral	(269, 270)
12		*Parainfluenza* viruses	*Paramyxovirus*		Cattle	Through direct contact	(273)
13	Re-emerging group	Orf virus infection (Ecthyma contagiosum)	*Parapoxvirus*		Wild and domesticated cattle, sheep, goats	By direct or indirect contact	(280, 281)
14	Rare Viral Zoonotic Infections group	African Horse Sickness (AHS)	Orbivirus	Africa, Asia, and Middle East, and Europe	Equids	Mosquito-borne	(283)
15		Bluetongue (BTV)	*Orbivirus*	Worldwide	Sheep, goats, and cattle	Mosquito-borne	(286)
16		Borna Disease (BD)	*Bornaviridae*		Horses, sheep, cattle, dogs, and cats	Exposure to contaminated saliva or nasal secretions	(289, 290)
17		Feline Calicivirus infection	*Vesivirus*		Cats	Direct contact	(292)
18		Foot and Mouth Disease (FMD)	*Aphthovirus*	Worldwide	Cattle, water buffalo, sheep, goats, and pigs	By close contact	(297)
19		Louping ill (LI)	*Flavivirus*	Various European countries	Sheep and goats	Tick-borne	(10)
20		Newcastle Disease (ND)	*Avulavirus*	Worldwide	Birds	By direct contact	(300)
21		Cowpox (CPX)	*Orthopoxvirus*	European countries and Eurasia	Small mammals and cattle	By direct contact	(303)
22		Pseudocowpox virus Infection	*Parapoxvirus*	Worldwide	Cows	By direct contact	(305)
23		Bovine papular stomatitis	*Parapoxvirus*	Worldwide	Cattle	Through direct or indirect contact	(308)
24		Rotavirus diseases	*Rotavirus*	Developing countries	Calves and foals	Contact with contaminated objects	(312)
25		Norovirus infection	*Norovirus*		Calves	Food or water-borne, by contact and aerosol route	(315, 316)
26	Potential zoonotic viral infections group	Astrovirus infection	*Astrovirus*			Food and water-borne	(316)
27		Phlebovirus Infections	*Phlebovirus*	Mediterranean Basin	Vector-borne	(21)	
28		Lumpy Skin Disease (LSD)	*Capripoxvirus*		Cattle	Blood-feeding arthropods borne	(20, 75)
29		Hepaciviruses	*Hepacivirus*		Domesticate cattle?	?	(327)

Parasitic Diseases with Zoonotic Characteristics							
1	Trematode zoonoses	*Fascioliasis*	*Fasciola hepatica* spp.	Worldwide	Sheep, cattle, ruminants, and humans	Food-borne	(334)
2		*Dicrocoeliosis*	*Dicrocoellum dentricum*	Worldwide	Livestock, humans	Food-borne	(336)
3		*Schistosomiasis*	*Schistoma* spp.	Worldwide	Humans	Water-borne	(338)
4	Cestode Zoonoses	*Echinococcosis*	*Echinococcus* spp.	Worldwide	Cattle, buffalo, sheep, goat, pigs, dogs, and humans	Food-borne	(343)
5		*Taeniasis*	*Taenia saginata*	Worldwide	Cattle, pigs, sheep, and humans	Food-borne	(348)
6		*Cysticercosis*		Worldwide	Cattle, pigs, sheep, and humans	Food-borne	(348)
7		*Coenurosis*	*Taenia multiceps*	Worldwide	Small ruminants, sheep, cattle, and humans	Food-borne Water-borne	(350)
8		*Dipylidiasis*	*Dipylidium caninum*	Worldwide	Pet animals, dog, cats, and humans	Food-borne	(353)
9		*Hymenolepiasis*	*Hymanolepis* spp.	Worldwide	Humans	Food-borne, water-borne, Poor sanitation	(355)
10		*Mesocestoidiasis*	*Mesocetoides* spp	Worldwide	Dogs and cats	Food-borne	(357)
11	Nematode Zoonoses	*Angiostrongylosis*	*Angiostrongylus* spp.	Worldwide	Humans and dogs	Food-borne	(358)
12		Ascariasis	Ascaris *lumbricoides*	Worldwide	Humans	Food-borne	(359)
13		Cutaneous Larva Migrans (CLM)	*Ancylostoma* spp. *Necator americanus*, *Uncineria stenocephala* and *Bunostomum phlebotomum*	Areas with moist and warm climate	Dogs, cats, wild animals, and humans	By walking barefoot on sandy beaches or contacting moist soft soil, that have contaminated with animal feces	(362)
14		*Dirofilariasis*	*Dirofilaria* spp.	Worldwide	Dogs and humans	Mosquito-borne	(363)
15		*Filariasis*	*Wuchereria bancrofti* *Brugia* spp.	Worldwide	Humans, felines, and monkeys	Mosquito-borne	(365)
16		*Gnathostomiasis*	*Gnathostoma* spp.	Worldwide	Humans	Water-borne Food-borne	(45)
17		*Onchocerciasis*	*Onchocerca* spp.	Worldwide	Humans and animals	Simulid-borne	(367)
18		*Strongyloidiasis*	*Strongyloides stercoralis*	Worldwide	Humans, dogs, and cats	Soil-transmitted	(370)
19		*Toxocariasis*	*Toxocara* spp.	Worldwide	Humans, dogs, and cats	Contaminated with dog or cat feces, food-borne	(353)
20		*Trichinellosis*	*Trichinella* spp.	Worldwide	Humans and animals	Food-borne	(374)
21	Zoonotic Parasitic Protozoans	*Leishmaniasis*	*Leishmania* spp.	Mediterranean Basin	Dogs, cats, cattle, and equids	Vector-borne	(21, 454)
22		*Toxoplasmosis*	*Toxoplasma gondii*	Throughout the world	Mammal and bird species	By congenital, carnivorism and fecal-oral route	(23, 393)
23		*Sarcosporidiosis*	Sarcocystis spp.	Worldwide	Some mammalians, and in some avian	By oral route	(399)
24		*Giardiasis*	*Giardia* spp.	Worldwide	Domesticated animals	Water, food borne, and by direct physical contact	(405, 406)
25		Amoebiasis or Amoebic Dysentery	*Entamoeba histolytica*	Worldwide		Fecal-oral transmission	(407, 408)
26		*Cryptosporidiosis*	*Cryptosporidium* spp.	Globally	Mammals, birds, reptiles, amphibians, and fish	Water-borne	(412, 413)
27		*Rhinosporidiosis*	*Rhinosporidium seeberi*		Fish and amphibians	By the contact	(417)
28		*Cystoisosporiasis*	*Cystoisospora* belli	Tropical and subtropical regions in the world	Monkey, dog, pig, rat, mouse, Guinea pig, and rabbit	Food/water-borne	(419, 420)

two strains of the agent can be distinguished by genetic analysis. One strain is found only in humans worldwide, while the other also occurs in flying squirrels (*Glaucomys sabrinus* and *G. volans*) in the USA (55). The primary vector of person-to-person transmission is the human body louse (*Pediculus humanus corporis*). Lice are infected when they feed on the blood of infected patients and excrete *R. prowazekii* in the feces as they feed on a new host. Transmission occurs when organisms in the louse feces are rubbed into the bite wound or other breaks in the skin (55). The rickettsia is also infectious by inhalation or contact with the mucous membranes of the mouth and eyes. In most parts of the world, humans are the only reservoir host for *R. prowazekii*. Infections can become latent and later recrudesce; humans with recrudescent typhus are capable of infecting lice and spreading the disease (56). It was reported that typhus epidemics were seen in Erzurum and nearby cities during the years of World War I in Turkey (57).

Tick-borne Typhus is one of the oldest rickettsial diseases also called Boutonneuse fever or Mediterranean Spotted Fever (MSF). In Turkey, several cases of MSF associated with *R. conorii* have been reported in humans (58-63). Recently, *R. hoogstraali* and two human pathogenic species (*R. aeschlimannii* and *R. slovaca)* were detected in ixodid ticks in Turkey (64, 65). In addition, in the Thrace region of Turkey, *R. conorii* was also isolated from the skin lesions in three of 10 patients with MSF and was identified molecularly in the biopsy materials from 9 of 10 patients (66); *Rickettsia* spp. were found positive in the pools of ticks collected from tortoises (67).

Rickettsialpox is a mite-transmitted bacterial zoonotic disease. The causative agent is *Rickettsia akari*, a member of the spotted-fever group of rickettsiae. The disease causes mild, self-limited, febrile illness characterized by eschar formation at the mite bite site, followed by the onset of systemic symptoms and a more generalized papulovesicular rash. The pathogen is originally found in mice (usually the house mouse), and humans may be infected by the bite of an infected mite, *Liponyssoides sanguineus* (68). In Turkey, a clinical rickettsialpox case has been described in a 9-year-old boy from the Nevsehir province (69).

Murine typhus is a zoonotic infection in rats, cats, and humans caused by *Rickettsia typhi* and occurs worldwide. Recently, the infection is also described as a disease of travelers (70). The causal agent may be transmitted to humans by the bite of infected rodent fleas (*Xenopsylla cheopis*) and possibly cat fleas (*Ctenocephalides felis*). Two clinical cases of endemic or murine typhus were also reported in Istanbul, Turkey (71).

Wolbachia endobacteria are the most widespread intracellular endosymbiont of arthropods and nematodes. Their interactions with their hosts are often mutualistic rather than parasitic (72). Recently, the prevalence of *Wolbachia* endobacteria were determined via molecular techniques in the mosquito populations in Turkey (73, 74) and in the chewing lice species collected from the Angora goats (75).

Candidatus Rickettsia vini is a newly named rickettsial bacterium belonging to the spotted-fever group that has been molecularly detected in *Ixodes arboricola* ticks (76). In Turkey, *Candidatus R. vini* was detected in *I. arboricola* ticks collected from birds in the Kizilirmak Delta (77).

Lyme Disease (LD), the most common tick-borne zoonotic infection with clinical significance of humans and domesticated animals in the northern temperate zone, was first described in the USA in the late 1970s, and the causal agent was described as a tick-borne spirochete *Borrellia burgdorferi* in 1982. The environmental risk of LD is measured by the density of infected questing ticks and more specifically by the density of infected nymphs of genus *Ixodes*, as nymphs appear to be the most important epidemiological stage (39). In Turkey, Lyme borreliosis is also one of the most important tick-borne zoonotic disease, and its causal agent *Bor. burgdorferi* was isolated from *I. ricinus* ticks collected from cattle in the Black Sea region in 1998 (78). The spirochetes of *Borrelia* were present in an unfed tick nymph (79). Meanwhile, some *Bor. burgdorferi sensu lato* strains were characterized molecularly (80), and a novel *Borrelia* sp. was also isolated from *H. aegyptium* ticks collected from tortoises (*Testudo graeca*) (81), and the spirochete was named as *Bor. turcica* sp. nov (82). A clinical Lyme case was observed in a dog in 2007 (83), and anti-*Bor. burgdorferi* antibodies were also detected in dogs and horses in Turkey (84). In contrast, a few reports on LD cases in humans have been documented in some parts of Turkey (85-88). The seropositivity rate was reported as 17% in the patients with a history of tick bite in Central Anatolia (89). However, a serological study showed that the seropositivity rate for LD was found to be 10% in 50 patients having symptoms compatible with LD at the Erciyes University Hospital in the Kayseri province (90). In the Marmara region, three LD cases have been confirmed serologically and by *in vitro* cultivation with two of the three cases detected in the residents of Istanbul, while the third was described in a tourist from the USA (88). Meanwhile, *Bor. burgdorferi* was also isolated from questing *I. ricinus* ticks sampled by flagging from parks and rural areas in the Thrace region of Turkey (44). In the same region of Turkey, another similar field study was performed on ticks, which were collected from tortoise and *Rickettsia* spp., and *Bor. burgdorferi s.l.* were molecularly detected in the tick pools (67). Meanwhile, another study was conducted to investigate the presence of *Bor. burgdorferi* in tick samples collected from humans, domestic and wild animals, and the ground as unfed (questing) in 12 different provinces, including Agri and Erzurum in Eastern Anatolia; Ankara, Cankiri, Yozgat, and Kirsehir in Central Anatolia; Artvin, Giresun, and Corum in the Black Sea Coast; Kocaeli and Bolu in Marmara; and Mardin in Southeastern Anatolia regions of Turkey. *Bor. burgdorferi sensu stricto* was also isolated from unusual tick species, such as *H. marginatum*, *H. excavatum*, *Hae. parva*, and nymphs of *Hyalomma* spp. (64). Epidemiologically, these results reveal that Turkey has a high-risk potential for zoonotic LD.

Tick-borne Relapsing Fever (TBRF) Can be either louse-borne (LBRF) or tick-borne (TBRF). LBRF is caused by a human-restricted pathogen, spirochete *Borrelia recurrentis*, and transmitted by the body louse *Pediculus humanus*, while TBRF is caused by *Borrelia* spp. and is associated with the bite or coxal fluid of argasid ticks of the genus *Ornithodoros* in a wider endemic geographic area of the world, spanning Africa, Asia, Europe, Eurasia,

and the Americas with different *Borrelia* tick vector complexes implicated in the transmission in each area (39, 91, 92). In Turkey, the presence of relapsing fever with a spirochete of the Crocidurae group *Bor. crocidurae* was shown in *Ornithodoros erraticus* ticks collected from rodent holes in the southeastern areas near the Syria border (93). During the Balkan War and the First World War, some outbreaks were noted among the Ottoman and Turkish army (94).

Tularemia is an important arthropod-transmitted zoonotic bacterial infection caused by the *Francesilla tularensis* and comprises a range of clinical syndromes ranging from mild to very severe intensity. The majority of cases occur in the northern hemisphere, particularly in the rural or semirural environments (39). In Turkey, tularemia is also an important disease, which has reemerged in 1988, and the first outbreak was recorded in 2005. Almost all cases were recorded as oropharyngeal tularemia due to the ingestion of contaminated food or water (95). The first case associated with the outbreak was diagnosed near Kayseri in 2009 in Central Anatolia, and the region was described as an endemic area for tularemia (96), but no positivity was detected using molecular techniques in the pools of mosquitoes and ticks collected near the Kayseri area (18).

Bartonellosis or Cat Scrath Disease is another zoonotic vector-borne infection of humans and animals that is caused by an excluded rickettsilaes bacteria *Bartonella* spp. The causal agents *Bar. bacilliformis* and *Bar. quintana* are transmitted by sand flies (*Lutzomyia* spp) and by the human body louse, respectively, while the other agent *Bar. henselae* is commonly transmitted to humans through the bite or saliva-contaminated scratch of cats that are the natural reservoirs for the bacteria (97). *Bar. henselae* has a large distribution in the northern hemisphere (98). Domestic cats represent the main reservoir of the pathogen, and the main vector of the infection is the cat flea (99). However, the trans-stadial transmission of *Bar. henselae* by *I. ricinus* ticks was also shown (100). In Turkey, a case of bartonellosis in a domestic cat was reported (101). However, the seropositivity rates of *Bar. henselae* were 18.6% in cats (101), 6% in human blood donors (102), and 16.9% in kidney transplant patients (103) and 22.2% in cattle breeders and veterinarians (104), while the seroprevalence of *Bar. vinsonii subsp. berkhoffii* was recorded as 6.6% in dogs (105) in Turkey. In addition, the seropositivity rates of *Bar. henselae* in domestic cats varied in distinct provinces, such as Bursa, Adana, Aydin Burdur, Kayseri, and Istanbul, where they were 41.3%, 33.9%, 27.5%, 32.3%, 7.9%, and 12.5%, respectively; the average seropositivity of *Bar. heselae* in cats was found to be 27.9% in Turkey (106).

Hemoplasmosis is one of the bacterial infections of humans and animals caused by the *Mycoplasma* spp. (107). Although the infection is mainly described as vector-borne and transmitted by blood-feeding arthropods, such as ticks and fleas, the disease might also be transmitted through other routes, such as mechanically with contaminated operation tools or blood transfusions and vertically in the intrauterine period (108). *Rhipicephalus appendiculatus* transmits the infection to dogs by co-feeding (109). In Turkey, a clinical case of feline hemoplasmosis associated *M. haemofelis* was reported (110).

Q fever is caused by an excluded rickettsiales bacterium *Coxiella burnetii*. A number of hard and soft tick species, including *Amblyomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Rhipicephalus*, and *Ornithodoros*, have been documented to harbor the *C. burnetii* (111-113). Recent studies have shown that ticks harbor *Coxiella*-like bacteria, which are potentially tick-specific endosymbionts. For instance, *Coxiella*-like bacteria and possibly *C. burnetii* have been detected in the tick species *Haemaphysalis bispinosa*, *Hae. hystricis*, *Dermacentor compactus*, *Der. steini*, and *Amblyomma* sp., which were collected from wildlife and domesticated goats in different locations of Malaysia (114). Q fever is also an endemic and zoonotic infectious disease of humans and animals in Turkey. It was reported that cows, sheep, goats, and dogs might serve as reservoirs of *C. burnetii,* and *Ornithodorus lahorensis* ticks also harbor the agent; the disease is disseminated throughout Turkey, although the epidemics among humans are relatively rare (115). Recently, IgG seropositivity of *C. burnetti* in women with an abortion history and in women with healthy births in the central Black Sea region of Turkey was reported as 15.6% and 11.1%, respectively, (116).

Plague or Black Death is another zoonotic bacterial disease transmitted from rodent to rodent and from rodent to man via flea bites. Humans can also be infected by direct contact with infected animal tissues. Pneumonic plague may result from direct human-to-human transmission. The causative agent of the disease is the bacterium *Yersinia pestis*. Urban plague describes the situation where plague circulates among wild rodents. The infection is maintained in the rat population by fleas, such as *Xenopsylla cheopis* (Asia, Africa, Europe, and the Americas), *X. astia* (southeast Asia), and *X. brasiliensis* (Africa, India, and South America). Rarely, plague is spread directly from person to person by fleas, such as *Xenopsylla* species and the so-called human flea *Pulex irritans* (117). The first recorded appearance of the plague in Europe was at Messina, Sicily, in the Middle Ages (October 1347). It is thought that it arrived on trading ships that likely came from the Black Sea, past Istanbul and through the Mediterranean. It is estimated that a quarter of the people living in Europe were killed from the Black Death at that time. Within the last decade, human plague cases have been reported from countries in Africa, America, and Asia. Between 1990 and 1996, there were 16,005 cases of plague and 1214 deaths (7.6%) reported to the WHO (117). It is noted that the last plague outbreak involving 32 human cases in Turkey was recorded in 1947 in Akcakale, a town located on the Turkish-Syrian border (15). There is no official record of plague in Turkey since then.

Anthrax is an infection of humans and other mammals caused by the bacterium *Bacillus anthracis,* a Tier 1 biologic agent. Anthrax spores persist for a long time under changing environmental conditions and can be easily found in nature; they can also be produced in the laboratory. Although the vast majority of human cases are related to direct contact with infected carcasses or to handling of contaminated products from morbid animals, the transmission of the disease has been demonstrated by a wide variety of tabanid and mosquito species and with stable flies (*Stomoxys* spp) (118). The disease has wide distribution in the world and is also an endemic zoonosis in Turkey. A total of 967 (464 from animals and 503 from humans) anthrax

cases were reported from Eastern Turkey between 1992 and 2004 (119). In contrast, a total of 26,954 human anthrax cases were recorded by the Turkish Ministry of Health between 1960 and 2005, with 6861 cases reported between 1990 and 2005 (120). Although the incidence rate of anthrax in humans is decreasing (≤150 cases per year between 2011 and 2016) in Turkey, regional outbreaks still present a risk to human and animal health. The prominent clinical form recorded is cutaneous anthrax (120, 121). Recently, in April 2017, two pumas died at the Kayseri Zoo Park, and the etiologic agent was identified as *B. anthracis* by laboratory examination. The source of the infection was considered consumption of a carcass of cattle that had died of unknown reasons (personal communication with Professor M Doganay).

Brucellosis is a zoonotic infection with significant health and economic problems worldwide. The causal agents of the infection are *Brucella abortus*, *B. melitensis*, *B. ovis*, *B. suis*, and *B. canis*. The disease is mainly food-borne and is transmitted to humans through the consumption of unpasteurized/raw dairy products and rarely by eating undercooked meat. In addition, the bacteria may also enter the body by inhalation or by contact. In Turkey, brucellosis is a known disease since the First World War and its incidence has been increasing over the years. In 1999, 11,462 cases were notified to the Ministry of Health, with the incidence rate being 17.41/100,000. In the last decade, the annual recorded cases in human have been decreasing below 6,000. Predominant etiological agent is also *B. melitensis* (122). Although several control and eradication measures have been applied, brucellosis remains an endemic disease in many regions and leads to a large economic loss in cattle and in small ruminants with serious public health problems (23, 123). The prevalence of brucellosis was shown to be 32.9% in tested animals (124).

Campylobacteriosis is a common food-borne zoonotic infection of humans with gastroenteritis. The causal agent of the disease is most commonly *Campylobacter jejuni*. The agent is transmitted to humans by ingestion of contaminated food (usually unpasteurized/raw milk and undercooked poultry) and drinking of contaminated water (water-borne). The infection is also transmitted by contact with contaminated poultry, livestock, or household pets, particularly puppies (125). Meanwhile, animals farmed for meat are the major source of campylobacter enteritis. In Turkey, campylobacter gastroenteritis has been reported as a more common disease in children (126).

Clostridial diseases are caused by many clostridial bacteria both in humans and domestic animals, but these pathogens are seldom considered zoonotic agents. *Clostridium botulinum* and *C. tetani* lead neurotoxicoses in humans and domestic and wild animals, but there is no evidence for transmission among the species. *C. septicum* causes malignant edema in domestic animals and humans, and the signs and the lesions of infection are generally the same in both; however, there is no evidence for direct transmission between animals and humans. However, it was suggested that indirect transmission of entrotoxigenic *C. peringes* type C and *C. difficile* is possible via foods (i.e., in retail meats) (127). In Turkey, limited *C. difficile* infection cases have been reported in the patients with antibiotic-associated bloody diarrhea in some provinces such as Kayseri (128), Bursa (129), and Istanbul (130).

Tetanus is also another clostridial disease characterized with muscle rigidity and spasms. The agent of infection is *Clostridium tetani*, which is generally found in soil, dust, and manure. The pathogens usually enter through a break in the skin, such as a cut or puncture wound by a dirty contaminated object. Tetanus in neonates is primarily related to insufficient sanitation and lack of hygiene. Neonatal tetanus is actually preventable by immunization in many developing countries, and it has already been eliminated in most of the developed countries. In Turkey, the incidence of tetanus cases in humans has been reduced by improving hygiene conditions and implementation of tetanus vaccine in the last decades (131, 132).

Enterohemorrhagic Escherichia coli (EHEC) infection is an important coliform water-borne zoonotic disease seen worldwide. Cattle are important reservoirs of Shiga-like toxin-producing *Escherichia coli* (SLTEC) O157:H7 EHEC, which causes hemorrhagic colitis and hemolytic uremic syndrome in humans. The infected cattle can shed low levels of *E. coli* O157:H7 for a long term. The most important EHEC reservoir cattle can also carry unusual EHEC strains, such as EHEC O104:H4. Humans acquire EHEC by direct contact with carrier cattle or sheep, their feces, infected people, and contaminated soil or water or via the ingestion of undercooked meat, other animal products, contaminated vegetables and fruit, and other foods (133). In Turkey, limited data are available regarding EHEC O157 in humans and animals. Although the incidence of *E. coli* O157:H7 has been reported as varying up to 40% in gastroenteritisassociated children (134, 135), verocytotoxin producing *E. coli* O157 was molecularly detected in only one case (136). In contrast, verocytotoxin producing *E. coli* O157 was also isolated from clinically healthy cattle samples in the Hatay province of the Mediterranean region (137) and in the carcasses of cattle and abattoir environment in Istanbul in the Marmara area (138).

Erysipeloid is a rare skin bacterial infection of humans caused by *Erysipelothrix rhusiopathiae* and *Ery. tonsillaru* and occurs more commonly in individuals, who handle fish and raw meat. The disease has economic importance for farmed animals, including swine, turkeys, chickens, and sheep. People acquire the disease through contact with infected animals (particularly pigs), fish, or birds. The pathogen enters the body through existing skin wounds, such as cuts, scratches, punctures, or splinters. The infection does not spread from person to person (139). In Turkey, a few rare cases of erysipeloid in humans were reported (140, 141).

Glanders or Malleus is one of the oldest known, highly contagious and re-emerging infections and often causes fatal zoonotic disease in equids, such as horses, mules, and donkeys. These solidungulate animals serve as a natural reservoir role for the pathogen. The causal agent of the disease is *Burkholderia mallei* (formerly *Pseudomonas mallei*). It was reported that this bacterium has been listed as a potential agent for biological warfare and bioterrorism under Center of Diseases Controlcategory B (142). The pathogen organism is transmitted to the animals either directly or indirectly from secretions and excretions of

infected animals. The infection occurs subclinically in horses, and the agent organisms are found in the lesions and discharges of the skin and nasal mucosa. Thus, chronic infected horses can serve a carrier role for the epidemiology of the disease. Mules and donkeys are acutely infected animals, and the organisms are excreted in feces, urine, saliva, and tears. The major mode of transmission among solipeds is the respiratory route and ingestion of feed and water contaminated by nasal discharge, or sputum of sick animals, or direct contact with fomites. Glanders has been eradicated from many countries by statutory testing, elimination of infected animals, and import restrictions. However, it persists in some Asian, African, and South American countries. The infection should be considered a re-emerging disease and may be imported by pet or racing equids into glanders-free areas (143). The transmission of *B. mallei* from infected equines to humans is uncommon, and the person-to-person transmission is also rare. The main routes of zoonotic transmission of *B. mallei* in humans involve direct invasion of a cut, abrasion, or laceration of the skin and; inhalation; and by attack to mucous membranes (144). The first zoonotic human case was reported in a French veterinarian in 1793 (142), and recently, a clinical glanders case was determined in a microbiologist at the U.S. Army in 2000 (145). Professionals who are in close contact with sick horse, such as veterinarians, farmers, horse traders/fanciers, laboratory workers, and other workers in slaughterhouses and horse stable and soldiers are at occupational exposure to glanders. In Turkey, glanders is one of the compulsory notifiable diseases. To control and eradicate glanders, a national project was conducted by the Ministry of Agriculture between 2000 and 2001. In the project scope, a total of 235,286 equines were screened for glanders, and 3509 were found positive. All of the positives were culled as compensation. The economic impact of the disease was devastating for Turkey. In same period, no clinical cases of glanders were observed in tested horses and mules, while only one glanders case was reported from a donkey with clinical sings. In recent years, approximately 10,000 pedigree horse sera were tested using the complement fixation test (CFT) and all of the tested sera were found negative for glanders (146). It was reported that the history of human cases of glanders goes back to 1890s when some army and civil veterinarians became sick during the struggle programs against glanders between 1901 and 1934 and died of the disease (147). In the following decades, limited human cases of glanders were also reported from some parts of Turkey (148-150).

Leprosy is a serious human disease caused by *Mycobacterium leprae*. The transmission of the disease from an infected person to others is possible by close contact. However, the transmission of animal leprosy to man may be possible with armadillos that are the only other known natural hosts of the pathogen organism. The disease was a serious health problem almost 60 years ago in Turkey (151), but no leprosy case is seen in the country today. The disease was eradicated with systemic surveillance and treatment, intensive control measures, improvement in general health conditions, and with good coordination of health institutions in Turkey (152).

Leptospirosis is a zoonotic disease caused by *Leptospira interrogans* and occurs worldwide. The infection predominantly affects some professionals who are in close contact with infected animals or their urine. The incidence of leptospirosis was found to be relatively high in humans (153) as well in animals (154, 155) in Turkey.

Listeriosis is a sporadic bacterial zoonotic infection caused by *Listeria monocytogenes* and affects a wide range of animals, including man and birds. Encephalitis or meningencephalitis in adult ruminants is the most commonly recognized clinical form of the disease. The disease is primarily a winter-spring infection of feedlot or housed ruminants. Grazing animals ingest the organism and animal-to-animal transmission occurs via the fecal-oral route. The transmission of listeriosis to man is possible by close contact or through handling of aborted material; nosocomial infection is also seen in hospitals. *L. monocytogenes* is an important cause of severe infection in patients with impaired cell-mediated immunity, neonates, pregnant women, the elderly, and transplant recipients. Human infection is generally observed as a food-borne disease. Various clinical forms, such as central nervous system infection, sepsis, endocarditis, gastroenteritis, and rarely other clinical forms, were reported in humans in Turkey (156). Several serosurveys indicate that seroprevalance of *L. monocytogenes* was relatively high in healthy animals and reported as 44.9% in cattle (157), 25.8% in sheep (158), 40.29% in horses (159), and 22.3% in dogs (160) in different regions of Turkey. Meanwhile, it was declared that the prevalence of *L. monocytogenes* was 42.2% in slaughterhouse workers in Ankara (161).

Mycobacteriosis is a chronic or acute, systemic, granulomatous disease that occurs in aquarium and culture fish. Several species of *Mycobacterium* cause the infection. The two most important species in fish and humans are *Mycobacterium marinum* and *M. fortuitum*. The source of *M. marinum* infection is contaminated water. In the past, human outbreaks of *M. marinum* were sporadic and most commonly associated with swimming in contaminated pools. In humans, breaks in the skin serve as an entry point for the organism during contact with contaminated water sources or infected fish. In fish, transmission can occur by consumption of contaminated feed, cannibalism of infected fish or aquatic detritus, or by entry via injuries, skin abrasions, or external parasites. In Turkey, *Mycobacterium* spp. were detected in fish samples in the Mersin province (162). In contrast, avian mycobacteriosis is also an important disease that has been reported widely in pet birds, captive wild birds, as well as poultry and occurs worldwide (163). Recently, a case of avian mycobacteriosis was detected in a wild bird (*Buteo rufinus*) in the Kars province in Turkey (164).

Pasteurellosis is an important zoonotic disease caused by *Pasteurella* species, which are highly prevalent among animal populations where they are often found as part of the normal microbiota of the oral, nasopharyngeal, and upper respiratory tracts. Many *Pasteurella* species are opportunistic pathogens that can cause endemic disease and are associated increasingly with epizootic outbreaks. Zoonotic transmission to humans usually occurs through animal bites or contact with nasal secretions, with *P. multocida* being the most prevalent isolate observed in human infections (165). In Turkey, bovine pasteurellosis is one of

the prevalent infections and leads to important economic losses (166). Meanwhile, cellulitis due to *Pasteurella multocida* in a 5-year-old girl bitten by a dog (167) and acute osteomyelitis due to *P. multocida* in a 70year-old diabetic man bitten by a cat have been reported (168).

Psittacosis is a zoonotic infectious disease of birds caused by *Chlamydophila psittaci*. The disease is also known as parrot fever or avian chlamydiosis. *C. psittaci* can be transmitted among birds by inhalation of infectious dust or airborne particles, such as feathers, and by ingestion of infectious material including carcasses. Humans usually get the infection by inhalation of contaminated dust, feathers, or aerosolized secretions and excretions. In Turkey, *C. psittaci* was detected in pet birds (169) and in some waterfowls in different zoos (170), while there is no official report on human chlamydiosis.

Salmonellosis is a widespread food-borne contagious zoonotic infection both humans and animals worldwide caused by *Salmonella enterica* subspecies enterica serovar Typhimurium. Domestic animals and wild animals may serve as carriers in the epidemiology of the disease. The disease is typically transmitted to humans by consumption of *Salmonella*-contaminated food, with eggs being the most blamed food (171). In Turkey, few studies have been performed on salmonellosis in dogs (172) and in poultry (173). Recently, different *Salmonello* serotyps were detected in turkey ground meat and meat parts, and *S. corvallis* was shown to be the predominant serotype in poultry meat in Turkey (174). Although salmonellosis is considered a threat for public health, limited reports on confirmed cases of human salmonellosis were documented in Turkey. In a study that was conducted to investigate surveillance of enteric pathogens of public health importance, a total of 177 *Salmonella* strains were isolated from different patients during the period between 2008 and 2011 in Ankara. *Salmonella* Enteritidis was found as the most frequent *Salmonella* serovar. Its prevalence was detected as 61.4% with one *Salmonella typhi* strain isolated (175). An outbreak of Salmonella Enteritidis due to consumption of contaminated patisserie products was reported in 433 persons in Kadirli county of Osmaniye province located in the Mediterranean region of Turkey in 2014 (176).

Streptococci are gram-positive and aerobic bacteria that cause several disorders, including pharyngitis, pneumonia, endocarditis, sepsis, and wound and skin infections. The wound and skin infections are seen in man and animals due to dog and cat bites or rarely wild predatory animal bites or rodent bites as well (177, 178). The numbers of bacterial isolates vary depending on the type of wound, which is commonly mixed as aerobic anaerobic infections (179). *Streptococcus* species are frequently isolated from dog bite wounds. *Streptococcus mitis* was found as the most common species among different members of the genus (180). In Turkey, the reports on the cases of wound and skin infections in animals and in man due to dog and cat bites are limited. In a retrospective study, 114 bite wounds were recorded in dogs and cats between 1999 and 2003 at small animal clinics of Veterinary Faculty of the Aydin province in the Aegean region of Turkey (181). Meanwhile, a total of 25,480 dog and cat bite cases were recorded in humans between 2005 and 2009 in Ankara (182). Recently, the number of animal-inflicted human wound cases was reported as 205 between 2013 and 2014 in the Erzurum province in Eastern Anatolia, Turkey (183).

Tuberculosis (TB) is one of the most devastating and oldest known zoonotic disease in humans and occurs worldwide. The estimated global annual incidence rate of human TB is almost 128 new cases/100,000 populations (184). Although human TB is caused particularly by *Mycobacterium tuberculosis*, other major causative agents, such as *M. bovis, M. caprae*, *M. avium*, and *M. marinum,* can also cause human tuberculosis. *M. bovis* and to a lesser extent *M. caprae* are the main causative agents of bovine TB. These zoonotic pathogens are transmitted to humans by close contact with infected cattle or consumption of contaminated animal products, such as unpasteurized milk (185). In Turkey, the total number of human TB was reported as 16,551 while the rate of new cases of human TB was shown as 22/100,000 between 2005 and 2010 (186). Meanwhile, the prevalence of tuberculosis in cattle was reported as 0.38%–1.49% in Turkey (124).

Vibrio diseases may be mainly classified into two different infections groups: Vibrio cholera (caused by V. cholerae) and noncholera *Vibrio* (caused by *V. parahaemolyticus* or *V. vulnificus*). Most of these *Vibrio* infections are related to consumption of contaminated food or water and hence these infections are considered as food-borne or water-borne diseases. Poor sanitation and adverse environmental conditions after natural disasters, such as hurricane, earthquake, and tsunami, may also increase the risk of *Vibrio* infections. Humans can acquire *Vibrio* infections by ingestion of raw or undercooked shellfish. Vibriosis is also an economically important disease of cultured fishes, such as gilthead sea bream (*Sparus aurata*). Initial infection is probably water-borne; however, once established in fish, the infection spreads by contact. Some epizoitics can also be seen because of the use of infected marine fish in the feeds of healthy fish. The zoonotic transmission of fish vibriosis is possible by ingestion of infected fish tissues (187). In Turkey, studies on vibriosis are very limited. However, fish vibriosis was diagnosed in cultured gilthead sea bream in the Aegean Sea coast farms of Turkey (188). There is no official report on cases of human vibriosis in Turkey.

Yersiniosis is a food-borne zoonotic infection caused mostly by eating raw or undercooked contaminated foods with *Yersinia enterocolitica*. *Y. enterocolitica* and other *Yersinia* species were isolated from ground beef in Aydin (189). In another study that was conducted to investigate the incidence and pathogenicity of *Y. enterocolitica* in the Northeast Anatolia regions of Turkey (provinces of Kars, Igdir, and Ardahan), a total of 750 food samples, composed of ice cream, raw milk, feta cheese, chicken drumsticks, and minced meat were tested and 57 samples (7.6%) were evaluated positive for *Yersinia* spp; 18 (2.4%) of these isolated from 6 feta cheese, 4 ice cream, 2 chicken drumsticks, 4 minced meat, and 2 raw milk samples were determined as contaminated with pathogenic *Y. enterocolitica* (190). However, *Y. enterocolitica* and *Y. pseudotuberculosis* strains were isolated from humans in the Van province in East Anatolia, Turkey (191).

Actinomycosis is caused by anaerobic *Actinomyces* species *A. israelii* and *A. bovis*. The disease occurs rarely in humans, but

frequently in cattle, and the infection is called "lumpy jaw" because of large abscesses seen on the necks of infected cattle. *A. israelii* and *A. bovis* are normal commensal species in humans and in cattle, respectively. The infection develops due to a predisposing factor in the buccal cavity, such as dental problem or periodontal disease (192). The rare zoonotic transmission of the disease may be seen by contact with infected animals (193). In Turkey, a total of 167 cattle with actinomycosis were treated at the surgical clinic of Veterinary Faculty between 1957 and 1971 in Ankara (194). However, a total of 50 *A. israelii* strain were isolated from cervico-vaginal regions of women who were introduced to gynecology clinics of Medicine School between 2002 and 2004 in the Van province in Eastern Anatolia (195).

Actinobacillosis is a bacterial zoonotic disease caused mostly by *Actinobacillus lignieresii*. The most common form of the disease occurs as mouth actinobacillosis in cattle and is called "wooden tongue." However, the infection affects sheep as well. Actually, the pathogen is considered a microorganism of normal rumen flora of sheep and cattle. The organism enters via damaged tissues in the mouth of ruminants. Cutaneous route was indicated for zoonotic transmission of the infection in humans (36). In Turkey, two cattle with clinical actinobacillosis were treated in Ankara (194), whereas there is no report on actinobacillosis in humans.

Arcanobacteriosis is a zoonotic infection characterized with granuloma caused by facultative anaerobic bacteria *Arcanobacterium* species, *A. haemolyticum*, and *A. pyogenes*. The infection can be transmitted by close contact from animal to animal, from animals to humans, or even from human to human (36, 196, 197). *A. pyogenes* leads summer mastitis in cows with huge economic losses (197) and causes thoracic pyogranuloma formation in dogs (198), while causes endocarditis in man (196). However, the insect transmission of summer mastitis in cows at a cattle herd was successful experimentally via *Hydrotaea irritans* flies (199). In Turkey, a total of 51 *A. pyogenes* strains were identified from samples collected from cattle and sheep in the Konya province of Central Anatolia (200). Meanwhile, the prevalence of *A. haemolyticum* was reported as 2% in children with tonsillopharyngytis in Istanbul (201).

Dermatophilosis is a zoonotic bacterial infection caused by *Dermatophilus congolensis*. The infection is rare in humans but is frequent in horses, dogs, cats, and ruminants, particularly in cattle infested with ticks. In Turkey, a few cases of dermatophilosis in animals (202) and in humans have been reported (203).

Nocardiosis is a bacterial disease in immunocompromized hosts caused by opportunistic species belonging to the *Nocardia asteriodes* complex. The pathogens can be found in environment, such as soil, decomposing vegetation, and other organic matter as well as in fresh and salt water. People with cancer or people taking steroid treatments are at risk for nocardiosis, and the infection often happens via several ways, such as inhalation (pulmonary nocardiosis), traumatic inoculation (cutaneous nocardiosis), and hospital-acquired (extra pulmonary nocardiosis) (204-206). In Turkey, a solitary case with granulomatous nocardial pleurisy was documented in a dog in Ankara (207). However, a total of 53 cases with mostly pulmonary nocardiosis were reported in humans between 1997 and 2004 (208); recently, a few new cases with clinical nocardiosis were also diagnosed in man in distinct areas of Turkey (209, 210).

Fungal Zoonotic Diseases in Turkey

Fungal Zoonotic Diseases are significant health problems in man and in animals worldwide. Today, many fungal zoonotic diseases have been described in the world and some of them also occur in Turkey (Table 1).

Aspergillosis is a respiratory and non-contagious fungal infection caused by opportunistic *Aspergillus* species and occurs relatively rarely in humans, while it is a common and dangerous disease for birds. Although *A. fumigatus* is most common in humans, other common species, including *A. flavus* and *A. niger,* also cause problems in humans and in birds (211). Warm and moist environment, poor ventilation and insufficient sanitation, and long-term storage of feed, are predisposing conditions for aspergillosis and can increase the amount of the spores in the air. Spores often become airborne and spread to the environment by wind and can enter into the respiratory system by inhalation (212). In Turkey, aspergillosis has been detected predominantly in the homes of asthmatic patients (213, 214). Meanwhile, it was reported that aspergillosis is a prevalent fungi infection in pigeon herds, birds of zoo, geese, dogs, and horses (215).

Blastomycosis is a zoonotic fungal infection caused by *Blastomyces dermatitis*, and the disease occurs in several endemic geographical areas, such as North America. The fungus mainly thrives in moist soil and decomposed matters, such as wood and leaves. The infection is transmitted to humans and animals by inhalation the fungal spores via the airway from the environment or by contact with contaminated soils. In Turkey, a case of blastomycosis in a 47year-old female was reported (216).

Candidiasis is a zoonotic infection caused by particularly *Candida albicans*. Humans mainly serve as reservoirs, while animals only occasionally. *Candida* is present in the normal flora of humans and animals present on the skin, intestinal tract, and genital area of women; they generally do not cause any problems. However, the fungi sometimes lead to infections on the skin and in the mucous membrane of the mouth and the vagina. The transmission of disease is possibly via direct contact. In Turkey, *Candida albicans* was isolated from the fecal samples of cage birds in Istanbul (217). In contrast, different *Candida* species were isolated from the oral cavity of 65 of 125 healthy people between the ages 17 and 67 years in Istanbul, and the prevalence of *C. albicans* was found as 48% (218).

Coccidioidomycosis is a fungal infection caused by *Coccidioides immitis* and *C. posadasii*. The disease occurs in non-human mammals, such as cattle, cats, horses, dogs, and wildlife and is transmitted through environmental exposure. The causative pathogens of the disease are found particularly in warm, arid, and desert areas of the Western Hemisphere. The zoonotic transmission of the infection to humans has not been reported yet. However, any person who resides in or travels to the endemic area can become infected with *Coccidioides* spp. after inhalation of airborne arthroconidia (219). Recently, an imported coccidioidomycosis case has been detected in a 41-year-old other-

wise healthy Turkish man who visited Texas area in the USA and returned to Turkey (220).

Cryptococcosis is a zoonotic and serious fungal disease worldwide caused by opportunistic *Cryptococcus neoformans*. The disease is considered to be acquired by inhalation of the infectious propagule from the environment in endemic areas and occurs in three forms in humans, such as cutaneous, pulmonary, and meningitis. Its prevalence has been increasing over the past 20 years for many reasons parallel to the increase in the incidence of acquired immunodeficiency syndrome (AIDS) and the expanded use of immunosuppressive drugs. The infection is also common in livestock animals, dogs, cats, birds, and wild life. Soil, fowl manure, and particularly dropping and nest of pigeons could be sources for disease. In Turkey, it was reported that the prevalence of *C. neoformans* varies between 1% and 35% in natural sources, and most of the human cases were clinically characterized with meningitis (221).

Histoplasmosis is a zoonotic fungal infection caused by *Histoplasma capsulatum,* and occurs worldwide in different forms, such as pulmonary and systemic infections in humans. The pathogen lives in the environment, mainly in the contaminated soil with fowl manure in the bat caves. Birds are not susceptible to the disease, but the pathogen causes infection in various animals, such as dogs, cats, farm animals, and other wild mammals besides humans. The causative agent is transmitted to the host by the inhalation of the spores (222). It was asserted that Turkey may be an endemic area for histoplasmosis by some earlier reports (223). Recently, a case report has been documented on histoplasmosis in humans (224).

Dermatophytosis is a widespread fungal infection of the skin caused by three types of fungi called trichophyton, microsporum, and epidermophyton, which infect both humans and animals. The infection on the skin clinically reflects typical enlarging raised rings called "ringworm." The spores of these fungi may survive for a long term in the soil. Humans and animals can acquire the infection by direct contact with contaminated soil, and the disease can also spread via contact with infected hosts. In an investigation conducted to determine the prevalence of dermatophytosis in the introduced patients in the dermatology clinic of Medical School in Elazig province in Eastern Anatolia, several fungi were isolated from 142 of 651 samples (21.8%). The prevalence of *Trichophyton rubrum*, *T. mentagrophytes*, *T. violaceum*, *T. tonsurans*, *Epidermophyton floccosum*, and *Microsporum canis* in the isolates were diagnosed as 70.4%, 15.4%, 2.11%, 0.7%, 2.8%, and 4.2%, respectively (225). However, the prevalence of dermatophytosis in cattle, sheep, goats, and cat displayed in the Van province in the same region of Turkey were 33.3%, 18.1%, 33.3%, and 47.1%, respectively (226).

Sporotrichosis is an infection caused by the saprophytic fungus *Sporothrix schenckii* worldwide. It is characterized by skin, lung, and circulate types. The pathogen is present in the soil and on various plant matters, such as sphagnum moss, rose bushes, and hay. Humans can acquire the infection by contact with the spores of the fungus in the contaminated environment. The skin form of the disease is the most common and sometimes has been associated with cat scratches. Skin sporotrichosis is frequently seen in cats and horses, and infected cats can also play a role in zoonotic transmission of the infection. Hence, the disease is a major and close hazard for veterinarians. In Turkey, sporotrichosis is rare (227), but a few cases have been reported. A case of subcutaneous sporotrichosis was reported from a 48-year-old man in Kayseri in Central Anatolia (228). *Sporothrix schenckii* was isolated from a patient with nodular lymphangitic cutaneous sporotrichosis in the Edirne province of the Thrace region (227).

Penicilliosis is an emerging fungal zoonotic disease caused by *Penicillium marneffei*. *P. marneffei* has an enigmatic epidemiology, and more investigations are needed to understand its zoonotic or sapronotic transmission. This opportunistic fungus is generally seen in immunocompromized individuals, particularly in human immunodeficiency virus positives (229). The pathogen lives in the soil as its natural habitat and endemically occurs in south Asian countries. Bamboo rats and dogs can serve as reservoirs for the pathogen in endemic areas; important points about the zoonotic nature of its transmission is remains unknown (230). *Penicillium* spp was found as predominant allergen (46%) in a study that was carried out to investigate fungus species at atmospheric air of elementary schools in the Denizli province of the Aegean region, Turkey (231).

Malassezia infection or Pityriasis is a fungal infection caused by *Malassezia pachydermatis.* The infection affects both humans and animals. Malassezia species can be involved in skin disorders, such as pityriasis versicolor, seborrheic dermatitis, atopic eczema, and folliculitis and occur at higher population densities on scalps with dandruff than on scalps without dandruff. The zoonotic transmission of pityriasis is possible mechanically through hands (232). Patients under total parenteral nutrition and immunocompromized patients with an increased length of stay in intensive care units are at risk for *Malassezia* infections. Dogs and cats become infected with *M. pachydermatis* that are normally present on their skin and in the ear canal (233). In Turkey, a limited number of studies on pityriasis have been performed to date (234-236).

Adiaspiromycosis is a rare chronic pulmonary disease caused by *Emmonsia crescens*, *Emm. Parva*, and *Emm. pasteuriana* and effects both humans and animals. The disease is mainly characterized by the presence of large adiaspores in the lungs of infected humans and animals. Among the etiologic agents, *Emm. crescens* is prevalent in continental Europe and England, whereas *E. parva* occurs in Asian, African, and American continents. *Emmonsia* species are environmental pathogens and their transmission to the host is possible by inhalation of their spores (230). In Turkey, some adiaspiromycosis cases were reported from several small wild mammals (237).

Pneumocystosis is a fungal disease caused by *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii*) that primarily leads to pulmonary infection in AIDS or in immunocompromized patients (238, 239). The airborne transmission of *Pneumocystis* sp. from host-to-host has been demonstrated in rodent models (240). In Turkey, pneumocystis pneumonia due to *P. carinii* in AIDS patients was reported in 1990s (241, 242). The prevalence of *P. jirovecii* was also displayed as 54% in the respiratory samples introduced to the parasitology laboratory

between 2003 and 2011 in the Samsun province of the Black Sea region (243).

Microsporidiosis is an opportunistic fungi infection of humans. The infection is caused by several microsporidian species, such as *Encephalitozoon cuniculi*, *Enc. intestinalis*, *Enc. Hellem*, and *Enterocytozoon bieneusi*. The infection occurs in immune-deficient individuals with persistent diarrhea. Microsporidial species also infect a wide range of animals, including birds, raising the concern for zoonotic transmission. Microsporidian spores are relatively resistant to harsh environmental conditions and exist in water sources. Humans and animals get the infection by ingestion or inhalation of the spores (244). A study in Turkey, which was conducted to investigate the prevalence of *Enc. intestinalis* and *Ent. bieneusi* in cancer patients under chemotherapy at the Erciyes University Hospital in Kayseri showed that 65 of 93 patients (69.9%) with cancer were found positive; 43 (46.2%) of the positive samples were identified as *Enc. intestinalis*, while the 9 were determined as (9.7%) *Ent. Bieneusi*, and the other 13 (14%) were diagnosed as mixed infections (245). However, a study was performed to investigate the molecular epidemiology of microsporidian infections in dogs around Kayseri in the Cappadocia region, and 41 of 282 stool samples (14.5%) were found positive for microsporidiosis; 35 of 41 positive samples (85.3%) were identified as *Enc. intestinalis*, while the reaming 6 (14.6%) were detected as *Enc. cuniculi*. In the same study, three haplotypes that showed 99.4% identity to each other were characterized within the *Enc. intestinalis* isolates. However, only one haplotype was displayed in the sequences of *Enc. cuniculi* isolates and this haplotype was described as *Enc. cuniculi* Genotyp III (dog genotype), and no polymorphic region was found in the sequences of the *Enc. cuniculi* isolates (246). Furthermore, *Enc. cuniculi* and *Ent. bieneusi* were molecularly detected from household cats in the Samsun province of the Black Sea region (247).

Viral Zoonotic Diseases in Turkey

Globally, a total of 95 zoonotic viruses have been identified and listed under the entitled "spillover and pandemic properties of zoonotic viruses with high host plasticity" and their general transmission categories were also grouped (248). Several zoonotic viruses that are transmitted to humans by direct or indirect route cause severe infections in Turkey (Table 1) as well as globally. These infections were categorized according to their clinical manifestations and epidemiological characteristics, as indicated by Venkatesan et al. (249) into groups (i) encephalitis, (ii) rash and arthralgia, (iii) hemorrhagic fever, (iv) emerging, (v) re-emerging (vi), rare zoonotic, and (vii) potential zoonotic viral infections. The specific diagnosis of these infections generally involve virologic tests, such as virus neutralization test, complement fixation and hemagglutination-inhibition, enzyme-linked immunosorbent assays; further analysis is required for molecular detection and characterization of the causative viruses (250, 251). Vaccines are not available for the majority of these diseases. However, recent advances and intense investigations toward the development of new generation vaccines are encouraging for the future of control programs against viral infections. Currently, some measures, such as prophylactic and therapeutic, are available for the control of limited number of viral infections, whereas the implementation of vector control programs are basically required for most of viral diseases.

Encephalitis group zoonotic viruses are RNA viruses of the Rhabdoviridae, Flaviviridae, Togoviridae, Reoviridae, and Bunyaviridae families and are transmitted to humans by mosquitoes and ticks, except rabies virus in Rhabdoviridae family, which is transmitted by the bite of an infected host. The symptoms of viral encephalitis are associated with clinical manifestations of neurological disorders, headache, fatigue, aches in muscles, fever, vomiting, double vision, confusion, and agitation or hallucinations. The reported viral zoonotic infections with encephalitis manifestation in Turkey are shown in Table 1.

Rabies is a lethal form of encephalitis caused by the *Rabies lyssavirus* belonging to the genus *Lyssavirusvirus* of the Rhabdoviridae family. The disease is still effective and has great zoonotic importance in Turkey. Confirmed 39 cases of human rabies were reported by the Ministry of Health in a 15-year period between 1992 and 2007. Of the cases, 29 (74%) were related to dog bites, while the others were closely connected with wild animals (252).

Tick-Borne Encephalitis (TBE) is an important infection of humans caused by the tick-borne meningoencephalitis virus belonging to the genus *Flavivirus* in the family Flaviviridae. The infection is prevalent in a large endemic area of Asia and Europe, including Turkey. In Turkey, the seropositivity of the infection was reported in the range 1.4%-20.5% (10).

West Nile Virus (WNV) is an infection that has a worldwide distribution. The infection is mainly transmitted by mosquitoes. The virus has been isolated from several mosquito species. Especially *Culex* species have found to be infected with the virus. In 2010, the first outbreak of WNV infection, including 12 laboratory-confirmed and 35 suspected cases, were identified in Turkey. The patients were from different provinces, mainly located in the western part of the country (253). In Turkey, the seropositivity of the infection was reported in the range 1%-16% in humans, while 1%-37.7% in domestic animals (35, 254).

Rashes and arthralgia group viruses consist of a few viruses that belong to *Alphavirus* in Togaviridae family. Rashes and arthralgia are clinically seen in the virus-infected patients. In Turkey, the reported viral zoonotic infections causing rash and arthralgia are presented in Table 1.

Chikungunya virus (CHIKV) infection is a mosquito-borne zoonotic disease with rashes and arthralgia characteristics caused by CHIKV belonging to the genus *Alphavirus* of the Togoviridae family. The infection is prevalent in Africa and Asia. However, in Ankara, a case of CHIKV infection was diagnosed in a 55-year-old Turkish woman who had lived in India, New-Delhi, for 3 years (255). More recently, *Alphavirus* was also found by molecular assays in pools of mosquitoes collected from the Thrace region of Turkey (256).

Hemorrhagic fever group zoonotic viruses consist of 16 pathogens that belong to Arenaviridae, Bunyaviridae, Flaviridae, and Filoviridae families, causing infections generally associated with extensive bleeding. Most of viruses in this group are transmitted

by vector arthropods, such as mosquitoes and ticks. In Turkey, the reported hemorrhagic fever viruses are shown in Table 1.

Crimean-Congo Hemorrhagic Fever (CCHF) is a tick-borne zoonotic contagious disease caused by a virus belonging genus *Nairovirus* in Bunyaviridae family, which is transmitted by tick species of the Ixodidae family. Wild and livestock animals serve as amplifiers of the CCHF virus in field conditions. The infection occurs in a large area of sub-Saharan Africa, Eastern Europe, Russia, the Middle East and western China. In Turkey, it was reported that the infection was first observed in 2002 in the Black Sea region and then spread to the rest of the country (10, 257).

Dengue fever (DENF) is a zoonotic infection caused by DENF virus (DEN-1, DEN-2, DEN-3, and DEN-4 serotypes) belonging to genus *Flavivirus* of the Flaviviridae family. The infection is transmitted to humans by *Aedes aegypti* mosquitoes and occurs worldwide. In Turkey, a case of DENF virus was diagnosed in a 40-year-old patient who has visited India and the virus was identified as DEN-3 serotype (258).

Emerging group zoonotic viruses: An emerging disease means previously unknown and newly identified infectious agent that causes public and animal health problems either locally or globally. This group has serious potential threats for human health with economic impacts, and their current trends have been going upwards. Thus, these viruses have been defined as "a zoonosis that is newly recognized or newly evolved or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector range" by the WHO/ Food and Agriculture Organization of the United Nations (FAO)/ World Organization for Animal Health (OIE) in Geneva (259). The last 30 years have seen a significant increase in emerging viral diseases in humans, and almost 70% of the infections were categorized as zoonotic infections (2, 260). The major source of emerging zoonotic viruses is increasing wildlife, particularly bats which play important epidemiologic roles for some viruses, such as Hendra and Nipah, SARS, and MERS virus. Toward the investigation of these viruses and to prevent current diseases (or possible infections), the One Health approach has been developed. In this scope, it was reported that a horse vaccine also called "One Health Vaccine" can be used to prevent the transmission of Hendra virus from horse to human (261). In Turkey, the reported emerging zoonotic viruses are shown in Table 1.

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a zoonotic infectious disease caused by a virus belonging to genus Betacoronovirus in the subfamily Coronovirinae of the Coronaviridae family, and MERS-CoV was isolated from bats. Infected patients with MERS-CoV commonly have fever, cough and shortness of breath as clinical symptoms, and in most of the cases, gastrointestinal symptoms, such as diarrhea, have also reported. There is no vaccine or medication that protects against MERS-CoV (243), and close dromedary camel contact is a major risk for human infection (262). In 2015, 971 laboratory-confirmed cases of human infection with MERS-CoV were reported to WHO, including at least 356 deaths. Most of these cases have been reported from several Middle East countries including Turkey (263).

Avian Influenza (H5N1) is a zoonotic infection caused by viruses adapted to birds that serve as a natural reservoir for the infection. Although influenza A is adapted to birds, it can also stably adapt and sustain person-to person transmission. The transmission of the infection is mainly by contact between infected and healthy birds, although it can also be spread indirectly through contaminated equipment. The virus can be found in the secretions and droppings of the infected birds. A highly pathogenic infection is spread to people often through direct contact with infected poultry, such as during slaughter or plucking. The infection occurs as global avian influenza pandemics and cause big economic losses (261). The infection is also prevalent in Turkey, and its economic impact was reported at almost 7.5 million US dollars/per day and total loss was expressed as over 231 million US Dollars for 2 months in 2006 (264). A total of 625 patients with suspected H5N1 virus infection were treated at the University Hospital between 2005 and 2006 in the Van province, and eight of them were diagnosed as H5N1 positive. At the same period, additional four confirmed cases of H5N1 were reported from different areas of Turkey, including the Black Sea region and central, southeast, and eastern Anatolia (265).

Swine Influenza is a highly contagious respiratory zoonotic viral infection caused by influenza A viruses of the Orthomyxoviridae family. The most common subtypes of influenza virus in swine are H1N1, H1N2, and H3N2. The disease in swine occurs within a herd either as an epizootic or enzootic form, which infect the respiratory tract of pigs and result in a barking cough, decreased appetite, nasal secretions, and listless behavior; the virus can be transmitted to humans. Swine flu viruses may mutate so that they are easily transmissible among humans. Swine flu is transmitted from person to person by inhalation or ingestion of droplets containing virus from sneezing or coughing. In Turkey, a study was conducted to investigate the seroprevalence following the first wave of pandemic influenza A (H1N1) in 2009, the pandemic H1N1 seropositivity was found to be 24.1% for Ankara and 27.7% for Diyarbakir (266).

Hemorrhagic Fever with Renal Syndrome (HFRS) virus is a group of clinically similar diseases caused by various viruses, such as Hantaan, Dobrava, Saaremaa, Seoul, and Puumala, belonging to genus *Hantavirus* in Bunyaviridae family. HFRS comprises several diseases, such as Korean hemorrhagic fever, epidemic hemorrhagic fever, and nephropathia epidemica. Rodents are reservoirs for Hantaviruses, and humans can become infected by direct contact with infected rodents. Although individual transmission is possible, it is extremely rare. HFRS occurs commonly in a large area of Asia, Southeast Asia, and Europe (261). An outbreak of HFRS with 23 confirmed cases was reported as an emerging disease from Zonguldak and Bartin provinces in the Northwest part of Turkey in 2009 (267, 268).

Hepatitis E is a liver disease caused by hepatitis E virus, which is a small RNA virus with at least 4 genotypes. The transmission of the disease is possible by the fecal-oral route, principally via contaminated water. Hepatitis E virus occurs worldwide, although the prevalence is highest in East and South Asia (261). In Turkey, limited epidemiological studies on hepatitis virus have been conducted in children in various provinces. The seropositivity of

hepatitis E virus was 2.1% in Ankara of Central Anatolia (269), 12.4% in the Denizli province of the Agean region (270), and 4.2% in the Van province of Eastern Anatolia (271).

Parainfluenza viruses (PIVs) belong to the Paramyxoviridae family and have 5 subtypes, such as Parainfluenza 1, 2, 3, 4a, and 4b. Nosocomial infections are also common, particularly among young infants. Human parainfluenza viruses (hPIVs) can be transferred through direct person-to-person contact (with infected secretions) and via respiratory droplets (261). In Turkey, outbreaks were reported in children in the Izmir province between 2000 and 2005, and Parainfluenza type 3 was isolated from 96 of the 178 (53.9%) viral specimens (272). In another study, the seropositivity of Parainfluenza 3 was found to be 18% in 15 dairy cattle farms in East and Southeast Anatolia regions of Turkey (273).

Re-emerging group zoonotic viruses: Re-emerging infectious diseases include infectious agent that had fallen to such low levels that it was no longer considered a danger for public and animal health problem, but became reactive again and showed an upward trend in the incidence or prevalence in humans and animals both locally and worldwide. Re-emerging zoonotic viral infections can emerge when viruses expand their host range (for example monkey poxvirus and equine morbillivirus) or the disease can be a result of intrinsic properties of the virus itself, such as high mutation rate (ie, influenza A virus and foot and mouth disease [FMD] virus) (274). Most re-emerging viral zoononeses involve infections with hemorrhagic and neuropathological viruses that are arthropod-borne (yellow fever virus; Zika virus) (275), by rodents (Hanta virus), or by nosocomial infections (Ebola virus). The re-emergence and increase of these group of infections are also a consequence of anthropogenic environmental changes, such as distortion of the ecological balance and major agricultural changes (276). Additionally, complex interactions among ecology, socioeconomic and demographic structures, health care, and human/animal behaviors also affect the re-emergence of zoonotic viral disease (249). The reported re-emerging viral zoonotic infections from Turkey are listed in Table 1.

Orf virus infection or Ecthyma contagiosum is one of the re-emerging zoonotic viral infections caused by a virus belonging to genus *Parapoxvirus* (PPV) in Chordopoxvirus subfamily of the Poxviridae family. The Orf virus often affects different hosts, such as wild and domesticated cattle, sheep, goats, and humans. The disease is transmitted to humans by direct or indirect contact with the infected material. The first case of Orf in humans was clinically manifested as solitary skin lesion in 1934 (277). In Turkey, the Orf virus infection has reemerged during the last two decades, and case reports and Orf outbreaks related to Orf in both animals and humans are available (278, 279). The human case of Orf virus infection with a pyoderma-like lesion on the left indicator finger was diagnosed in a 37-year-old man in 2011 in Ankara, and the virus was molecularly characterized (280). Later another case of Orf virus infection with similar manifestations on the right hand thumb was reported from a child (281).

Rare Viral Zoonotic Infections group: Various viral infections, which originate from animal pathogens, can sometimes cause nonspecific febrile illness in humans. The transmission of these diseases are commonly possible by contact with infected animal (FMD particularly serotype O, buffalo pox), by handling of such organisms in laboratory conditions (bluetongue and Newcastle disease), by sexual contact (simian immune deficiency virus), by bite or scratch (monkey B virus), via vectors (semliki forest virus, African horse sickness, and louping ill [LI]), or through food or water (caliciviruses, such as swine vesicular exanthema, feline calicivirus, and rabbit hemorrhagic disease virus). Recently, it was reported that animal rotaviruses and the Eyach virus cause mild infections in humans (249). The reported rare viral zoonotic infections in Turkey are listed in Table 1.

African Horse Sickness (AHS) is a vector-borne and non-contagious disease of equids caused by the African horse sickness virus belonging to the genus *Orbivirus* within the Reoviridae family. The virus is transmitted to the hosts *Culicoides* species (282). The disease occurs in a large area of Africa, Asia, and Middle East region and has been reported in Europe (Iberian Peninsula). The infection was seen in a limited period between 1959 and 1966 in Turkey (283).

Bluetongue (BTV) is an insect-borne and non-contagious viral infection of ruminants caused by the Bluetongue virus (BTV) belonging to the genus *Orbivirus* of the Reoviridae family. The infection has a global distribution between latitudes of approximately 40–50°N and 35°S in Africa, Europe, Middle East, and the Mediterranean regions, Indian subcontinent, the Americas, and Asia (284). The global distribution and nature of BTV infection has changed significantly in recent years, and climate change, particularly global warming has been implicated as a potential cause of this dramatic event. BTV pandemics with devastating economic impact on the cattle industry have been especially seen due to the populations of different new Palearctic vectors, such as *Culicoides chiopterus*, *C. dewulffi*, *C. obsoletus*, *C. scotius*, and *C. pulcaris*, expanding their range in some parts of Europe (285). It was reported that BTV infection is a prevalent disease with almost 30% seropositivity among the herds of sheep, goats, and cattle in many parts of Turkey (286), but zoonotic transmission of the infection has not been recorded in the country until today.

Borna Disease (BD) is a viral infection with neurological and psychiatric syndromes of animals and humans caused by BD viruses (BDV) 1 and 2 of the Bornaviridae family. BDVs have a wide host range and have been determined in some domesticated animals, such as horses, sheep, cattle, dogs, and cats as well as wild life. The transmission of these viruses is probably via intranasal exposure to contaminated saliva or nasal secretions (287). A correlation between BDV infection in animals and humans was demonstrated via autopsy in human brains (288). In Turkey, antibodies to BDV were first detected in the sera of 82 of 323 (25%) clinically healthy horses in the Marmara region (289). Recently, the seropositivity of the infection in the distinct regions of Turkey was reported as 4.9% in horse, 12% in sheep, 4% in goats, 14% in cattle, and 6.6% in cats (290). There is no official report on the cases of human BDV infection in Turkey.

Feline Calicivirus (FCV) infection is a widespread respiratory disease of cats caused by a virus of the genus *Vesivirus* of Caliciviridae family. Cats can be infected after coming into con-

tact with other infected cats in shelters. The disease can occur in cats of any age, but younger kittens under 6 weeks are most susceptible (291). In Istanbul, Turkey, FCV was detected in 17 of 220 (8%) cats that had clinical oral lesions (292). There is no official report related to FCV infections in humans in Turkey.

Foot and Mouth Disease is a widespread and most contagious and notifiable disease of cattle, water buffalo, sheep, goats, and pigs caused by a virus (seven serotypes: O, A, C, SAT1, SAT2, SAT3, and Asia1) belonging to the genus *Aphthovirus* of the Picornaviridae family. The infection can be very rapidly spread among animals by aerosols of infected animals and contaminated equipment. The disease occurs worldwide as outbreaks and can occasionally be fatal and cause huge economic losses (293). Rare cases of human FMD may be observed due to close contact with infected animals. The highest risk to European Union countries is through legal and illegal imports of infected live animals and contaminated meat or dairy products from infected countries that are consumed by animals. International travelers bringing back food from endemic countries could also spread the disease. The FMDV can survive for long periods in a range of fresh, partially cooked, cured, and smoked meats and in inadequately pasteurized dairy products (294). The control program requires a close collaboration among veterinary office, health service, and local authorities. The control measures of FMD depend on restricting the movement of farm animals in the endemic region and immunization with vaccines in a vaccination regime. Several outbreaks of FMD have been reported in Turkey (295, 296). The official FMD status of Turkey has been shown in the list of OIE (297).

Louping Ill is a tick-borne infection of sheep and goats caused by the LI virus (LIV) belonging to the genus *Flavivirus* of the Flaviviridae family. The LIV characteristically causes encephalomyelitis of sheep. The epidemiological occurrence of the disease is closely related to the distribution of its primary vector tick *Ixodes ricinus* (298). The disease has been reported from various European countries, including England, Norway, Greece, and Bulgaria, as well as Turkey (10). There is no report human LIV infection cases in Turkey.

Newcastle Disease (ND) is a widespread, contagious, and notifiable infection of aves caused by a virulent strain of paramyxovirus type 1 (APMV-1) belonging to the genus *Avulavirus* of the Paramyxoviridae family. The transmission of the disease is possible by direct contact with affected birds and inhalation or ingestion of contaminated material. The virus survives in the environment, especially in the feces. It is an essential requirement for workers and staff to wear gloves, mask, and coveralls and to use of disinfected equipment and supplies to minimize the potential risk of zoonotic transmission of the disease. The infection occurs worldwide and causes devastating economic losses in the poultry sector (299). In Turkey, a total of 549 cases of ND in poultry have been reported from various regions between 2007 and 2014 (300). There is no report on the cases of human ND in Turkey.

Cowpox (CPX) is presently a rare zoonotic viral infection caused by *Cowpox virus* belonging to the genus *Orthopoxvirus* of the Poxviridae family. The zoonotic transferal of the infection is first seen in milkers, who touch the udders of infected cows. The infection is mostly restricted to small mammals rather than cattle (301). The transmission of the disease from pet rats to humans has also been observed in four different cases in France (302). It was reported that cases of cowpox are seen in European countries and also in Eurasia including Turkey (303).

Pseudocowpox virus (PCPV) Infection is a zoonotic viral skin disease caused by PCPV belonging to *Parapoxvirus* within the Chordopoxvirinae subfamily of the Poxviridae family. The virus is widespread worldwide and is transmitted to humans by direct contact with infected cows. The infection affects particularly milkers and farm workers. Clinically, the mild sores can be seen on udders and teats of the infected cows, and on hands of the infected milkers. Most recently, the isolation and identification of Pseudocowpox virus was performed from an infected Angus bull with lesions on the surface of the penis in Idaho, USA (304). In Turkey, PCPV was first isolated and characterized both from an infected cow and from a milker in a farm near the Milas district of Mugla (305).

Bovine papular stomatitis (BPS) is a zoonotic infection caused by *Bovine popular stomatitis virus* (BPSV) belonging to the genus *Parapoxvirus* of the Poxviridae family, and occurs worldwide in cattle. The infection has occupational zoonotic spreading among farmers, veterinarians, and butchers. The zoonotic transmission of the infection is through direct or indirect contact with infected animals (306). BPS virus infection is clinically seen with erosive lesions on the muzzle, lips, hard palate, oral mucosa, tongue, and esophagus in infected calves. In human, BPSV infection is often associated with nodules and pustules on the hands and rarely on the face (307). In Turkey, an outbreak of BPSV infection has been reported in a dairy herd in the town of Tire near Izmir (308).

Rotavirus diseases are epidemiologically important viral zoonotic infections for public health, particularly in children as well in calves and foals. Rotavirus infections are characterized by acute watery dehydrating diarrhea in various hosts, including birds and mammals. The infections are caused by different types of viruses belonging to the genus *Rotavirus* within the Reoviridae family. Rotaviruses are enteric pathogens that cause a large number of child deaths each year in developing countries, and rotavirus infections are mainly acquired by the fecaloral route, including fomites and person-to-person contact with contaminated objects (309). However, the cases of Rotavirus-associated enteritis are most frequently seen in calves and in foals, and to combat against Rotavirus infections, vaccines are available for infants and children (310, 311). In Turkey, a study was conducted to investigate the etiology of diarrhea cases between September 2004 and December 2005. At the end of the study, the prevalence of Rotavirus was determined as 39.7%, and the serotype G1P of Rotaviruses was also found as dominant (312).

Norovirus infection is a very contagious disease caused by the Norwalk virus belonging to the genus *Norovirus* of the Caliciviridae family. Humans can be infected via different ways, such as contaminated food or water, or by touching contaminated surfaces, or by contact with an infected person who has norovirus illness, or by fecal-oral, or through aerosol route. The

infection leads to acute gastroenteritis characterized by nausea, vomiting, watery diarrhea, and abdominal pain (313). In Turkey, norovirus was found positive in samples of mussels in the Izmir city of the Agean region (314) and in some samples of ready-to-eat food items in Istanbul of the Marmara region (315). Additionally, a large multipathogenic gastroenteritis outbreak was reported from Erzurum located in the Eastern part of the country in 2012, and etiologic agents of the outbreak were identified as astrovirus, norovirus, *Shigella sonnei*, and *E. coli* (316). In contrast, bovine norovirus was detected through molecular techniques in calves (317).

Astrovirus infection is caused by a type virus belonging to the genera *Astrovirus* and *Mamastrovirus* in the family Astroviridae. The main mode of astrovirus transmission is by contaminated food and water, and it cause gastroenteritis in humans, particularly in children and the elderly individuals (318). In Turkey, astrovirus was identified as an agent in large multipathogenic outbreak, which was seen in Erzurum in 2012 (316).

Potential zoonotic viral infections group Expansions of human interest in nature damages the ecological balance among animal–human ecosystems. The emergence of zoonotic diseases due to changes in animal/human host interface is considered e a major threat for public health (319). The trend of increasing zoonotic virus emergence is expected to continue (259). In this scope, the foamy retroviruses of bovine, feline, and equine can be given as examples of potential viral zoonotic disease transmission to humans (319, 320). Moreover, a novel tick-borne phlebovirus with zoonotic potential was isolated from ticks in Australia and shown to be closely related to two other newly discovered zoonotic phleboviruses Severe Fever with Thrombocytopenia Syndrome Virus and Hunter Island Group Virus, which were responsible for severe disease and deaths in humans in four separate countries from Asia and North America (321). However, the zoonotic status of Lumpy Skin Disease (LSD) virus is still controversial. LSD was propounded as "potential for zoonotic spread to humans" (322), whereas the disease was shown as "not zoonose" in the list of EFSA (323, 324). The potential zoonotic viral diseases in Turkey are given in Table 1.

Hepaciviruses belong to the genus *Hepacivirus* in Flaviviridae family, and include hepatitis C and hepatitis GB virus B (HCV and GBV-B) types. Humans serve as natural hosts for these viruses. HCV is transmitted by infected blood transfusion between humans. HCV was also identified in domestic cattle from Germany (325). However, the zoonotic transmission of Hepaciviruses was investigated using Hepacivirus NS3/4A proteases (interfere with mitochondrial antiviral-signaling protein [MAVS] signaling) in both cognate animal hosts and humans. Human MAVS was found as susceptible to cleavage by these non-human viral proteases, indicating that it does not pose a barrier for zoonotic transmission to humans (326). In Turkey, the seropositivity of HCV was detected as 1.5% in sera collected from 1374 people who live in five distinct regions of the country (327).

Phlebovirus contains known disease agents of animals, including humans, that can be carried by different vectors (eg, phlebotomine sandflies, mosquitoes, and ticks) (328). Four serotypes of phleboviruses, sand fly Sicilian virus, sand fly Cyprus virus, sand fly Naples virus, and Toscana virus have been circulating in the Mediterranean Basin including Turkey (21).

Lumpy Skin Disease (LSD) is a pox disease of the cattle characterized with nodules on the skin and transmitted mechanically via blood-feeding arthropods, including some hard ticks. *Rhipicephalus (Boophilus) decoloratus*, *Rhi. appendiculatus*, and *Amblyomma hebraeum* ticks serve trasmitters in the epidemiology of LSD in the endemic areas (329). An LSD outbreak was first recognized in cattle associated with the nodular clinical symptoms in August 2013 in Turkey (330). In the following months, the infection has spread countrywide, and a total of 3504 LSD cases were recorded between August 2013 and December 2014 (331). Recently, an LSD outbreak with huge economic devastation has been reported by official government veterinarians in May and June of 2016 in the Aegean region of Turkey, and more than 500 cattle infected with LSD virus have been culled for the control of the disease (10).

Parasitic Diseases with Zoonotic Characteristics in Turkey

To date, various parasitic diseases with zoonotic characteristics caused by distinct parasite species of helminthes, protozoa, and arthropods have been reported from different regions subtropically located in Turkey (Table 1). These diseases can often cause serious public health problems and lead to greater economic devastation in livestock industry and may also promote poverty in some regions of Turkey as well throughout the world (26, 154). The life cycle of parasites is very complex, and it can be varied as monoxene and heteroxene. Combating parasitic zoonoses is also extremely difficult, and the control measures are mainly related to the management of livestock as indoor or outdoor, chemical usage, and vector control. Vaccines are not available for immunization against zoonotic parasitic disease in Turkey.

Trematode zoonoses are caused by mainly *Fasciola* spp and *Schistosoma* spp and to lesser extent by other trematode species, such as *Dicrocoellium dentriticum* that occur worldwide. Fascioliasis is a most prevalent parasitic disease of the liver in ruminants, sheep, and cattle caused by the common liver fluke *Fasciola hepatica* as well as by *F. gigantica*. The infection frequently occurs with acute and chronic forms in sheep and causes huge economic losses due to deaths and productivity losses (332), but also affects cattle. Humans are infected by eating some vegetables contaminated with the infective stage of metacercariae of the parasite. The WHO has accepted that fasciolosis is an important zoonotic infection of humans after 2,594 human cases were reported from 42 countries between 1970 and 1990 (333). In Turkey, 53 cases of human fascioliasis were reported from the Mediterranean region between 1998 and 2003 (334), and the seroprevalence of *F. hepatica* was detected as 5.6% in humans in the Van province in Eastern Anatolia (335). However, a case of human dicrocoeliosis caused by *D. dentricum* was reported from the eastern part of Turkey (336). Another important zoonotic disease is schistosomiasis caused by penetration of free-swimming larva form (cercariae), which is able to actively penetrate human skin. The disease is caused by five *Schistoma* species (*S. mansoni, S. japonicum, S. mekongi, S. intercalatum,* and *S. haematobium*). The disease causes global health problem

and affects nearly 200 million people in the endemic areas of the world (337). In Turkey, a case of urinary schistosomiasis was detected in a man who had visited Nigeria (338). Briefly, cases of fasciolosis, dicrocoelliosis, and schistosomiasis in humans have been reported as zoonotic trematode infections from Turkey (Table 1).

Cestode Zoonoses can be grouped within two super families: Cyclophyllidea and Pseudophyllidea. Cyclophyllidea contains various species with zoonotic characteristics in different families, such as Taeniidae, Dipylidiidae, Hymenolepididae, and Mesocestoididae, while Pseudophyllidea includes a few zoonotic species of the Diphyllobothriidae family. *Taenia saginata*, *T. solium*, *T. multiceps*, *Echinococcus granulosus*, and *E. multilocilaris* in Taeniidae; *Dipylidium caninum* in Dipylidiidae; *Hymenolepis nana* and *H. diminata* in Hymenolepididae; *Mesocestoides linatus* in Mesocestoididae; and *Diphyllobothrium latum* and *Spirometra mansoni* in Diphyllobothriidae are major and prevalent zoonotic species of cestodes in the world. The zoonotic cestodes belonging to family Taeniidae are of paramount importance in the economic structure of developing countries, including Turkey, and lead to huge losses (28). The animals, such as cattle, buffalo, sheep, goats, and pigs serve as intermediate hosts for *Echinococcus granulosus*. Humans get the echinococcosis after accidental consumption of foods contaminated with eggs of *Echinococcus* species that are shed in the feces of the definitive carnivorous host/animal. Taeniasis is another zoonotic infection for which pig and cattle are intermediate hosts for *Taenia solium* and *Taenia saginata*, respectively, and humans serve as definitive/final hosts. Neurocysticercosis, such as coenurosis, which is caused by *T. multiceps,* is one of the important neurological problems in animals, such as sheep and cattle, and this type of neurologic disorder can also occur in humans. Besides important animal and human health concern, particularly in sheep breeding, the economic losses arising due to these infections are enormous. *Dipylidium* infection is an ingested vector-borne zoonotic disease of dogs, cats, and humans. Dogs, cats, some wild carnivores, and humans can be infected by swallowing fleas (*Ctenocephalides canis*, *C. felis* and *Pulex irritans*) or by chewing lice (*Trichodectes canis*), which are infected with the larval form (cysticercoids) of a cyclophyllid cestode, *D. caninum*. The parasite mostly infects dogs and cats, but is occasionally found in humans, particularly young children. Hymenolepiasis caused by *Hymenolepis nana* and *H. diminuta* is actually classified as a neglected zoonotic disease. These worms thrive in the intestine of rats in warm climate conditions, and the eggs of these parasites can spread to the environment by feces of infected rats. The secondary host, which is an insect in the order of coleopteran, acquires the parasite from the contaminated environment and then the parasite develops as cysticercoid form within the insect. Humans and other animals are infected by eating foods or materials contaminated with infected insects. Humans can also acquire *H. nana* infection directly by ingesting the eggs of the parasite through contaminated food or water. In an infected person, it is possible for the worm to complete the entire lifecycle in the intestine (by autoinfection). Mesocestoidiasis is a zoonotic infection caused by *Mesocestoides lineatus* and *M. variabilis*. *Mesocestoides* spp. require a three-host life cycle to complete their development. The definitive hosts are primarily carnivores that become infected after eating meat contaminated with tetrathyridia of the parasite. Humans are not definitive hosts, but can serve as such after eating undercooked meat containing tetrathyridia of the parasite. In the case of human mesocestoidiasis, mild gastrointestinal symptoms, such as nausea, diarrhea, abdominal discomfort, and vomiting can be seen. *M. lineatus* infections are prevalent in a large area of Europe, Asia, Africa, and North America, whereas *M. variabilis* infections occur in North America. Other important parasitic zoononoses are pseudophyllid cestodes, such as *Diphyllobothrium latum* and *Spirometra* spp. Dogs and humans acquire the infection by eating raw or undercooked fish, which are infected with the third larval stage (plerocercoid) of the pseudophylliid cestode *D. latum*. Epidemiologically, diphyllobothriasis occurs worldwide in areas where raw fish is consumed. Sparganosis is a rare zoonotic cestode infection caused by *Spirometra mansoni*, *S. ranarum*, *S. mansonoides*, and *S. erinacei*. Dogs, cats, and other mammals are definitive hosts, while humans can play role of accidental host in the life cycle of the parasite. The infection is transmitted to humans by the ingestion of contaminated water or ingestion of a second intermediate host, such as a frog or a snake. The transmission of the infection is also possible by contact between a second intermediate host and an open wound or mucous membrane of the hosts. Once a human is infected, the sparganum (plerocercoid) migrates to various tissues and organs, such as brain and eyes. The subcutaneous location of the sparganum causes a painful nodule, while the migration to the brain results in cerebral sparganosis, and the migration to the eyes results in ocular sparganosis. Sparganosis is a frequently seen zoonotic disease in eastern Asia, but cases have also been reported from distinct areas of the world. To prevent the infection, interventions of public health must be focused on sanitation of water and dietary in parallel to education of the people in rural areas in endemic regions (339).

Echinococcosis is one of the most important parasitic zoonotic infections in Turkey of huge economic impact (30). The disease is seen in two forms: Cystic Echinococcosis (CE) and Alveolar Echinococcosis (AE). CE caused by *Echinococcus granulosus sensu stricto* is prevalent throughout the country (340), while AE caused by *E. multilocilaris,* occurs sporadically, and some human cases of AE have been reported mostly from the Eastern Anatolia region of Turkey (341). Epidemiologically, the prevalence range of CE in domesticated animals varies between 3.5% and 58.6%, depending on intermediate hosts, such as sheep, goats, and cattle, and their managements and the different regions of Turkey (22). The prevalence can even reach 90% in sheep in some regions of the country (340). Although the present number of stray dogs and owned dogs, which are of critical importance for epidemiology of CE, is unknown in Turkey, the rising population of dogs is an increasing nuisance and seriously threatens both public health and the health of farm animals. The prevalence of CE in dogs has been reported widely to vary between 0.32% and 40% in different areas of Turkey. However, the regularly reported number of cases of CE in humans is 52,124 in the period of 16 years between 1990 and 2005 in Turkey. This official statistical data from Ministry of Health of

Turkey reveals that 3,257 new CE cases are seen per year in humans. This incidence of CE in humans is very high and is a serious unacceptable threat for public health. The seroprevalence of CE in the Izmir area, which represents the western part of Turkey, has been reported as 291 per 100,000 inhabitants (22). In contrast, it was reported that most number of patients with complaints of CE were observed in the regional hospitals in the Northeastern part of the country, such as Ataturk University Hospital in the Erzurum province (342). A total of 304 CE cases in humans were treated surgically at the Ataturk University Hospital between 1981 and 1996 in Erzurum (343). In addition, 156 children with hydatid liver disease were also treated at the same hospital between 1994 and 2011 (344). At the same hospital in Erzurum, patients with AE were also operated for liver transplantation due to hepatic alveolar echinococcosis (341, 345). The recent epidemiological data on CE cases in humans were expressed as follows: the regional incidence of CE varied depending on epidemiological differences and ranged 0–79 per 100,000 population; the prevalence of CE was also reported as 50–400 cases per 100,000; the average incidence of CE in Turkey was given as 3.4 per 100,000 inhabitants (346).

Taeniasis and cysticercosis are important cestode zoonotic diseases. Especially, bovine cysticercosis is a prevalent infection of cattle caused by the larvae (cysticercosis) of *Taenia saginata* and leads to huge economic losses in developing and industrialized countries. Cattle acquire the infection through ingestion of eggs, while the zoonotic transmission of this cestode is possible by consuming the meat of cattle infected with the larval stage of *T. saginata*. Humans are the definitive host and the larva develop into adult form of the parasite in the intestines of the infected humans. The clinical manifestations of taeniasis in humans are characterized by symptoms that include pain, unexplained weight loss, blockage of the intestine, and digestive problems. Some people with taeniasis may also experience irritation due to the parasite in the perianal area. A person with taeniasis often becomes aware of the infection by seeing the segments or eggs of *T. saginata* in their stool. Naturally, infected cattle do not exhibit any clinical symptoms but they cause financial losses due to downgrading, condemnation, extra handling, refrigeration, and transport of the infected carcasses in cattle industry. The main intervention to control of bovine cysticercosis is meat inspection according to the legislation status. The current epidemiological situation of bovine cysticercosis in European countries, including Turkey, is based on the detection of cysticerci in the carcasses of bovine animals during meat inspection at the slaughterhouse. Official reports about the meat inspection are considered an underestimation of the real prevalence, as meat inspection has a low sensitivity for the detection of cysts in muscles. In Turkey, it was reported that the prevalence of bovine cysticercosis ranged from 0.3% to 30% between 1957 and 1990, while the current prevalence of infection was shown to be nearly 5% (347). However, in a study that investigated the status of taeniasis and bovine cysticercosis in the Burdur and Afyonkarahisar provinces between 2009 and 2011, the prevalence of bovine cysticercosis in 1684 carcasses examined was detected to be 0.24%; the prevalence of taeniasis in humans in the examined 7644 stool samples was found as 0.1% (348).

Cerebral coenurosis is an important disease affecting small ruminants, particularly sheep, and causes significant economic losses in production. The infection is caused by larval stage (coenurus cerebralis) of *Taenia multiceps* and occurs worldwide. The life cycle of the parasite is commonly completed between host dogs and intermediate hosts, such as small ruminants. However, a rare case of cerebral coenurosis was seen in cattle and in humans (349). In Turkey, the prevalence of ovine coenurosis and bovine coenurosis was reported as 15.5% (350) and 0.47% (351), respectively. There is no official record on human coenurosis in Turkey.

Dipylidiasis is considered a potential risk for children and caregivers and companions living in the same houses. Definitely, pet animals, particularly dogs and cats are important companions in many households, contributing to the physical, social, and emotional development of children and the well-being of their owners. This close zoonotic potential threat should not be overlooked, and the possible flea infestations should be prevented on dogs and cats. In Turkey, the prevalence of *Dipylidium caninum* in stray dogs and in owned dogs was detected as 2.9% in the Afyonkarahisar province (352) and 2.8% in the Kayseri area (353). There is no official record about the cases of *D. caninum* infections in humans in Turkey.

Hymenolepiasis is a most common cestode infection in humans living in environments with poor sanitation and insufficient hygienic conditions in the parts of the world. Actually, this infection was shown to be one of the diseases considered an indicator of the relationship between disease and extent of good sanitation in a habitat. Humans can become infected by ingestion of the eggs of the parasite in contaminated food, water, or feces (354). The geographic distribution and prevalence of *Hymanolepis nana* infections were reported from some parts of the world, including Turkey (355). Additionally, a rare case of *H. dimunata* infection in a child was also recorded from Turkey (356).

Mesocestoidiasis is a prevalent cestode infection of dogs and cats in Turkey as well in the world. *Mesocetoides* spp occasionally induce peritoneal cestodiasis, which results in death in infected dogs and cats. The definitive host ultimately becomes infected after eating meat contaminated with tetrathyridia. In Turkey, the prevalence of *Mesocestoides lineatus* in dogs was shown to range 1%-19% (357). There is no official report on the cases of mesocestoidiasis in humans in Turkey.

Zoonotic nematode infections are prevalent diseases in a large part of the world and affect millions of people. Zoonotic nematode diseases often may be classified as angiostrongylosis, anisakiasis, ascariasis, cutaneous larva migrans (CLM), dirofilariosis, filariasis, gnathostomiasis, onchoceriasis, strongyloidiasis, toxocariasis, trichinellosis, etc. The zoonotic nematode infections reported in Turkey are listed in Table 1.

Angiostrongylosis is an important nemadote disease caused by zoonotic *Angiostrongylus* species (*A. cantonensis* and *A. costaricensis*) within the Metastrongylidae family. The infection causes severe gastrointestinal or central nervous system disease in humans, depending on the species. *A. cantonensis*, the rat lungworm, is the most common cause of human eosinophilic menin-

gitis in Southeast Asia, Africa, and America, while *A. costaricensis* is the causal agent of abdominal or intestinal angiostrongyliasis in humans and frequently occurs in Latin America. Humans can acquire the infection by eating raw or undercooked snails or slugs infected with the parasite. The third *Angiostrongylus* species *A. vasorum* causes canine angiostrongylosis in dogs, and it is not a zoonotic nematode. In Turkey, a case of canine angiostrongylosis in a dog in Ankara was diagnosed (358), while cases of zoonotic angiostrongylosis have been not reported officially until today.

Ascariasis is the most common helminthic disease caused by *Ascaris lumbricoides*, which is a soil-transmitted nematode. The infection with a global prevalence of 25% infects over 1 billion people. The transmission occurs through ingestion of excreted eggs of *A. lumbricoides*. Humans are infected mostly in regions with poor sanitation, where the environment is contaminated with human feces. Particularly, pediatric ascariasis frequently occurs in children with manifestations associated with permanent abdominal pain, growth retardation, pneumonitis, intestinal obstruction, or hepatobiliary and pancreatic injury. Zoonotic ascariasis may be associated with pigs and the use of hog manure, but in most endemic areas, it is most likely transmitted person-to-person. The prevalence can vary depending on geographic regions of Turkey, and was reported as 45% in schoolchildren in the Sanliurfa province in the Southeast part of the country (359).

Cutaneous Larva Migrans (CLM) is a zoonotic parasitic skin infection caused by larvae of hookworm species (*Ancylostoma braziliense*, *A. caninum*, *A. duodenale*, *A. ceylanicum*, *A. tubaeforme*, *Necator americanus*, *Uncineria stenocephala*, and *Bunostomum phlebotomum*) in the super family Ancylostomatoidea. The infection mostly occurs in areas with moist and warm climate. Normally, these parasites live in the intestines of definitive hosts, such as dogs, cats, wild animals; humans are not the final hosts. The infective larvae, which live in soil, can penetrate the human skin and cause CLM. Humans can be infected with the infective larvae by walking barefoot on sandy beaches or contacting moist soft soil contaminated with animal feces. Occasionally, *A. caninum* larvae may migrate to the human intestine, and lead to eosinophilic enteritis and cause unilateral sub-acute neuroretinitis (360). In Turkey, the parasitological prevalence of *A. caninum* in playgrounds in parks was found as 0.4% in the Kayseri area (361). However, a case of CLM was diagnosed in a 27-year-old Australian woman who has visited Brazil with a trip to the Amazon in 2009 (362).

Dirofilariasis is a mosquito-borne zoonotic nematode infection caused by *Dirofilaria immitis*, *D. repens*, and *D. tenuis*. The infection affects both dogs and humans throughout the world. The pathogens are transmitted to hosts through the mosquito bites. In dogs, the infection is called "heartworm disease" caused by *D. immitis*. The disease causes pulmonary artery blockage, cough, exhaustion upon exercise, fainting, coughing up blood, and severe weight loss. In individuals infected with *D. immitis*, the disease leads to pulmonary "dirofilariasis." In Turkey, a molecular study carried out to investigate the potential vectors and relative mosquito infection rates of *D. immitis* throughout two mosquito seasons (2008-2009) around Kayseri located in Central Anatolian showed that 9/312 and 12/312 pools from *Ae. vexans* abdomens and thorax-heads were positive for filarial DNAs, respectively, whereas 3/241 pools of abdomens and thorax-heads from *Cx. pipiens* were positive for *D. immitis* DNAs (137). In contrast, several dirofilariasis cases in humans have been reported from some parts of Turkey. In one case, a white-colored and motile nematode (*D. conjunctivae*) was removed via a surgical operation from a 44-year-old Turkish woman, who presented with a 1×1.5 cm subcutaneous tumor in her occipital scalp (363). Recently, three ocular *D. repens* infection cases in humans were seen in June 2013 in the Marmara region, and the parasites were removed surgically, and antibiotic and anti-inflammatory therapies were applied post operatively (364).

Filariasis is a mosquito-borne lymphatic system disease of humans caused by several nematode species belonging to the genera *Wuchereria* and *Brugia* of the Onchocercidae family. The infection endemically occurs in many countries throughout the tropics and sub-tropics of Asia, Africa, the Western Pacific, and parts of the Caribbean and South America and affects over 120 million people. More than 90% of human infections are caused by *Wuchereria bancrofti*, and the remainder cases of filariasis are caused by *Brugia* spp. However, *Brugia malayi* can also cause infections in some animals, such as felines and monkeys. In Turkey, a case of filariasis was diagnosed in an 11-year-old girl patient who presented with swellings in both legs from Kozan, a town near the Adana province in the Mediterranean region of Turkey (365).

Gnathostomiasis is another zoonotic nematode infection in humans caused by the infective larvae of *Gnathostoma* spp (*G. spinigerum*, *G. binucleatum*, *G. doloresi*, *G. nippanicum*, *G. malaysiae*, and *G. hispidum*) of the Gnathostomidae family. The disease, also known as larva migrans profunds or nodula migratory eosinophilic panniculitis, occurs worldwide. The common manifestations of the infection include epigastric pain, vomiting, fever, appetite loss, and migration in the subcutaneous tissues with painful and pruritic swellings (CLM), and migration to other tissues (visceral larva migrans) may result in cough, hematuria, meningitis and ocular gnathostomiasis. A large group of animals, such as freshwater fishes, frogs, snakes, poultry, birds, cats, dogs, and wild felids, serve as definitive hosts for gnathostomiasis, while the crustaceans of the genus *Cyclops* play a role as intermediate host. Zoonotic transmission of the infection is possible by consuming raw or undercooked final hosts, such as freshwater fishes, poultry, or frogs. In Turkey, a case report related to eosinophilic panniculitis in a 50-year-old male patient was recorded at the Erciyes University hospital in the Kayseri province of Central Anatolia (366).

Onchocerciasis is a simulid-borne zoonotic nematode infection caused by *Onchocerca* species. The infection is seen with manifestations of subcutaneous nodule formation, dermatitis, and blindness in humans and animals. In Turkey, cases of onchocerciasis in cattle (367) and humans (368, 369) were reported.

Strongyloidiasis is a soil-transmitted zoonotic nematode disease caused by *Strongyloides stercoralis*. The infection occurs in humans, dogs, and cats worldwide. The hatching larvae in the

soil or water molts to infective third stage. The latter infects the host through skin and migrates to the heart and lung and is finally swallowed back to cause intestinal infection. However, in some cases intense pulmonary manifestations may occur. *Strongyloides stercoralis* has a unique feature of molting from parasitic form to infective stage within the body, rather than having a free-living stage and causing autoinfection. This may lead to latent infection for indefinite period in an immunocompetent person but fatal hyper or disseminated infection in immunocompromized individuals, such as patients of AIDS, organ transplant recipients, and cancer and other patients put on immunosuppressive therapy, in whom it can involve any organ of the body (370). In Turkey, a case of strongyloidiasis was identified in a 50-year-old woman patient with gastric perforation in the Erzurum province in Eastern Anatolia (371). Later, another case of strongyloidiasis was diagnosed in a dog with clinical manifestations, including severe watery diarrhea, pain during defecation, intermittent cough, vomiting, and emaciation in the Samsun province in the Black Sea region (372).

Toxocariasis is an important zoonotic disease caused by the larva of the roundworms in the genus *Toxocara* within the Toxocaridae family. Of the disease agents, *Toxocara canis* infects dogs, while *T. cati* infects cats. The infected dogs and cats shed the eggs of the parasite to the environment. Humans become infected by ingestion of the embryonated eggs (containing infective larva at stage 2) in contaminated areas, such as parks for children and game lands. Although it is rare, humans may also be infected by eating undercooked meat containing *Toxocara* larvae. Many people, who are infected with *Toxocara* spp do not have any symptoms of the disease, while some manifestations characterized with ocular toxocariasis and/or visceral toxocariasis can be seen in the affected people. In Turkey, toxocariasis is a prevalent zoonotic infection. The coprological prevalence of *T. canis* in stray dogs and in owned dogs was found to be 4.8% in Kayseri (353). Furthermore, the molecular prevalence of *T. canis*, *T. cati*, and *T. leonine* in playgrounds in parks was detected as 12%, 3%, and 7.5% in the Kayseri area, respectively (361). However, a case of visceral larva migrans with hypereosinophilia related to toxocariasis was determined in a 2.5-year-old child in Izmir province (373).

Trichinellosis (trichinosis) is the most prevalent zoonotic nematode disease caused by several species in the genus *Trichinella* of the Trichinellidae family. *Trichinella spiralis*, which is the classical agent of trichinellosis, is common in many carnivorus and omnivorus animals worldwide. The others, *T. pseudospiralis*, *T. nativa*, *T. nelsoni*, and *T. britovi,* have been recognized in mammals and birds worldwide, in Arctic bears, in African predators and scavengers and in carnivores of Europe and western Asia, respectively. Humans acquire trichinellosis by eating raw or undercooked meat infected with the *Trichinella* nematode, particularly pork or hunted wild animal meat. The zoonotic transmission is also possible even by tasting very small amounts of undercooked meat during preparation or cooking. Outbreaks of trichinellosis can be seen in areas, where multiple people consume the same *Trichinella*-infected meat. In Turkey, rare cases of trichinosis caused by *T. spiralis* were determined in domestic and wild pigs and in pork products (374). Later, several outbreaks of trichinellosis in humans have been reported from the Izmir province in the Aegean region (375-377) and from the Bursa province in the Marmara region (378). In recent years, the dramatic decrease in numbers of ruminants, particularly cattle and sheep population in Turkey, may be a predisposing factor for the outbreaks of trichinellosis, epidemiologically.

Leech infestations: Leeches are segmented worms belonging to the phylum Annelida and cause the parasitosis by blood feeding in animals and humans. However, some species within the subclass Hirudinea can be used for medical purposes in humans. *Hirudo medicinalis* is usually called the medical leech and has been used for medical purposes since ancient times, which is still used for some venous circulating problems in modern medicine. In the last decade, it has been used to follow-up some flab and re-implantation of graft after surgery by general surgeons to prevent venous congestion and maintain circulation (379). However, several important bacterial species belonging to the genus *Aeromonas*, which exist in the natural flora of the digestive tract of leeches, can cause infections in humans. Particularly, *Aeromonas hydrophila*, *A. media*, and *A. veronii biovar sobria* are known to be important pathogens for humans. These pathogens lead to pneumonia, sepsis, or gastroenteritis besides some tissue infections on skin and in some soft tissues. In addition, some leech species can play a vector role for some fungal, viral, and bacterial pathogens, such as *Serratia marcescens*, *Pseudomonas* spp, *Vibrio fluvialis*, *Streptococcus* spp, *Clostridium tetani*, classical swine fever virus, bovine parvovirus, feline calicivirus, equine arteritis virus, equine herpes virus type 1, *Rickettsia* spp, and *Bartonella* spp (380-382). Leeches can also transmit several *Trypanosoma* spp to fish (382). In Turkey, some cases of leech infestations were reported from humans and animals. It was reported that a total of 13 parasitic leech species (3 species from marine fish, 8 species from freshwater fish, 1 species from brackish water fish, and 1 species from aquarium fish) have been recorded in different parts of Turkey (383). A rare adverse effect caused by artificial infestation with about 14 leeches on both legs was diagnosed in a 42-year-old woman patient who was referred to the emergency service with painful and itchy lesions on her feet and legs in the Adiyaman province in southeastern Turkey (384). In another case of leech infestation, a leech with dark-brown color was removed by surgery from the floor of the mouth of a 10-year-old child, who was referred to the emergency service of the city hospital in Yozgat in Central Anatolia (385).

Zoonotic Parasitic Protozoans (Protozooses): A number of parasitic protozoa with zoonotic characteristics cause serious infections in humans and animals, and lead to economic losses in Turkey as well as globally. The reported zoonotic protozoan infections from Turkey are listed in Table 1.

Leishmaniasis is a most important vector-borne zoonotic disease caused by several *Leishmania* species in the Trypanosomatidae family. The infection mostly occurs in two clinical forms: visceral leishmanisis and cutaneous leishmanisis. The disease affects both humans and animals, such as dogs, cats, cattle, and equids. The transmission of the disease agents is through the bite of infected Phlebotomine sand flies in the Psychodidae family

(386). Zoonotic visceral leishmaniasis (ZVL) is caused by *Leishmania infantum* and cutaneous leishmaniasis (CL) is caused by *L. tropica* and *L. infantum* in Turkey (21). These diseases in humans are compulsory notifiable diseases in Turkey for years. The ZVL occurs in the Aegean and Mediterranean regions endemically. However, the infection has been reported sporadically in other regions of the country as well. It is consistent with Mediterranean type and mostly seen in infants. *Leishmania* strains isolated from human/dogs in different regions were identified as *L. infantum* MON-1 and MON-98 by multilocus enzyme electrophoresis, also known as zymodeme analysis. In Turkey, CL has been spreading from endemic regions to other regions because of different epidemiological factors. CL with different clinical types was reported from numerous provinces, but more than 90% of the cases were concentrated in the southeastern regions, eastern Mediterranean and Aegean of the country. According to Ministry of Health's official records, 46,003 new cases were reported between 1990 and 2010. Major migrations that have arisen due to the civil wars in Syria in recent years have made CL much more important for public health in Turkey. Twelve specific microsatellite markers have been identified in the analyses made on the isolates obtained from Turkish and Syrian patients in Sanliurfa region where 45% of the cases of CL detected in Turkey are seen (387). The result suggests that *L. tropica* is a more complicated zoonotic protozoan parasite than is suspected. This of course not only made the struggle more difficult, but also created a potential danger especially for the epidemiology of CL (387). Additionally, in a study performed to demonstrate the effects of Syrian civil war on the epidemiology of CL in the Gaziantep province in southeast part of Turkey, a total of 567 people were hospitalized with the suspicion of CL, and 263 (46.4%) of them were found positive by parasitological examination. Overall, 174 (66.15%), 88 (33.46%), and 1 (0.38%) of the positive patients were grouped as Turkish, Syrians, and Afghan, respectively. Tissue samples on slides obtained from 34 CL suspected patients were also analyzed using polymerase chain reaction (PCR), and 20 of them were found positive. Eighteen (9 Turkish and 9 Syrians) of the PCR positive samples were identified as *L. tropica*, while two (1 Turkish and 1 Syrian) were *L. infantum* (388). These molecular epidemiological findings indicate that public health in Turkey and other European countries is under threat of new *L. tropica* and *L. infantum* strains. In contrast, Canine Leishmaniasis (CanL) is another serious form of the disease that occurs in dogs and wild canids. Dogs can be infected with several *Leishmania* species, but the most important clinical form of canine leishmaniasis is viscerocutaneous leishmaniasis caused by *L. infantum*. CanL mainly occurs in the Mediterranean Basin. The infection is also prevalent in dogs in Mediterranean and Aegean regions of Turkey. Another form of the infection is feline leishmaniosis caused by *L. infantum*, which sporadically occurs in domestic cats in various parts of the world. It was reported that a case of clinical feline leishmaniosis caused by *L. infantum* was seen in Agean region of Turkey (330).

Toxoplasmosis is the most prevalent zoonotic protozoan disease throughout the world caused by three infective forms (sporozoite, bradyzoite, and tachyzoite) of *Toxoplasma gondii*, which has 3 strain types (I, II, and III) in the Toxoplasmatinae subfamily. The infection could lead to serious global health problems in humans. The transmission of *T. gondii* is possible by congenital, carnivorism, and fecal-oral route. *Toxoplasma gondii* is a protozoan parasite that infects nearly all mammal and bird species worldwide. In the life cycle of *T. gondii*, all members of Felidae family serve as definitive hosts, while birds and all mammals, including man play a role as an intermediate host. Usually asymptomatic, toxoplasmosis can be severe and even fatal to many hosts, including people, particularly causing abortions in cattle and sheep that lead to huge economic losses in livestock industry (389). Elucidating the contribution of genetic variation among parasites to the patterns of disease transmission and manifestations has been the goal of many studies for the molecular epidemiology of toxoplasmosis. In a study that focused on the geographic variation of *T. gondii* strains, most genotypes of the parasite were detected as locale specific, but some were found conserved across continents and closely related to one other, indicating a recent radiation of a pandemic genotype (390). In Turkey, the seroprevalence of *T. gondii* was detected as 43% in domestic cats (391), 68.57% in dogs (392), 1.9% in horses (393), 66% in cattle (23), 33.76% in sheep (23), 63.2% in goats (394), 1.66% in domestic fowls (395), and 9.09% in prey birds (396). The general prevalence of toxoplasmosis ranged between 39.5% and 78% in animals (397). However, the prevalence of toxoplasmosis in different groups of humans, such as (i) hospital patients, (ii) people who are occupationally in close contact with animals or working in meat industry, (iii) apparently healthy people, and (iv) a special group that contains homosexuals and hemodialysis patients were reported as 13.9%–85.3%; 20.7%–57.6%; 23.0%–43.7%, and 16.3%- 76.6%, respectively (397).

Sarcosporidiosis is an important disease of animals and humans that occurs worldwide, and causes serious economic losses in livestock industry. Although the infection in humans is rare, it was reported that recent international attention on sarcocystosis has concentrated on recurrent outbreaks of muscular sarcocystosis among tourists visiting Malaysia (398). Animals and humans can be infected by the oral route with developmental stages of several *Sarcocystis* species. *Sarcocystis* species require both definitive and intermediate hosts to complete their life cycle. In the cases of intestinal sarcocystosis, humans can serve as definitive hosts for two species acquired from eating undercooked meat: *S. hominis* from beef and *S. suihominis* from pork. Clinical manifestations, such as nausea, stomachache, and diarrhea in humans with intestinal sarcocystosis, can be varied depending on the number of cysts ingested and appear more severe with pork than with beef. Humans can play a role as intermediate hosts for *S. nesbitti*, which is a species with reptilian definitive host. Humans can be infected by ingesting the sporocysts of the parasite from feces-contaminated food or water and the environment. In infected people, diagnosing the infection is difficult at the early phases, but some clinical signs, including fever, headache, and myalgia may be evident, and later, intramuscular cysts characterized with myositis can develop. Presumptive diagnosis related to travel history to tropical regions, elevated serum enzyme levels, and eosinophilia can be confirmed by finding sarcocystis in muscle biopsy material. There is no vaccine or

confirmed effective antiparasitic drug for muscular sarcocystosis, but anti-inflammatory drugs may reduce the disease symptoms. Prevention strategies are also discussed (398). In Turkey, several *Sarcocystis* species have been detected in some mammalian intermediate hosts, such as sheep, goats, cattle, water buffaloes, horses, donkeys, and pigs and in some avian intermediate hosts, such as turkey and partridges, and some *Sarcocystis* species were also identified in definitive hosts, such as dogs and cats (399). There is no official report on cases of zoonotic sarcaoproidiosis in humans in Turkey.

Giardiasis is one of the most common zoonotic intestinal protozoan diseases caused by *Giardia* spp in the Giardiinae subfamily and occurs in humans and animals worldwide, particularly in developing countries; WHO has classified this infection as a neglected disease (400). One species in *Giardia* genus *Giardia duodenalis* (syn. *Giardia lamblia* and *Giardia intestinalis*) causes giardiasis in humans and domesticated animals, including livestock, dogs, cats, and wildlife; hence, giardiasis is considered a zoonotic disease (401, 402). Direct evidence that human giardiasis can be an example of a zoonosis, ie, a human infection acquired from non-human hosts under "natural" conditions (via ingestion of *G. duodenalis* cysts excreted by animals) is limited (403). *Giardia* cysts have environmental resistance and survive for a long time under natural conditions (over 65 days at 4°C). After ingestion of the cysts by the host, primarily, the walls of cysts are broken down by bile salts, low pH, stomach acids, and some other factors. After this excystation, the trophozoites are released in the duodenum, undergo repeated mitotic division, and finally develop into an environment resistant cyst form. These cysts can pass through the intestine via feces and spread to the environment by contaminated water, food, and fomites and by direct physical contact. The most important epidemiologic aspect for giardiasis is to understand the host range of different *Giardia* species and strains/genotypes (assemblages), the potential for cross-species transmission, and risk and environmental factors involved in the exposure to the pathogen. This is particularly important in determining the zoonotic potential of *Giardia* infections in domestic animals and in determining the human disease burden attributable to parasites of animal origin (402, 403). A significant association between the occurrence of *Giardia* infections in calves and calf handlers has been shown in a study in Bangladesh (404). In Turkey, *G. intestinalis* was identified in 5 of 30 small ruminants (19 kids and 11 lambs) with neonatal diarrhea at clinics of a veterinary faculty in the Burdur province of the Mediterranean region (405). However, changes in serum cytokine levels were determined in 92 giardiasic children infected with *G. lamblia* at a Medical Centre in the Malatya province located in the eastern part of the country, and all of the sick children were treated using metronidazole (406).

Amoebiasis or Amoebic Dysentery is an intestinal disease caused by an anaerobic parasitic amoebozoan protozoa, *Entamoeba histolytica* of the Entamoebidae family. The reservoir of *E. histolytica* is man. The infection is seen worldwide but often affects anyone, who lives in tropical regions with poor sanitary conditions. The disease causes mild to severe colitis and hepatic amoebiasis in infected individuals. The fecal-oral transmission of the infection is possible by ingestion of the infective cysts via contaminated water or food or flies or fomites. Workers or personnel at departments of laboratory animals may be infected from fecal matter contaminated on skin or on clothing. The disease also occurs clinically with chronic and mild colitis in animals, such as dogs and monkeys. *E. histolytica* can be found in the large intestine of rats as a commensal, but sometimes it can cause amoebic dysentery too. In Turkey, the disease is also a prevalent infection among humans. In a study, trichrome-stained 49 smear samples of 51 patients were found positive for *E. histolytica/dispar* at clinics of the Ege University Hospital in the Izmir province of the Aegean region, Turkey (407). A case of amoebic liver abscess caused by penetration of amoebic trophozoites of *E. histolytica* was diagnosed at the clinics of a university hospital in the Istanbul province (408).

Cryptosporidiosis is another important water-borne zoonotic protozoan disease caused by several apicomplexan parasites belonging the genus *Cryptosoridium* in the Cryptosporidiidae in the subphylum of Apicomplexa family and occurs globally with a devastating economic impact on the livestock industry. *Cryptosporidium* species infect both the gastrointestinal and respiratory tracts of a wide variety of animals (mammals, birds, reptiles, amphibians, and fish), including man. The infection is one of the major problems of farm animals, particularly *C. parvum* is seen as the most common entero-pathogen during the first weeks of life of newborn calves, lambs, goat kids, and piglets, and is thought to be a critical agent in the etiology of the "neonatal diarrhea syndrome" in newborns (409). The majority of human infections are caused by either *C. hominis* and/or *C. parvum*, and the disease mainly involves the infection of jejunum and ileum, resulting in a watery diarrhea. The infection may involve the biliary tract, stomach, and lungs in immunodeficient and immunosuppressed individuals (401). The persistent diarrhea and malabsorption can seriously threaten the life of the infected person, particularly in patients with AIDS (410). A significant association between the occurrence of Cryptosporidium infections in calves and calf handlers has been shown in a study in Bangladesh (404). A vaccine is not available for immunization against cryptosporidiosis, and an etiologic specific treatment option has also not been practiced for the infection. However, antidiarrheal medicine may be used to slow down the diarrhea. Actually, the major control measures of the infection are limited to sanitation, good hygienic conditions, and education. In Turkey, cryptosporidiosis is also a prevalent disease, and its prevalence in humans was reported in the range 4.9%-39.08% (22). In contrast, several molecular epidemiological studies have been performed for bovine cryptosporidiosis in the calves in different parts of Turkey. In one of these investigations, the molecular prevalence of crytospridiosis was found as 20.7% in neonatal calves with diarrhea in different localities of the Nevsehir province of the Capadoccia region, and *C. parvum* was detected as predominant species with a 15.3% prevalence (411). Another molecular study was conducted on cryptosporidiosis in cattle (up to 2 months calves with diarrhea and others) to investigate their reservoir importance for the epidemiology of disease in the Burdur area of the Mediterranean region, and *C. parvum*, *C. ryanae* and *C. bovis* parasites were identified related to bovine cryptosporidiosis and the total prevalence the disease was

detected as 37.2%, with *C. parvum* as the predominant parasite in the region (412). Conversely, in the Konya province of Central Anatolia, only *C. parvum* was detected molecularly related to bovine cryptosporidiosis in clinically diarrheic calves that were up to 2 months old (413).

Rhinosporidiosis is a chronic granulomatous infection of humans caused by a protist, *Rhinosporidium seeberi*, in Mesomycetozoea. The analysis of the aligned sequence and inference of phylogenetic relationships showed that *R. seeberi* is a protist from a novel clade of parasites that infect fish and amphibians. The disease usually manifests as vascular friable polyps that arise from the nasal mucosa or external structures of the eye in infected individual. The etiologic pathogen organism causes similar infections in amphibians and fish (414). Another molecular work has demonstrated evidence that *R. seeberi* may have host-specific strains (eg, human vs dog versus swan) (415). Humans generally acquire the infection by contact of the nasal mucosa with infectious material when bathing in ponds contaminated by animal feces (416). In Turkey, a case of cutaneous rhinosporidiosis localized in the nasal philtrum in a patient, who had a polyploid lesion was diagnosed at the clinics of the Akdeniz University Hospital in the Antalya province (417).

Cystoisosporiasis (formerly Isosporiasis or human cocciddiosis) is a food/water-borne intestinal infection of humans caused by the coccidian protozoan parasite *Cystoisospora belli* (formerly *Isospora belli*) in the Sarcocystidae family. The infection often occurs in the tropical and subtropical regions of the world. Humans are infected by ingestion of sporulated oocysts of the parasite via contaminated food and/or water. The infection clinically manifests as watery diarrhea in sick individuals. It was experimentally demonstrated that *Isospora belli* can cause infection in animals, such as monkey, dog, pig, rat, mouse, guinea pig, and rabbit (418). Hence, *Cystoisospora belli* may be regarded as a potential zoonotic coccidian pathogen. In Turkey, a few cases of cystoisosporiasis were reported in some immunosuppressed individuals (419, 420).

Arthropod zoonosis: Arthropods can be found on humans and/or animals as ectoparasites and can adversely affect both humans and animals in several ways. They also live as urban pests (421). The ectoparasites or vectors can contaminate stored food and transmit many pathogens or introduce diseases in new and/or instable geographic areas epidemiologically. There are direct nonallergic effects, such as tissue damage due to stings and bites, as well as vesicating fluid exposure, and tissue infestation by the larval stages of the parasites themselves (e.g., myiasis). Additionally, some venoms produce necrosis in hosts tissues and some others can lead to neurological effects. Indirect effects on human and animal health comprise disease transmission (as a vector) and allergic reactions due to bites, irritations, and stings as well as reactions to some structures on arthropods, emanations, or secretions on arthropods (422). Basically, the attacks of arthropods on humans and animals could be classified as insect infestation or acar infestation, depending on the origin of the parasite. Besides being vectors for various diseases, the species of arthropods that have zoonotic importance in the orders of Blattaria, Coleoptera, Diptera, Hemiptera, Hymenoptera, Lepidoptera, and Siphonaptera can cause direct infestations in humans and animals. The reported arthropod infestations in Turkey are as follows:

Bugs in Blattaria are commonly named as cockroaches. Cockroaches are the most important pests of the urban area and occur primarily in the tropical and subtropical regions of the world. Some cockroach species in the genera of *Periplaneta* and *Blattella* occur in caves and in animal barns, particularly in the animal feed deposits and feed with animal waste or organic matter. Cockroaches adversely affect human health via sometimes biting sleeping children, entering into ear canals of humans, and mechanical contamination of food with many pathogens (423). In Turkey, *Blattella germanica* was found to harbor intestinal parasites of public health importance (424).

Coleoptera (Beetles) have a very low medical and veterinary importance. However, some coprophagous and necrophagous species of beetles in the families of Dermestidae and Silphidae have been suspected of mechanically spreading the spores of *Bacillus anthracis* (423). Darkling beetles in Tenebrionidae family cause the infestation of feeds in chicken houses and may transmit *Salmonella* bacteria from infected chickens mechanically, leading to high economic losses in the poultry sector. Both larval and adult forms of the lesser mealworm beetle *Alphitobius diaperinus* may transmit *Salmonella typhimurium* and *S. chester* from infected chickens. In contrast, the small hive beetle, *Aethina tumida* of the Nitidulidae family causes severe infestation and leads to the destruction of honey bee colonies with huge economic losses. If the beetle infestation is sufficiently heavy in a honey bee colony, it may cause bees to abandon their hive. The presence of hive beetles can be an early marker in the detection of the Colony Collapse Disorder for honey bees. In addition, the beetles can also be a pest for stored combs with honey/without honey (425). In Turkey, there is no study related to beetles with medical and veterinary importance. However, in a study, several species of dung beetles in Scarabaeidae family have been reported from the Black Sea region of Turkey (426).

Diptera (true flies) is one of the largest insect orders in the world and includes many species, which have medical and veterinary importance in the Nematocera and Brachycera suborders. Most commonly, flies in this order cause serious infestations both in humans and in animals. Most of them also serve vectorial roles for the transmission of several diseases, which lead to huge economic losses in different regions of the world, particularly in the tropical and subtropical areas. Nematocera suborder contains many flies with conspicuously long antennae, such as mosquitoes, black flies, midges, and sand flies, while Brachycera include flies with short antennae, such as horse flies, deer flies, house flies, stable flies, and tsetse flies. Some flies of Diptera can also cause cases of myiasis via their maggot type larva both in humans and in animals (427).

Mosquitoes are one of the most important ectoparasitic flies in the Culicidae family and commonly cause serious infestations of both humans and animals. Particularly, they inflict more human suffering than other hosts. Mosquito bites can lead to severe skin irritation through an allergic reaction to the saliva of mosquitoes, which causes the red bump and itching on the skin of the

infested individuals; additionally, severe mosquito infestations may lead to anemia and even deaths as seen in the old periods of human history. Every year nearly over one million people globally die from mosquito-borne infections. However, mosquitoes also transmit several pathogens, such as viruses and parasites, to some susceptible animals, such as dogs and horses. The mosquito-borne diseases include West Nile virus (WNV), Eastern equine encephalitis, dengue, encephalitis, yellow fever, chikungunya, St. Louis encephalitis, LaCrosse encephalitis, Western Equine encephalitis, Zika virus, human malaria, avian malaria, filariasis, and dirofilariasis. In Turkey, a total of 55 mosquito species have been reported (428). Recently, in a study conducted to investigate the potential vectors of *Dirofilaria immitis* using molecular techniques in Central Anatolia region of Turkey, *Aedes vexans* and *Culex pipiens* were detected as vectors in the Kayseri region of Central Anatolia (429). In another study performed to detect *Culex pipiens* biotypes in the Kayseri region using a real-time PCR technique, *Cx. pipiens* form *pipiens*, hybrids of *Cx. pipiens* form *pipiens*, and *Cx. pipiens* form *molestus* were identified as biotypes among the genomic DNA isolates (430). However, in a study that was carried out via molecular techniques to investigate avian *Plasmodium* parasites and to determine the hemosporidian parasite lineages in mosquito samples in the Kayseri area of Central Anatolia region, Turkey, the samples of *Cx. pipiens*, *Cx. theileri*, *Ae. Vexans*, and *Culiseta annulata* were found positive for avian malaria and avian hemosporidian parasites, and *Cx. pipiens* was also shown as a major vector of avian *Plasmodium* parasites (431).

Black flies are small but powerful flies with autogenous and anautogenous characteristics in the Simuliidae family and can be formidable pests for humans, domestic animals, and wildlife, affecting virtually all facets of outdoor life. Black flies are distributed worldwide with the exception of Antartica and some oceanic islands. The black fly *Simulium* (*Wilhelmia*) *lineatum* is among the most widely distributed members of the Simuliidae family, ranging from the British Isles to eastern China (432, 433). Occasionally, some severe infestations of black flies at the level of disasters also lead to devastating economic losses in some countries. The public health importance of black flies is commonly related to the blood-seeking females and the disease agents they transmit. The females transmit the nematodes *Onchocerca volvulus* (river-blindness) and *Mansonella ozzardi* (mansonelliasis) to humans, and they are also suspected of the Altamira syndrome in humans in Brazil. However, black flies can transmit some other pathogens, such as *Onchocerca lienalis* and *Leucocytozzoon* spp to bovids and to birds, respectively. Black flies can also cause multideaths of animals, which are seen suddenly, particularly in cattle due to simulotoxicosis and toxic shock (434). In Turkey, some *Simulium* species have been reported, which showed pest characteristics and caused outbreaks (432, 433, 435, 436). In contrast, in a study that was performed for molecular detection of blood-feeding preferences of *Simulium* species in Central Kizilirmak Basin of Turkey, *Onchocerca* sp and *Leucocytozoon* sp were detected in the samples of *Simulium* spp. collected from the area (437). In last three decades, two cases of simulotoxicosis in cattle herds with over 100 sudden deaths were observed in the Erzurum province of eastern Turkey (438). In a study, which was conducted to investigate the economic costs associated with a 2006–2007 outbreak of *Simulium (Wilhelmia)* spp. in the Cappadocia region of Turkey, the economic losses were calculated as US$ 5.45 million according to 2013 prices (27).

Biting Midges are very small flies belonging to the Ceratopogonidae family and occur in the temperate and tropical areas of the world. Biting midges infest both humans and animals and cause discomfort. In addition, biting midges serve as vectors for a number of viruses, protozoans, and nematodes. Among the more important viral diseases are Oropouche fever in humans; bluetongue and epizootic hemorrhagic in ruminants; and African horsesickness in equines (439). In Turkey, a total of 57 *Culicoides* spp were reported from different localities in Marmara, Aegean, Mediterranean, Central Anatolia, and the Eastern and Southeastern Anatolia regions (440). In a different study conducted to investigate *Culicoides* spp by molecular techniques in the ecosystem of Sultan marshes near the Kayseri province in Central Anatolia, a total of 10 *Culicoides* spp were identified, and *C. circumscriptus* and *C. nubeculosus* complexes were found as the predominant species in the ecosystem (441).

Sand flies are an important hematophagous group belonging to the genera *Phlebotomus* and *Lutzomyia* of Phlebotominae subfamily in the Psychodidae family. During crepuscular time or at night, the females of sand flies feed on various mammals, reptiles, and birds. These bloodfeeding flies include the primary vectors of leishmaniasis, bartonellosis, and pappataci fever. In the old world, lesihmaniasis was transmitted to humans and animals by *Plebotomus* spp, while the *Lutzomyia* spp spread leishmaniasis in the new world (442). In Turkey, a total of 19 *Phlebotomus* spp were reported from distinct regions, such as Aegean, Mediterranean, Southeastern Anatolia, and Western Black Sea (443). Meanwhile, it was reported that four serotypes of phleboviruses, and phlebovirus RNA were determined in the Mediterranean region and around the Ankara province in Turkey, respectively (35).

Horse flies and deer flies belong to the Tabanidae family and attack humans and animals. They are large hematophagus and their adult feeding activity is diurnal, but occasionally crepuscular or nocturnal. In the most temperate areas, tabanids are primarily nuisance pests of humans. In this regard, they can pose economically significant problems for local tourism. Tabanids transmit some pathogens as biological (for *Loa* and *Elaeophora schneideri*) and mechanical (for Equine infectious anemia, bovine leukemia, hog cholera, *Anaplasma marginale*, *Francisella tularensis*, *Bacillus anthracis*, *Besnoitia besnoiti*, *Trypanasoma evansi*, and *Try. vivax*) vectors (439). In Turkey, a total of 161 species belonging to 11 genera of Tabanidae family were reported from different regions (444).

Muscid flies can be grouped ecologically as filth flies (house fly, stable fly, garbage fly, false stable fly, little house fly, and latrine fly), dung flies (horn fly and face fly), and sweat flies (sweat flies). Muscid flies also can be grouped depending on their mouthparts as biting (stable fly, *Stomoxys calcitrans*; Horn fly, *Haematobia irritans*; and Bufffalo fly *Hae. irritans exgua*) and nonbiting flies (house fly, *Musca domestica*; bazaar fly, *M. sor-*

bens; bush fly *M. vetustissima*; face fly, *M. autumnalis*; false stable fly, *Muscina stabulans*; little house fly, *Fannia canicularis*; garbage fly, *Hydrotaea* spp.; sweat flies, *Hydrotaea* spp.), and all the important muscid flies are anautogenous that require proteins to complete their first gonotrophic cycle. Except for house fly, their seasonal patterns in abundance differ among the species, years, and locations. Most muscid flies of medical and veterinary importance are multivoltine, developing through two or more generations per breeding season. Adults of some important flies affect humans commonly as nuisance, occasionally as vector of several pathogens, and rarely as agents of myiasis. The cosmopolitan house fly and stable fly have more medical importance than others (445). In Turkey, a total of 11 species belonging to the Muscidae family have been reported from the Cukurova area (446).

Myiasis is the invasion of a living vertebrate animal by larvae of myiatic flies in the superfamilies Tipuloidea, Psychodoidea, Stratiomyoidea, Asiloidea, Platypezoidea, Syrphoidea, Tephritoidea, Ephydroidea, Carnoidea, Muscoidea, and Oestrroidea and are classified as accidental, facultative, obligatory, and emporary. Myiasis can also be categorized as gastrointestinal, urogenital, ocular, nasopharyngeal, auricular, and cutaneous depending on the site of larval invasion (447). In Turkey, several cases of myiasis in humans were reported from different regions (448-450).

Hemiptera are the kissing bugs and bed bugs, which are annoying nocturnal pests that feed on humans and animals by sucking blood. Kissing bugs in the Reduviidae family transmit *Trypanosoma cruzi* in some countries of Central and South America. The bed bugs *Cimex lectularius* of the Cimicidae family are external parasites of humans. In Turkey, actually, *C. lectularius* is one of the prevalent ectoparasites in houses and also in the coops for poultry, but its infestations were not documented sufficiently. However, a report related to *C. lectularis* infestation in a 46-year-old woman with poor personal hygiene was recorded in the Sakarya province of the Marmara region (451).

Hymenoptera order contains ants, bees, and wasps, and these insects are abundant throughout most of the world and constitute a significant proportion of all insects. A number of species of ants, bees, and wasps occasionally are harmful to humans and animals, and cause problematic cases, such as poisoning, allergies, and anaphylaxis (452). In Turkey, recently, a fatal case caused by massive honey bee stings on a 10-year-old boy who was subjected to 5989 honey bee attacks was reported from the Erciyes University Hospital in the Kayseri province, and this case was also shown as the highest number of honey bee stings in the literature to date (453).

Lepidoptera order includes the species of moths and butterflies, which are recognized as economic pest of the cultivated plants on which their larvae feed. However, adult moths also can be a nuisance because of their attraction to lights and often entering homes at night, but butterflies are rare pests. In most cases of a medical-veterinary nature, it is the caterpillar larval stage that is involved. Some urticating caterpillars of the Limacodidae, Megalopygidae and Saturniidae families cause urticaria and moth dermatitis in humans, while the majority of caterpillars within the Lasiocampidae, Notodontidae, Thaumetopoidae, and Lymantriidae families induce abortions in pregnant mares and also in dromedary camels due to the ingestion of the larval forms during grazing in the infested areas (454). There is no official report on urticating caterpillar infestations in both humans and animals in Turkey.

Siphonaptera (fleas) are hematophagous and morphologically unique ectoparasites, and they feed by sucking blood on different warm-blooded hosts, including man, worldwide. Most fleas in the Pulicidae family, with other important fleas belonging to the Ceratophyllidae, Leptopsyllidae, or Vermipsyllidae have medical or veterinary importance. Occasionally, members of other families, notably the Hystrichopsyllidae and Rhopalopsyllidae, also feed on humans and domestic animals. Human flea (*Pulex irritans*), cat flea (*Ctenocephalides felis*), dog flea (*Ctenocephalides canis*), oriental rat flea (*Xenopsylla cheopis*), and chigoe (*Tunga penetrans*) can cause zoonotic infestations in both humans and animals. Fleas can cause considerable discomfort and occasionally lead to secondary infections of bite wounds. The bites of fleas can cause dermatitis and allergic reactions. In addition to the intense irritation, fleas transmit various diseases, such as myxomatosis, Q fever, tularemia, murine typhus, sylvatic epidemic typhus, plague, murine trypanosomiasis, rabbit trypanosomiasis, canine filariasis, double-pored tapeworm (*Dipylidium caninum*), rodent tapeworm (*Hymenolepis diminuta*), and Dwarf tapeworm (*Hymenolepis nana*) (455). In Turkey, in a study that was conducted to investigate the species of fleas around Ankara, 9 species of fleas belonging to 6 genera of 4 families were identified morphologically, and *Pulex irritans*, *Ctenocephalides canis*, *Chaetopsylla globiceps*, and *Ctenocephalides felis* were identified as prevalent species, with the prevalence of 31.91%, 29.79%, 23.89%, and 11.92%, respectively (456).

Zoonotic scabies is a rare form of canine scabies, also called pseudo scabies in humans. Sarcoptic mange in dogs is caused by *Sarcoptes scabiei* var. *canis* belonging to the Sarcoptidae family and affects body parts of dogs, which are devoid of hair, such as the head, chest, abdomen, neck, face, ears, elbow, and hocks. Basically, each species of the mite prefers one specific type of host, and it does not live long or reproduce away from the preferred host. However, occasionally humans can be infested with sarcoptic mange by close contact with infested dogs. Intense pruritis and irritation due to hypersensitivity reactions are seen as major clinical manifestations in infested individuals. The incubation period is shorter, the symptoms are transient, and the infestation is self-limiting. A case of a zoonotic sarcoptic mange caused by *Sarcoptes scabiei* var. *canis* in a 56-year-old man was reported from India (457). In Turkey, frequently cases of sarcoptic mange with manifested local or generalized forms in dogs are seen and treated with local or systemic acaricides (458). There is no official report on zoonotic mange in Turkey.

Ticks are obligate blood-sucking zoonotic ectoparasites belonging to the families Argasidae, Ixodidae, and Nuttalliellidae and are very important biological vectors for many pathogens of human and other animal diseases after mosquitoes (459). Ticks can cause serious direct damages to their hosts as well annoyance and "tick worry," skin lesions, predisposition for myiasis,

loss of blood, tick paralysis, tick toxication, allergy, anaphylaxis, and meat allergy (48, 460). Tick infestations and TBDs of animals can cause huge economic losses, particularly in the cattle industry in many countries in the subtropical regions of the world, including Turkey (9, 459, 461). The current status of tick species in Turkey showed 47 species (8 argasid and 39 ixodid) in the last century (10). In addition, almost 19 TBDs have been reported in animals and men, involving 4 protozoa (babesiosis, theileriosis, cytauxzoonosis, and hepatozoonosis), 1 filarial nematode (acanthocheilonemasis), 10 bacterial agents (anaplasmosis, ehrlichiosis, aegyptianellosis, TBT, Candidatus Rickettsia vini, Lyme borreliosis, TBRF, tularemia, bartonellosis, and hemoplasmosis), and 4 viral infections (TBE, Crimean-Congo Hemorrhagic Fever (CCHF), louping ill (LI), and LSD in Turkey (20).

Chiggers (larvae of Trombiculidae), bird and rodent mites (Dermanyssus gallinae and Lyponyssus bacoti), Cheyletiella spp, and house dust mites (Dermatophagoides spp) can cause rare zoonotic infestations, such as cutaneous reactions by close contact worldwide. Occasional asthma cases can be seen in children due to the inhalation of metabolites of house dust mites (462). In Turkey, a case of dermatosis caused by *Cheyletiella* sp. in a patient, who was a pet owner has been reported as a zoonotic mite infestation at the Sakarya University Hospital (463).

Unconventional zoonotic agents: The bovine spongiform encephalopathy (BSE) or "mad cow disease" and Creutzfeldt-Jakop disease (vCJD) are classified among unconventional zoonotic diseases by OIE and WHO. BSE is a central nervous disease caused by an agent named "prion" or "infectious protein." The infectious protein is transmitted to cattle via feeding of infected meat and/or bone meal, and then is found in the central nervous tissue, causing neurological disorders after an incubation period of 4–5 years ("mad cow"). The coincidence of the emergence of a variant form of vCJD in humans provides some evidence that the BSE agent might have crossed a species barrier. This is not scientifically proven but is the "precautionary principle" is suggested by OIE and WHO. There is no official report about both BSE and vCJD in Turkey.

CONCLUSION

In this review, we focused on the assessment of zoonotic infections in Turkey with a holistic approach. Turkey's natural conditions allow exposure to many diseases, including zoonotic infections in animals and humans in different regions (10, 48, 441). Numerous zoonotic diseases, including 37 bacterial, 13 fungal, 29 viral, 28 parasitic (3 trematodes, 7 cestodes, 10 nematodes, and 8 protozoan) totaling to 107 infections have been reported in Turkey to date, almost one-half of the zoonotic diseases described in the world. Sixteen of these infections (9 bacterial (tuberculosis, *E. coli* infection, salmonellosis, brucellosis, leptospirosis, chlamydiosis, anthrax, Q fever, and campylobacteriosis), 3 viral (hepatitis E virus, rabies, and CCHF), and 4 parasitic (cryptosporidiosis, leishmaniosis, echinococcosis, and cysticercosis) diseases) have also been evaluated as among the most important infections for Europe and are among the 21 zoonotic diseases, which were high priority in Europe as determined and listed by the experts of Discontools (464-466). Additionally, many ectoparasitic zoonoses within 15 different arthropod groups have also been reported in Turkey. The main zoonotic transmission routes of the reported diseases and ectoparasites from Turkey are shown in Fig 1. Obviously, this high zoonotic burden found in Turkey is an important problem and a major threat to both public health and animal health. In addition, these diseases are a threat to the country's economic welfare when it is evaluated within the scope of the current understanding of "diseases are both the cause of poverty and the consequences of poverty." The severity and extent of the threat and danger can be better understood in light of the large migrations that Turkey has faced on regional basis in recent years. However, the same zoonotic dangers pose a threat to the rest of the world, especially for other European countries. It is unavoidable that hunger and misery dominates when the demographic and socioeconomic structures change dramatically at times of major migrations as we observed in the last decade. These conditions further promote poverty and poor hygiene and provide a rich environment for the parasitic, bacterial, vector-borne, and zoonotic diseases to flourish. Therefore, Turkey and the European countries are facing an increasing threat of various zoonotic pathogens today.

The epidemiological characteristics of many diseases are known on a molecular basis, allowing the capability to develop new and much more effective strategies in combat. Successful results can be obtained by using new generation drugs, such as antibiotics, antifungals, and antiparasitic preparations, in the treatment of many bacterial, fungal, and parasitic diseases, particularly in animals and humans. In addition, many viral diseases can be controlled with developed vaccines, and vaccine development studies are continuing for some viral diseases such as CCHF. Conversely, great success has been achieved by the usage of various acaricides and insecticides in the control of many vectors and thus vector-borne diseases. Unfortunately, resistance against these chemicals in vectors has developed due to the widespread usage of the chemicals thus leading to a new problem. In addition, the usage of intensive insecticide and acaricide caused environmental pollution and the death of non-target living creatures, such as bees, fish, and others. Today, we are faced with another serious problem, Antimicrobial Resistance (AMR). AMR and drug-resistant infections are now one of the biggest health threats that mankind faces in the coming decades. Considering the current adverse conditions, the health of the people, the animals, and the safe environment are facing danger (467). Therefore, the solution of the problem requires the new global approaches.

It may be useful to investigate the historical interactions of human populations and zoonotic diseases and to recall all the devastating consequences of economic losses.

In the early periods of history, high death and birth rates have had enormous impact on the demographics of populations, often leading to distributions shaped like a pyramid. Many children were born but few reached to adulthood. This meant that a large portion of the population depended on relatively few. Resources per capita were few; the population was poor because people were dying of disease, and few were working and producing. Under these conditions, deaths caused poverty, but according to Malthusian doctrine, poverty causes deaths. In

this category, poor living and working conditions, which might give rise to low resistance to disease as well as more obvious factors, such as disease itself, wars, and famine directly affect the life of the people. Essentially, inadequate food supplies by themselves do not cause massive die-offs. High death rates during famines are typically caused by people migrating to where they perceive food is in greater abundance. In this situation, the congregation of a large numbers of people spread infectious diseases; particularly, during famines and wars people typically died from infections, such as typhus, cholera, typhoid fever, diarrheal diseases, influenza, and other infections. Any increased morbidity that accompanies the disease environment also will has negative effects on productivity. This situation will exacerbate the effects of the disease and increase poverty. It is true that inadequate nutrition may reduce the effectiveness of the immune system in combating disease; as a consequence, those who already have compromised immune systems, such as the infirm, the elderly, and the very young individuals are disproportionately likely to die (468). In modern times, a concept has been accepted that diseases, including zoonotic infectious diseases can be a reason and also a consequence of poverty, as mentioned above. However, in the same period, the close interest of people caused the imbalance in nature. A consistent theme that arises across studies of emerging zoonoses is the anthropogenic nature of identified risk factors. *Homo sapiens* has dramatically altered the ecological landscape in which other species and their pathogens function. It is accepted that almost four-thirds of the diseases that arise are acquired from animals. Actually, this situation shows us how artificial the separation is between the human species and the rest of the natural world. The growing understanding of the links between environmental disturbances and disease may require an extension of the "One Medicine" concept to include not only animal and human health, but planetary health as well (319). Particularly, global warming affects the behaviors of vector arthropods and causes a generation of aggressive insect populations as seen in simuliids (435) or biting midges (439). Similarly, ticks cause a global challenge (20, 48, 459, 469, 470). Current local potential arthropod vectors, which have existed in the region for a long time and have been adapted to the region, are ready for the transmission of pathogens among humans, livestock, and wild animals. Naturally, increasing populations of vector arthropods can lead to increasing spread of zoonotic vector-borne diseases among animals and humans living in these tropical and subtropical areas (471).

Advanced information related to parasites and pathogens, sanitation, and hygiene (354) and the progress made in integrated economy and new biological views introduce new perspectives into the historical development of humanity and economies. Hence, in the last two decades, WHO has generated a new concept based on One Health for combating infectious, particularly zoonotic diseases (14). In this scope, WHO has purposed to generate "Healthier livestock and Wealthier People in a Reliable Ecosystem." For this aim, primarily, to prevent and control many infectious diseases and ectoparasites, including vectors, have been re-evaluated by the international coordination of the FAO, the OIE, and WHO. Following this initiative, a network named "Global Early Warning System (GLEWS)" has been established by WHO, OIE, and FAO for combating major animal diseases, including zoonoses (472). This network also is linked with national stakeholders to assist in early warning, prevention, and control of animal diseases and their zoonotic threats, and the International Food Safety Authorities Network to ensure food safety. Early warning of outbreaks and the prediction of their spreading capacity to new areas, particularly to the enzootic instable regions, is an essential principle for the control of endemic diseases. This principle is a fundamental and indispensable rule in international animal trade. Early warning and response is based on the concept that dealing with a disease epidemic in its early stages is easier and more economical than having to deal with it once it is widespread. The major mission of GLEWS is to provide multidisciplinary risk assessment for a zoonotic disease globally. For instance, for public health, an early warning for any outbreak with a known zoonotic potential will give adequate time to enable control measures that can prevent human morbidity and mortality, and as well economic losses. Also, this system gives an opportunity to discovery of new previously unknown human infectious diseases, which have emerged and will continue to emerge from the animal reservoir. However, both global warming and deterioration of the balance of the nature are essentially a management error. These negativities that are created as a result of over-demand all over the world will be corrected with the right decisions. While struggling at an international level against "global warming" at the global level, a number of additional social projects to prevent "environmental changes" can be required. At this point, for example, concurrent support from international sports organizations and their national partners can be provided. In this framework, messages about the dramatic destruction created by environmental changes to the masses of the people around the world can be provided in several types of international sporting events, such as the World Soccer Championship and so on. It should not be forgotten that all projects owned by the people can reach success. The positive impact of these projects will also have a widespread impact on the global scale. In this framework, the notion of "respect for nature" can be included among the concepts, such as "respect" and "enjoy responsibility," which are widely used in every step of the global scale sports in recent years, and the "environmental changes" can be noted and some urges can be achieved urgently. Moreover, at this point, it is at least reminded that what they do to administrators and politicians is not true.

From a public health and animal health perspective, prevention and control of diseases, including zoonotic infections, which have been reported from Turkey, should be realized with the coordination of national and international stakeholders based on the One Health concept. In accordance with the One Health concept, the development of advanced research projects for controlling zoonotic diseases by expert researchers from all related scientific disciplines should be top priority. In addition, the administrative and political decisions that impact climate change, urbanization, land use, and industrial and agricultural pollution should be consistent with ecological and epidemiological findings on diseases,

including zoonoses, in Turkey. We also suggest that a regional program utilizing the One Health Concept that considers an interdisciplinary approach would be imperative to combat zoonotic infections given that country borders are insignificant for disease transmission. Turkey should provide leadership to bring together the agencies and appropriate researchers under the auspices of international organizations to help shape a global policy for zoonotic diseases control in the region.

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Amerika Kıtasına Seyahat Edenlerde Risk Oluşturabilecek Paraziter Enfeksiyonlar ve Alınacak Önlemler

Parasitic Infections in Individuals Travelling to America and Precautionary Measures

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ÖZ

Son 10 yılda uluslararası seyahat eden kişi sayısı giderek artmaya devam etmektedir. Çeşitli amaçlarla yapılan bu seyahatlerle birlikte paraziter hastalıkların bulaşma riski de artmaktadır. Risk olturan enfeksiyonlardan biri sıtma olup, bulaşabilecek türler *Plasmodium vivax* ve *Plasmodium falciparum* türleridir. Leishmaniasis vakalarının dağılımı ABD'nin güneyinden Arjantin'in kuzeyine kadar olan bölgelerde bildirilmiştir. Yılda ortalama 57.000 kutanöz ve mukokutanöz leishmaniasis vakasına rastlanırken, yaklaşık 4.000 visseral leishmaniasis vakası görülmektedir. Chagas hastalığı, 21 ülkede endemik ve her yıl yaklaşık altı milyon insanın etkilendiği bildirilmektedir. Bu kıtada 25 milyon insan schistosomiasis riski altında olup, bunların %90'ı Brezilya'da yaşamaktadır. Dünya Sağlık Örgütüne (DSÖ) göre Ekvator, Kolombiya, Brezilya, Guatemala, Meksika ve Venezuela'da seyahat edenlerin onchocerciasis ile bunun yanı sıra yaklaşık olarak 12,6 milyon insan lenfatik filariasis (%80'i Haiti'de) enfeksiyonuyla karşılaşma riski bulunduğu bildirilmektedir. Bu bölgelere yapılan seyahatlerde gerekli önlemler alınmadığı ve uygun profilkatik ilaçlar uygulanmadığı durumlarada önemli mortalite ve morbiteler görülebilmektedir.

Anahtar sözcükler: Amerika kıtası, parazit, seyahat, enfeksiyon, önlem
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ABSTRACT

Over the past decade, the number of international travels has increased. Hence, the risk of transmission of parasitic diseases has also increased. One of the risk infections is malaria; *Plasmodium vivax* and *P. falciparum* species can be transmitted. The distribution of leishmaniasis cases has been reported from the south of USA to the north of Argentina. Approximately 57,000 cases of cutaneous and mucocutaneous leishmaniasis occur annually, and approximately 4000 visceral leishmaniasis cases are observed. It is reported that Chagas disease is endemic in 21 countries, and approximately 6 million people are affected every year. In this continent, 25 million people are at a risk of schistosomiasis, and most (90%) are living in Brazil. According to the World Health Organization, individuals travelling to Ecuador, Colombia, Brazil, Guatemala, Mexico, and Venezuela are at a risk of onchocerciasis as well as infecting approximately 12.6 million individuals with lymphatic filariasis (80% in Haiti). Significant mortality and morbidity can be observed in cases where necessary precautions are not taken in individuals travelling to these regions and where appropriate prophylactic drugs are not administered.

Keywords: American, parasites, travel, infection, prevention
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GİRİŞ

Günümüzde uluslararası seyahat pek çok amaç doğrultusunda gerçekleşmektedir. İnsanlar başta turizm olmak üzere, çeşitli amaçlar için seyahat etmektedirler. Dünyada son 10 yılda uluslararası seyahat eden kişi sayısı önemli derece artmıştır. En son Birleşmiş Milletler Dünya Turizm Örgütü'nün paylaşımlarına göre, 2015 yılında uluslararası seyahat eden toplam kişi sayısının 1,2 milyara ulaştığı ve bunun 192,6 milyon'unun Amerika kıtasına seyahat ettiği bildirilmiştir (1). Seyahat sırasında kişilerin özellikle bazı enfeksiyonların endemik olarak görüldüğü bölgelere tercih

19. Ulusal Parazitoloji Kongresi ve Uluslararası Katılımlı Ekinokokkozis Sempozyumunda (5-9 Ekim 2015, Erzurum, Türkiye) sunulmuştur.

19th National Congress of Parasitology and International Participation in the symposium Echinococcosis (5-9 October 2015, Erzurum, Turkey) are presented.

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etmeleri durumunda ciddi sağlık problemleri ile karşı karşıya kalınmaktadır.

Son zamanlarda Kuzey, Orta ve Güney Amerika'da en çok ziyaret edilen ülkeler Amerika Birleşik Devletleri (ABD), Kanada, Meksika, Belize, Kosta Rika, Guatemala, Panama, Brezilya, Peru, Arjantin, Paraguay, Uruguay, Şili, Guayana, Venezuela, Bolivya ve Ekvator'dur. Bu ülkelere seyahat eden kişiler için risk taşıyan başlıca paraziter hastalıklar; sıtma, visseral, kutanöz ve mukokutanöz leishmaniasis (VL, KL ve MKL), Amerikan trypanosomiasis (Chagas Hastalığı), schistosomiasis, onchocerciasis ve lenfatik filariasisdir (LF). Bu paraziter enfeksiyonların bir çoğu aynı zamanda ihmal edilmiş tropikal hastalıklar listesinde yer almaktadır (2). Seyahat öncesinde gidilecek ülkenin hangi tür paraziter enfeksiyonlar bakımından risk taşıdığının araştırılması önerilmektedir (2, 3).

Bu derlemede, seyahat eden kişinin gideceği bölgede hangi tür parazitler ile karşılaşabileceği, bu hastalıklara karşı ne gibi önlemlerin ve hangi profilaktik yöntemlerin uygulanması gerektiğinden bahsedilmektedir. Böylece paraziter enfeksiyonların oluşturduğu mortalite ve morbitelerin en aza indirilmesi açısından seyahat eden kişilere rehber oluşturması amaçlanmıştır.

Amerika Kıtasında Görülen Önemli Seyahat Parazit Enfeksiyonları

Sıtma

Sıtma, dişi *Anofel* cinsi sivrisineğin sokması sonucu *Plasmodium* spp.'nin neden olduğu ateşli paraziter bir enfeksiyondur. Sıtmaya neden olan *Plasmodium* türleri *Plasmodium falciparum, (P. falciparum) P. vivax, P. ovale, P. malaria* ve *P. knowlesi*'dir. En yaygın hastalık oluşturan türler *P. falciparum* ve *P. vivax* olup, *P. falciparum* en ciddi hastalık tablosu oluşturan türdür (4). Sıtma, sivrisinek sokması sonucu inoküle edilen sporozoitlerin 7-15 günlük bir inkübasyonu takiben başta titreme, ateş ve terleme ile karakterize klinik tabloyla seyreden vektör kaynaklı bir hastalık olarak tanımlanmaktadır. Bu klinik belirtilere ilave olarak kas ağrısı, yorgunluk ve kusma gibi belirtiler de görülmektedir. Özellikle *P. falciparum*'un neden olduğu sıtma tablosunda bazen ölümler gözlenmektedir (5). Dünya Sağlık Örgütü (DSÖ) verilerine göre 2015 yılında dünya çapında 212 milyon sıtma vakasının görüldüğü ve tedavi edilmediği takdirde yaklaşık olarak 429 bin sıtma nedeniyle hayatını kaybettiği bildirmektedir (6).

Kuzey Amerika

Meksika sıtma insidansı bakımından olumlu gelişme göstermekte ve son on yıllık dönem incelendiğinde bildirilen sıtma vakalarında önemli ölçüde azalma gözlenmiştir. Sadece ABD'yi ziyarete gelen insanlardan birkaç vaka rapor edilmiştir (7, 8). Meksika'da sıtma riski bulunan yerler Campeche, Chiapas, Chihuahua, Nayarit ve Sinaloa'dır. Bunun yanında Durango, Jalisco, Oaxaca, Sonora ve Tabasco sıtma enfeksiyonu açısından daha az riskli bölgelerdir (Şekil 1) (9). Centers for Disease Control and Prevention'ın (CDC) verilerine göre ülkeye seyahat edenler için sıtma riski düşük olup görülen türün %100 *P. vivax* olduğu bildirilmektedir. Ülkede sıtma enfeksiyonuna karşı bildirilmiş herhangi bir ilaç direnci bulunmamaktadır (9, 10).

Orta Amerika

Orta Amerikanın en küçük ikinci ülkesi olan Belize'de sıtma riskinin çok düşük olduğu daha önceki çalışmalarda bildirilmektedir. Bölgede bildirilen sıtma etkeni *P. vivax* olup daha önce bildirilmiş herhangi bir ilaç dirençi bulunmamaktadır (9).

Guatemala'da 1500 metre yüksekliğin altındaki kırsal bölgelerde sıtma riski bulunmaktadır. Sıtma bulaşma riski bu bölgede düşük olup, etken türlerin %97 *P. vivax* ve %3 *P. falciparum* olduğu bildirilmektedir. Ayrıca bildirilmiş herhangi bir ilaç direnci bulunmamaktadır (11).

El Salvador'da sıtma vakaları bildirilen yerler Guatemala'ya komşu Santa Ana ve Ahuachapan bölgesinin kırsal alanlarıdır. Bu bölgede bildirilen tür %99 *P. vivax* ve %1 *P. falciparum*'dur. Bu bölgede herhangi bir ilaç direnci bildirilmemiştir (9).

Panama'da 800 metre rakımın altındaki bölgelere seyahat edeceklerin sıtma bulaşma riski bulunduğu için dikkat etmeleri gerekmektedir. Bu bölgede etkenin %99'u *P. vivax* olmakla birlikte, % 1 oranında *P. falciparum'*dur. Panama kanalının doğusunda klorokine karşı direnç geliştiği bildirilmiştir (9, 11).

Nikaragua'da, sıtma riski Atlántico Norte, Atlántico Sur, Jinoteca, Matagalpa, León, Chinandega, Managua ve Managua Gölü'nün kıyılarında mevcuttur. Bu bölgelerde görülen plasmodium türleri %90 *P. vivax* ve %10 *P. falciparum* 'dur. Ayrıca bölgede etken türler için bildirilmiş herhangi bir ilaç dirençi bulunmamaktadır. Nikaragua'nın düşük sıtma riski bulunan diğer bölgeleri için sivrisineklere karşı kişisel önlemlerin alınması yeterlidir (6, 9, 11).

Honduras'da sıtma bulaşma riski mevcuttur. Ülkeye seyahat eden kişilerin sıtma ile karşılaşma oranı orta seviyelerdedir. Bu ülkede sıtmaya karşı bildirilmiş herhangi bir ilaç dirençi bulunmamakdır. Honduras'da etken sıtma türleri %93 *P. vivax* ve %7 *P. falciparum* olarak bildirilmiştir (9, 11).

Haiti, *P. falciparum* için endemik olan ve prevelansının yaklaşık %2-3 olduğu bildirilen bir ülkedir. Bulaşma riski en sık Mart ile Mayıs ve Ekim ile Kasım arası olan yağışlı mevsimlerde yüksektir (9).

Şekil 1. Amerika kıtasında sıtma riski olan ülkeler (DSÖ, 2014'den değiştirilerek)

Dominik Cumhuriyeti'nin Santiago ve Santo Domingo şehirlerin dışında kalan yerlede sıtma riski bulunmaktadır. Bu ülkede bildirimi yapılan etken tür ise *P. falciparum*'dur (9, 11).

Güney Amerika

Brezilya'da sıtma riski daha çok Amazon ormanlarında bulunmaktadır. Ancak Brezilya'nın çoğu bölgesinde vektör sivrisinek türleri mevcuttur. Özellikle tarihi ve doğal güzellikleri ile turistlerin akınına uğrayan Acre, Amapá, Amazonas, Rondonia, Roraima Maranhão, Mato Grosso ve Para eyaletlerinde sıtma bulaş riski bulunmaktadır (Şekil 1). Espirito Santo, Goias, Mato Grosso do Sul, Piaui, Tocantins, Rio de Janeiro ve Sao Paolo eyaletlerin kırsal ve ormanlık alanlarına seyahat edenlere sıtma bulaşma riski daha düşüktür. Bu ülkede bildirilen etken türlerin %85 *P. vivax* ve %15 *P. falciparum*'dur. Ülkede klorakine karşı bildirilmiş ilaç direnci bulunmaktadır (9-12).

Peru'da sıtma riski düşüktür. Genellikle Amazon'un yağmur ormanlarına seyahat edenler için sıtma bulaşma riski bulunmaktadır (Şekil 1). Ayrıca, Iquitos, Puerto Maldonado, La Libertad ve Lambayeque'nin 2000 metre yüksekliğin altında kalan bölgelerinde sıtma vakaları bildirilmiştir. Ülkede bildirilen türler *P. vivax* ve *P. falciparum*'dur. Aynı zamanda klorokin direncide bildirilmiştir (6, 9, 11).

Korunma

Bu bölgelere hem uzun hemde kısa süreli seyahat edecekler için sıtmadan korunmanın birinci basamağı sıtma vektörü olan Anofel türü sivrisineklere karşı önlemlerin ve kemoprofilaksi kombinasyonun alınmasıdır. Bu tür sivrisineklerin beslenme alışkanlıkları nokturnal olması nedeniyle sıtma bulaşma riski daha çok gün batımıyla gün doğumu arasındaki dönemde gerçekleşmektedir. Bu zaman içerisinde özellikle vücudun açık kalan kısımlarına repellent (pyrethroid içeren) koruyucular sürülmelidir. Ayrıca, uzun kollu kıyafetler giyilmeli ve üzerine repellent uygulanmalıdır. Gece uykuda cibinlik ya da pyrethroid emdirilmiş cibinlikler kullanılmalıdır (9, 10). Seyahata çıkmadan önce kemofrofilaksi seçimi yaparken çeşitli faktörlere dikkat edilmelidir. Seyahat edilecek ülkede sıtma bulaşma riskinin olup olmadığı, var ise hangi *Plasmodium* türlerinin bulunduğu, hangi kemoprofilaktik ajan/ajanların kullanılacağı ve ilaç dirençinin olup olmadığı açısından araştırılması gereklidir. Bu endemik bölgelere seyahat etmeden önce, seyahat sırasında ve sonrasında kemoprofilaksilerin alınması önerilmektedir (13). Alınacak kemoprofilakside dikkate edilmesi gereken bazı noktalar bulunmaktadır (9, 14, 15):

- Hiçbir önlem ve tedavi protokolü kişiyi sıtmadan tam olarak koruyamadığı ancak uygulanacak iyi bir kemoprofilaksinin ölümcül ağır sıtmayı önlediği unutulmamalıdır.
- Çocuklarda kemoprofilaktif ilaçlar vücut ağırlığına göre hesaplanmalıdır.
- Günlük alınan ilaçlara (Atovakon, Proguanil, Doksisiklin) seyahatten en az bir-iki gün önce başlanmalıdır. Bu ilaçlar kısa süreli seyahat edenler için iyi bir ilaç seçimi olup sadece seyahatten döndükten sonra dört hafta ilaç alınması yerine yalnızca yedi gün alınması yeterlidir.
- Maksimum kan seviyesine ulaşması ve yan etkileri görülürse başka alternatif ilaca geçebilmek için; örneğin haftalık alınan klorokin ise seyahatten en az bir hafta önce ve meflokin ise iki-üç hafta önce başlanmalıdır. Klorokin ve Meflokin'in önemli bir avantajı da uzun süren seyahatlerde haftada sadece iki defa kullanılmasıdır. Ayrıca, hamileliğin tüm döneminde de kullanılabilir olduğundan dolayı tercih edilmektedir.
- Tüm profilaktik ilaçlar riskli bölgede bulunduğu sürece düzenli alınmalıdır.
- Karaciğerde bulunan hipnozoitler relapsa neden olmasın diye profilaktik ilaçların kullanımına riskli bölgeden ayrıldıktan sonra dört hafta daha devam edilmelidir. Ancak Atovakon ve proguanilin bir hafta kullanımı yeterlidir.
- Antimalaryal ilaçların yan etkileride bulunmakta fakat kişilerin aktivitelerini kısıtlamamaktadır.

DSÖ 2005 yılında yayınlamış olduğu bildirgede tüm dünyada sıtma açısından riskli bölgeleri dört bölümde ele alarak, uygulanması gereken önlemleri ve kulanılacak ilaçları şu şekilde belirtmiştir (16):

Tip 1 Sıtma Riskli Bölgelerde Önlemler: Bu bölgeler sıtma açısından risk taşımamakta ve kemoprofilaksi önerilmemektedir. Sadece sivrisineklerle savaş yeterlidir. Repellent ve pyrethroid emdirilmiş cibinlik kullanımı tavsiye edilmektedir.

Tip 2 Sıtma Riskli Bölgelerde Önlemler: Klorokin direncinin bildirilmediği ya da yaygın olmadığı bölgelerdir (Haiti, Dominik Cumhurihiyeti, Orta Amerika, Panama kanalının kuzey batısı ve Ortadoğunun bazı bölümleri). Klorokin tercih edilmektedir. Haftada tam bir doz yerine haftada iki kez (Pazartesi–Perşembe) verilmelidir. Tüm *Plasmodium* türlerine etkilidir.

Tip 3 Sıtma Riskli Bölgelerde Önlemler: Klorokin direncinin olduğu *P. falciparum* sıtmasının görüldüğü bölgelerdir (Afrika'nın çoğu bölgesi, Güney Amerika ve Bazı Asya ülkeleri). Bu bölgeler için klorokin–proguanil kombinasyonu önerilmektedir.

Tip 4 Sıtma Riskli Bölgelerde Önlemler: Klorokin ve diğer ilaçlara karşı direncin olduğu, *P. falciparum* sıtmasının çok fazla görüldüğü bölgelerde (Güney Asya, Kamboçya, Tayland, Güney Amerika ve Sahra altı Afrika) meflokin ilk tercihtir, bunun yanısıra doksisilin veya atovakuon- proguanil kombinasyonu da verilebilir.

Sıtma endemik bölgeye seyahatten sonra enfekte kişilerde genellikle etkene maruziyetten sonra ilk üç ay içinde semptomlar başlamaktadır. Kişiler etkene maruz kaldıktan en az bir hafta ile iki ay içinde ateşi olur ise sıtmadan şüphelinmeli ve hastanın *Plasmodium* ile enfekte olup olmadığı araştırılmadır.

Amerika kıtasında sıtma açısından endemik bölgelere seyahat edecek kişilerin seyahat öncesinde, seyahat sırasında ve sonrasında alması gereken profilaktif ajanlar Tablo 1'deki gibi bildirilmektedir (14-19).

Leishmaniasis

Leishmaniasis, 20'den fazla *Leishmania* spp.'den biri ile enfekte dişi kum sineklerinin ısırması ile bulaşan paraziter bir hastalıktır. Bu enfeksiyon tropik ve subtropik bölgelerde yaygın olup ihmal edilmiş tropikal hastalıklar listesinde yer almaktadır. İnsanlarda leishmaniasis üç temel klinik formu vardır. Bunlar VL, KL ve MKL olarak sınıflandırılmaktadır (19). En ciddi formu olan visseral leishmaniasisin klinik belirtileri hepatosplenomegali, anemi, pansi-

Tablo 1. Seyahat edilecek ülke ve bölgelere göre alınacak kemeprofilaktif ve alternatif önlemler

Amerika Kıtası	Tavsiye Edilen Kemoprofikalsi	Alternatif
Meksika		
Campeche, Chiapas, Chihuahua, Nayarit ve Sinaloa Eyaletlerinde	Atovakon/Proguanil, Klorokin, Doksisiklin, Meflokin veya Primakin	
Durango, Jalisco, Oaxaca, Sonora, Tabasco ve Othón P. Blanco ve Quintana Roo eyaletlerinde		Sadece Sivrisinekden Korunmak Yeterli
Belize		Sadece Sivrisinekden Korunmak Yeterli
Guatemala		
Escuintla Eyaleti	Atovakon/Proguanil, Klorokin, Doksisiklin veya Meflokin	
Guatemala'nın diğer tüm eyaletlerinde	Atovakon/Proguanil, Klorokin, Doksisiklin, Meflokin veya Primakin	
El Salvodor		Sadece Sivrisinekden Korunmak Yeterli
Panama		
Darien, Guna Yala ve Panama Este	Atovakon/Proguanil, Doksisiklin, Meflokin veya Primakin	
Ngäbe-Buglé Bölgesinde	Atovakon/Proguanil, Klorokin, Doksisiklin, Meflokin veya Primakin	
Nikaragua		
Región Autónoma Atlántico Norte (RAAN) ve Región Autónoma Atlántico Sur (RAAS)	Atovakon/Proguanil, Klorokin, Doksisiklin, veya Meflokin	
Nikaragua sıtma bulunan diğer bölgeşsrinde		Sadece Sivrisinekden Korunmak Yeterli
Honduras	Atovakon/Proguanil, Klorokin, Doksisiklin, Meflokin veya Primakin	
Haitii	Atovakon/Proguanil, Klorokin, Doksisiklin, veya Meflokin	Sivrisineklere karşı da önlem alınmalı
Dominik Cumhuriyeti	Atovakon/Proguanil, Klorokin, Doksisiklin, veya Meflokin	
Brezilya		
Acre, Amapá, Amazonas, Rondonia, Roraima Maranhão, Mato Grosso ve Para eyaletlerinde	Atovakon/Proguanil, Klorokin, Doksisiklin, veya Meflokin	
Espirito Santo, Goias, Mato Grosso do Sul, Piaui, Tocantins, Rio de Janeiro ve Sao Paolo eyaletlerinde		Sadece Sivrisinekden Korunmak Yeterli
Peru	Atovakon/Proguanil, Klorokin, Doksisiklin, veya Meflokin	

topeni, kaşeksi ve ateş ile karakterizedir. Kutanöz leishmaniasis, önce sineğin soktuğu bölgede kızarıklık, papül gelişmesi ile karakterize olmakta ve daha sonra lezyon büyüyüp kabuğu zor kaldırılabilen ülserleşme görülmektedir. Mukokutanöz leishmaniasis ise daha çok yüzde, kulak ve burun kıkırdak dokularında deri lezyonlarına sebep olmaktadır. Genellikle infiltratif mukoza ve deri tutulumu olup, ileri dönemlerde bütünüyle ya da kısmi ülseratif lezyonlar ile seyretmektedir (20, 21). DSÖ verilerine göre leishmaniasis dünyada 102 ülkede endemik olup 350 milyon insan risk altındadır (22, 23).

Son yıllarda yapılan araştırmalar sonucunda leishmaniasisin ölüm oranlarının yüksek olması ve geniş coğrafik dağılım göstermesinden dolayı Amerika kıtasında halk sağlığı problemi olarak görülmektedir. Amerika kıtasında görülen leishmaniasis vakaları ABD'nin güneyinden Arjantin'in kuzeyine kadar olan bölgelerde (Şili ve Uruguay hariç) dağılım göstermektedir (24). Bu bölgede yılda ortalama 57000 KL ve MKL, 4000 VL vakası bildirilmektedir (25).

DSÖ verilerine göre Amerika kıtasında KL 21 ülkede endemiktir (Şekil 2) (24, 26). Bu ülkeler ABD, Arjantin, Bolivya, Brezilya, Belize, Dominik Cumhuriyeti, Kolombiya, Kosta Rika, Ekvator, Elsalvador,

Şekil 2. Amerika kıtasında kutanöz ve visseral leishmaniasis riski olan ülkeler (DSÖ, 2015'den değiştirilerek)

Fransız Guyana, Guatemala, Guyana, Honduras, Meksika, Nikaragua, Panama, Paraguay, Peru, Surinama ve Venezuela'dır (25, 26). KL ve MKL etken türleri, *Leishmania* genusunun farklı türleridir. İnsanlarda enfeksiyona sebep olan *Leishmania* ve *Viannia*'nın cinsleri içerisinde yer alan 14 *Leishmania* türü bidirilmiştir. Bunlar; *L. (V.) braziliensis, L. (V.) peruviana, L. (V.) guyanensis, L. (V.) panamensis, L. (V.) lainsoni, L. (V.) naiffi , L. (V.) shawi, L.(V.) colombiensis, L.(V.) lindenbergi, L. (L.) mexicana, L. (L.) pifanoi, L.(L.) amazonensis, L. (L.) garnhami* ve *L.(L.) venezuelensis*'dir (27). Bu ülkelerde *Leishmania* spp.'nin bulaşma riski oldukça yüksektir. Özellikle doğa seyahatleri yapan kişiler için daha yüksek risk bulunmaktadır. Hatta endemik bölgelere kısa süreli seyahat eden insanlara bile *Leishmania* spp. bulaşabilmektedir (24, 25, 28).

VL, *Leishmania infantum*'un neden olduğu, *Lutzomyia* cinsi kum sinekleri tarafından bulaşan Latin Amerika'da endemik bir zoonotik hastalıktır (25). VL yaygın olarak dağlık bölgelerde, köylerde ve şehire yakın bazı bölgelerede yaşayan veya seyahat eden insanlarda görülmektedir (26). DSÖ verilerine göre Amerika kıtasınında yaklaşık 10 ülkede VL endemik olarak görülmektedir (Şekil 2) (22). Bu ülkeler Brezilya, Paraguay, Arjantin, Kolombiya, Bolivya, Guatemala, Honduras, Meksika, Nikaragua ve Venezuela'dır. Bu vakaların büyük bir kısmı (%96) Brezilya'dan bildirilmektedir (27-29).

Korunma

Bu bölgeye seyahat eden kişilerin *Leishmania* spp.'nin vektörü olan kum sineklerine karşı önlem alınması önerilmektedir. Özellikle doğa gezileri yapacak insanların daha dikkatli olmaları gerekmektedir (30, 31). Başlıca önlemler;

- Özellikle kum sineklerinin aktif olduğu güneş batımından doğumuna kadar geçen sürede açık alanlarda bulunmaktan kaçınmalıdır.
- Vücudun açıkta kalan yerleri en aza indirilmelidir. Bunun için uzun kollu gömlek, uzun pantolon ve çorap giyilmelidir.
- Giysilerin ve vücudun açıkta kalan kısımlarına repellentler uygulanmalıdır.
- İç mekanlarda hava akımı olşuturacak vantilatör ya da klima çalıştırılmalıdır.
- Kum sineklerinin gecemeyeceği kadar küçük gözenekli cibinlikler kullanılmalıdır.

Amerika Trypanosomiasisi (Chagas Hastalığı)

Chagas hastalığı ya da Amerika trypanosomiasisi, *Trypanosoma cruzi*'nin neden olduğu tropikal bir paraziter hastalıktır. Bulaşma vektör *Triatoma* türü böceklerin kan emmek için açtığı yere dışkısının teması sonucunda oluşmaktadır (32). Ayrıca, bu enfeksiyon kontamine olmuş kan ürünleri ve kontamine yiyecek ve içecekler ile de bulaşabilmektedir (9). Akut dönemde genellikle etkene maruz kalındıktan bir hafta sonra ateş, üşüme, miyalji ve yorgunluk gibi klinik belirtiler ortaya çıkmaktadır. Enfeksiyon bölgesinde Chagoma denilen, vektör böceğin soktuğu yerde oluşan sert ve eritematöz bir lezyon oluşmaktadır. Bu lezyonu takiben yüzde ve özellikle göz kapağında raş ve ödem gelişmektedir (Romana belirtisi). Chagas hastalığın kronik döneminde hepatosplenomegali, miyokardit, megakardiya, megaözofagus ve megakolon görülmektedir (33).

Chagas hastalığı Amerika kıtasında 21 ülkede endemik olup, yılda yaklaşık olarak 6 milyon insanı enfekte etmektedir. Enfekte kişilerin seyahat veya göç etmesi sebebiyle bu hastalık tüm Dünyaya yayılabilmektedir. Chagas hastalığı, Amerika kıtasında ihmal edilmiş enfeksiyon hastalıklarının en yaygınıdır. Yaklaşık 70 milyon insan risk altındadır. Bu hastalığın coğrafi dağılımı Şekil 3'te gösterilmektedir (25).

Kuzey, Orta Amerika ve Güney Amerika'da Chagas hastalığın riski olan ülkeler Arjantin, Belize, Bolivya, Brezilya, Şili, Kolombiya, Kosta Rika, Ekvator, El Salvador, Fransız Guyana, Guyana, Guatemala, Honduras, Meksika, Nikaragua, Panama, Paraguay, Peru, Surinema, ABD, Uruguay ve Venezuela'dır (34). Bu ülkelerin endemik bölgelerine seyahat edenler, yürüyüş, kamp ve doğa gezisi gibi açık hava etkinlikleri yapanlar büyük risk altındadır. *Triatoma* türü böcekler daha çok orman ekosistemi içinde çamurdan veya kerpiç tuğladan yapılmış kulubelerde bulunabilir. Bu tip yerlerde konaklayanların dikkatli olması gerekmektedir. Bunun yanı sıra, kontamine yiyecekler yenmesi (özellikle Brezilya'da açái meyvelerinin tüketilmesi) ve pastörize edilmemiş meyve suları içilmesiyle de bulaşma meydana gelebilmektedir (9, 34).

Korunma

Endemik bölgelere seyahat edenler, kendilerini *Triatoma* cinsi böceklerden şu şekilde korumalıdır (34);

- Seyahat sırasında vücudun açıkta kalan yerlerine repellent spreyler uygulanmalıdır.
- Açık renkli uzun kollu gömlekler, uzun pantolonlar ve şapkalar giyilmelidir.
- Orman bölgesinde *Triatoma* cinsi böceklerin en fazla bulunduğu palmiye ağaçları, taş ve tahta yığınlarından uzak yerler kamp konaklaması için tercih edilmelidir.
- Pyrethroid emdirilmiş cibinlikler kullanılmalıdır.

- Endemik bölgelerde seyahat sırasında pastorize edilmiş meyve suları tüketilmelidir. Ayrıca yemekler iyi pişirilmeli ve kabuğu soyulabilen meyveler tüketilmelidir.

Schistosomiasis

Schistosomiasis, *Schistosoma* spp.'ların neden olduğu akut ve kronik bir paraziter hastalıktır. Bu hastalık ihmal edilmiş tropikal hastalıklar listesinde yer almaktadır. *Schistosoma* spp. göller, nehirler, akarsular ve gölet gibi tatlı su kaynaklarında yaşayan salyangozlar tarafından suya salınan serkaryaların deriyi delmesi ile bulaş gerçekleşmektedir. Ayrıca enfekte içme sularında bulunan serkaryaların ağız mukozasından girmesiyle de bulaşma olabilmektedir (35). Bu parazitin sebep olduğu akut enfeksiyonda görülen klinik belirtileri yüksek ateş, terleme, titreme, ürtiker, ödem, karın ağrısı, kusma, ishal, karaciğer ve dalakta büyüme görülmektedir. Kronik enfesiyonda özellikle anemi, büyüme geriliği, hepatosplenomegali, kanlı mukuslu ishal, portal hipertansiyon, siroz, rektum prolapsusu, nörolojik komplikasyonlar ve ölüm ile sonuçlanmaktadır (36).

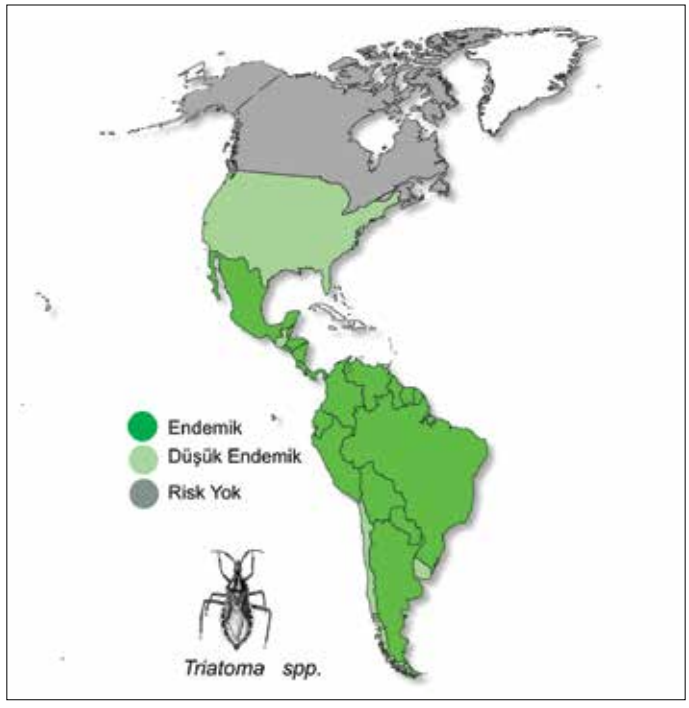
Bu hastalık tropikal ve subtropikal bölgelerde özellikle içme suyu sanitasyon koşullarının yetersiz olduğu yerlerde yaygındır. Tüm dünyada 200 milyondan fazla insanı enfekte ettiği tahmin edilmekte ve 700 milyon insanın riski altında olduğu bildirilmektedir (37). İnsanları enfekte edebilen esas olarak *Schistosoma haematobium*, *Schistosoma japonicum* ve *Schistosoma mansoni*'dir. Ancak *S. mansoni* Latin Amerika ve Karayip Ülkelerinde mevcut tek türdür (38). Amerika kıtasında 25 milyon insan risk altında olup, bunların %90'ı Brezilya'da yaşamaktadır. Brezilya'nın özellikle kuzeydoğusundaki bölgelerde bulunan tatlı su gölleri ve nehirlerinde büyük bir halk sağlığı sorunudur. Brezilya'nın dışında Venezuela yüksek riskli iken St.Lucia ve Surinam düşük riskli ülkelerdir (Şekil 4) (25, 39).

Korunma

- Schistosomiasisin endemik olduğu bölgelere seyahat edenlerin enfekte tatlı sular ile temastan kaçınmaları gerekmektedir.
- Nehir veya bataklıklardan geçilmesi gerekiyorsa su geçirmez çizmeler giyilmelidir.
- Enfekte sularla temasda bulunmak gerekirse çift katlı lastik eldiven kullanılmalıdır.
- Kaza ile enfekte su ile temasta bulunulursa enfeksiyon olasılığını azlatmak için vücudun açık yerlerine alkol sürerek kuru bir havlu ile ovulmalıdır.
- Banyo suyu kaynatılmalı veya su iki-üç gün bekletilmelidir.
- İçme suları tüketilmeden önce kaynatılmalı ya da klorlama yapılmalıdır.
- Sebzelerin enfekte su ile yıkandığı düşünülerek iyice pişirilmeli ve salata yemekten kaçınılmalıdır (40, 41).

Onchocerciasis (Nehir Körlüğü)

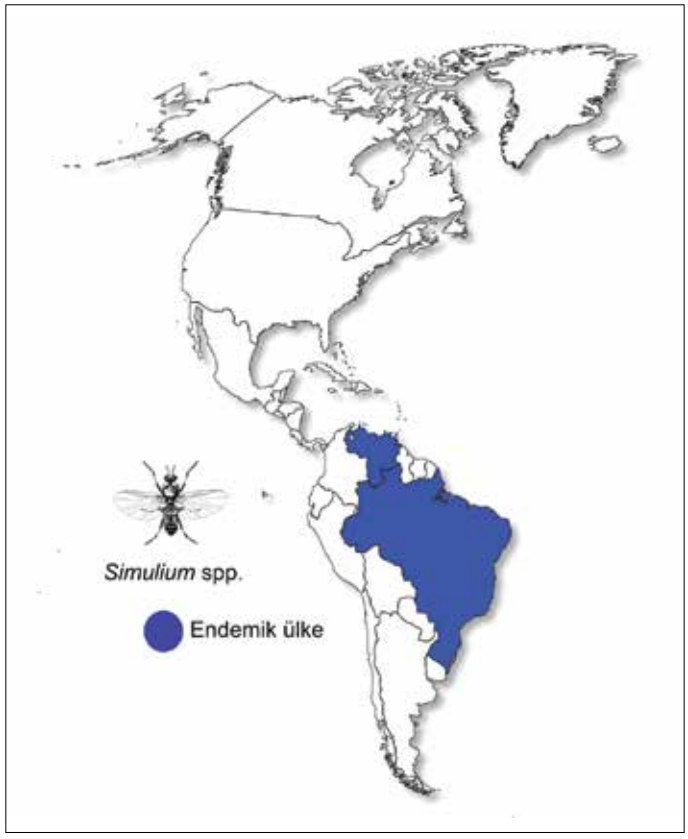
Onchocerciasis ya da Nehir Körlüğü hastalığı, *Onchocerca volvulus*'nun neden olduğu ihmal edilmiş tropikal hastalıklar listesinde bulunan bir paraziter hastalıktır. Bu parazit *Similum* türü karasineklerin ısırması sonucunda insanlara bulaşmaktadır. *Similum*'lar daha çok nehirlerin, derelerin ve verimli tarım arazilerin bulunduğu köylere yakın yerlerde bulunmaktadır (42). Onchocerciasis



Şekil 3. Amerika kıtasında Şagas hastalığı riski olan ülkeler (DSÖ, 2010'den değiştirilerek)

Şekil 4. Amerika kıtasında Schistosomiasis riski olan ülkeler (DSÖ, 2012'den değiştirilerek)

kaşıntılı papüller dermatit, subkutanöz nodüller, lenfadenit, görme kaybına ve körlüğe kadar ilerleyebilen oküler lezyonlara sebep olan bir enfeksiyondur (43).



Şekil 5. Amerika kıtasında Onchocrerciasis riski olan ülkeler (DSÖ, 2015'den değiştirilerek)

Şekil 6. Amerika kıtasında lenfatik filariasis riski olan ülkeler (DSÖ, 2015'den değiştirilerek)

DSÖ verilerine göre 2009 yılında Amerika kıtasında yaklaşık 500 bin kişi risk altındadır. Brezilya ve Venezuela endemik ülkelerdir (Şekil 5). DSÖ'nün 2016 verilerine göre onchocerciasis Kolambiya (2013) Ekvator (2014), Meksika (2015) ve Guatemala'dan (2016) eradike edilmiştir (25, 44).

Korunma

- *Similum* türü karasineklerin yaşam alanları olan nehir ve dere kenarlarından uzak durulmalıdır.
- Bu bölgere seyahat edenler *Similum* türü karasineklerin yaşam yerlerinden uzak yerlere kamp yapılması tercih edilmelidir.
- Kamp ve doğa gezileri yapanlar bu bölgelere ziyaret ettiklerinde repellentler kullanmalıdır.
- Seyahat sırasında vücuda repellent spreyler sıkılmalıdır.
- Pyrethroid emdirilmiş cibinlikler kullanılmalıdır.
- Açık renkli uzun kollu gömlekler, uzun pantolonlar ve şapkalar giyilmelidir.

Lenfatik Filariasis

Lenfatik filariasis'in üç etiyolojik ajanı, *Wuchereria bancrofti, Brugia malayi* ve *Brugia timori*'in vektörü olan sivrisineklerin ısırmasıyla insanlara bulaşan paraziter bir hastalıktır. Amerika kıtasında enfeksiyonun temel vektörü *Culex* türü sivrisineklerdir. Amerika kıtasında var olan tek tür *W. bancrofti* lenfatik filariasise neden olmaktadır (4). Çoğu enfeksiyon asemptomatiktir ancak lenfatik disfonksiyonlar yıllar sonra bacakta, skrotumda ve göğüste lenf ödemlere neden olabilmektedir. Lenfatik disfonksiyonu olan hastalarda akut dönemde ekstremitelerin etkilenmesinden dolayı ağrılı bir şişlik ve bakteriyel süperenfeksiyondan dolayıda ateş ya da titreme görülmektedir (45).

DSÖ'ye göre yaklaşık 12,6 milyon insan Amerika'da lenfatik filariasis enfeksiyonu riski altındadır ve bunların %80'i Haitii'de yaşan insanlardır. Şu anda Amerika kıtasında lenfatik filariasis açısından endemik 4 ülke mevcuttur. Bunlar; Brezilya, Dominik Cumhuriyeti, Guyana ve Haiti'dir (Şekil 6). Seyahat sırasında vektöre karşı kişisel önlemler alınmalıdır (25, 46).

Korunma

Bu ülkelere seyahat eden kişiler sivrisinek ısırmalarına karşı çeşitli önlem almalıdır (46). Bunlar;

- Güneş batımı ve doğumu zamanlarında dışarıda bulunmaktan kaçınılmalıdır.
- Vücudun açık kalan yerlerine repellentler kullanılmalıdır.
- Açık renkte ve kısa kollu giysiler giyilmemelidir.
- Geceleri ilaç emdirilmiş cibinlik kullanılmalıdır.

SONUÇ

Bu derlemede Amerika kıtasına seyahat edecek kişilerin hangi tür paraziter hastalıklar ile karşılaşma riski bulunduğunu konusunda bilgiler verilmektedir. Bu hastalıklara karşı seyahat öncesinde, sırasında ve sonrasında alınması gereken profilaktif ajanlar ve kişisel önlemlerden bahsedilmektedir. Böylece seyahat eden kişilerin paraziter enfeksiyonların bulaşma riskini en aza indirilmesinde rehber oluşturması amaçlanmıştır.

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A Rare Case of Blebharitis: Phthiriasis Palpebrarum

Nadir Bir Blefarit Nedeni Olgusu: Pitriazis Palpebrarum

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ABSTRACT

A six-year-old male patient was admitted to our hospital due to itching and scalding crusts that persisted 10-15 days in both eyes. Upon biomicroscopic examination, 5–6 semi-translucent, yellowish brown living lice attached to the upper eyelashes and a large number of eggs were observed. Following application of pilocarpine hydrochloride (Pilomann 2%, Bausch-Lomb) and topical proparacaine hydrochloride (Alcaine 0.5%, Alcon), the paralyzed parasites and eggs were manually removed by pulling with forceps. The lice were identified as adult forms of pubic louse, *Pthirus pubis*, and its eggs. The patient was treated with pilocarpine hydrochloride, which was applied thrice a day combined with pure vaseline. One week later, no lice or eggs were seen on the eyelashes.
Keywords: Phthiriasis palpebrarum, blepharitis, pilocarpine hydrochloride, vaseline
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ÖZ

Altı yaşındaki erkek hasta, her iki gözde10-15 gündür devam eden kaşıntı ve çekmekle çıkmayan kabuklar nedeniyle hastanemize başvurdu. Göz muayenesinde; her iki göz üst kapaklarının kirpiklerinde kahverengi kabuklanmalar görüldü. Biyomikroskopik incelemesinde; her iki göz üst kapaklarının kirpiklerine sıkıca tutunmuş, yengeç benzeri hareketli ayakları olan, yarı şeffaf, sarı kahverenkli, 5-6 adet canlı bit ve çok sayıda yumurtaları görüldü. Kirpik diplerine pilokarpin hidroklorid (Pilomann %2, Bausch-Lomb) damlatıldı. Topikal proparakain hidroklorid (Alcaine %0,5, Alkon) anestezisini takiben hareketsizleşen bitler ve yumurtaları tutundukları kirpiklerden penset yardımıyla dikkatli bir şekilde alındı. Kirpiklerden alınan örneklerin parazitolojik incelemesinde *Pthirus pubis* erişkin ve yumurtaları saptandı. Tedavi olarak Pilokarpin hidroklorid (Pilomann %2, Bausch-Lomb) ile birlikte kirpiklere günde 3 kez sıvı vazelin (petrolatum bileşiği) uygulaması önerildi. Kirpik diplerindeki bit ve yumurtalar bir hafta sonra tamamen ortadan kayboldu.
Anahtar sözcükler: Pitriazis palpebrarum, blefarit, pilokarpin hidroklorid, vazelin
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INTRODUCTION

Human lice are obligatory ectoparasites feeding on blood and humans are their only hosts. There are three types of human lice: the head louse Pediculus humanus capitis; the body louse Pediculus humanus humanus; and the pubic louse Pthirus pubis (1). These parasites cannot fly or jump and are transmitted through direct physical contact between two individuals. Although *P. pubis* usually involves the pubic/anal region, it can also infest the axilla, beard area of the face, chest hair, and rarely the eyelashes and eyebrows. *Phthiriasis palpebrarum* (PP) is a form of parasitosis occurring because of infestation of eyelashes with adult, nymph, and eggs of *P. pubis*, while *P. h. capitis* and *P. h. humanus* do not infest eyelashes. *P. pubis* is smaller (1.3-2 mm) and distinguished from other species by its strong second and third leg pairs. It is less mobile and therefore cannot easily displace itself from the initial contamination area (2). Adult females lay approximately three eggs per day (25-50 eggs during their life span), and the whitish oval eggs are attached

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to the hair on which the lice live (3). The development from egg to egg-laying adult takes from 22 to 27 days. The egg hatches and produces the first nymphal stage, which after three molts develops into nymph 2, nymph 3, and subsequently to either a male or female louse. The incubation period of the egg is 7-8 days. The average adult female lives for 17 days and the male for 22 days (1-3). *P. pubis* usually infests after puberty and is frequently sexually transmitted. Since transmission is possible with only close contact, the parasite is transferred from the pubic or axillary hair to the eyes by strong physical contact. It should be considered that *P. pubis* infestations can be associated with sexual abuse in children or sexual activity in adolescents (4). PP is a clinical entity that should be considered in the differential diagnosis of blepharitis in all age groups and can be easily missed if only the eye globe is taken into account during biomicroscopic examination and eyelid examination is overlooked.

CASE REPORT

A six-year-old male patient who was a preschool pupil experienced intense pruritus around the eyes and on his eyelashes for 15-20 days, and a whitish, hard-to-remove crust was observed. There was no hyperemia or irritation in the eyes. Eye examination revealed an intact eye vision. Biomicroscopic examination showed 5-6 semi-translucent, live adult *P. pubis* firmly attached to the upper eyelids with mobile legs resembling those of a crab and eggs attached with a translucent tubular sac surrounding the eyelash (Figure 1).

No hyperemia or follicular reaction on the edge of the eyelid or conjunctiva or other pathology in the anterior and posterior segments of the eye was observed. The family history revealed that he was the only child and lived with his parents. The parents did not complain of any symptoms suggesting pediculosis or phthiriasis. Ophthalmologic examination of the parents did not reveal any parasite in the eyelashes. The family stayed in a boarding house 15-20 days before the crusts and itching in the patient's eyelids appeared. All family members were directed for dermatologic examination to detect potential phthiriasis lesions in other body parts. Ample amount of pilocarpine hydrochloride solution (Pilomann 2%, Bausch-Lomb) was applied on both the eyes to cause paralysis of *P. pubis*. After five minutes, the movement of the parasites markedly diminished, and they were easily detached from the eyelashes. Following anesthesia by topical proparacaine hydrochloride (Alcaine 0.5%, Alcon), immobilized parasites and eggs were mechanically removed from the eyelashes with the help of a forceps. The family was advised to clean visible parasites using pilocarpine hydrochloride drops (Pilomann 2%, Bausch-Lomb) and to apply liquid vaseline on to base of the eyelashes for four days. During the follow-up examination one and two week later, no lice or eggs were observed on the eyelashes. The patient was cautioned during treatment and later on that his clothes and towels should not be shared with the family members.

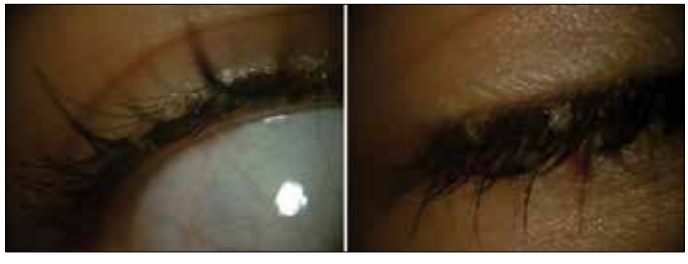

Figure 1. a, b. Slit-lamp examination: Phthiriasis palpebrarum. Mobile louse (a) embedded in the lid skin is seen at the base of the eyelashes and nits (b) attached to the eyelashes

The study protocol was approved by the Uludag University Human Research Ethics Committee (No: 2015-17/6).

DISCUSSION

Phthiriasis palpebrarum is a rare eyelid infestation caused by the pubic louse *P. pubis*, and it can be observed in people who live in crowded places and have poor hygiene (5). PP is a rare condition occurring due to infestation of eyelashes and eyebrows with pubic louse. Eyelashes are the most common site for lice infestation in children (3), and the parasite is acquired from parents through direct contact (6). Brown-reddish granular accumulations on the base of the eyelashes are sufficient for diagnosis, along with the observation of the lice and eggs on the lashes. Screening of the eyelashes and edges of the eyelids during eye examination, with or without marked itching, enables easy diagnosis of contagious parasitosis. The clinical findings of PP include blepharitis accompanied with itching, rash, and edema on the eyelids; follicular conjunctivitis; marginal keratitis; secondary bacterial infections; and rarely eyelid cellulites (7). PP is an uncommon cause of blepharoconjunctivitis. It might be observed as an isolated infestation of the eyelids and can be easily overlooked (8). No hyperemia or conjunctivitis was observed in the present case, while a mild itching was present. Shaving pubic and axillary regions, applying 1% permethrin shampoo on the infested regions, removing parasites from the eyelashes with a forceps, or cutting the eyelashes, are some of the treatment modalities. There are also studies suggesting that pilocarpine hydrochloride, liquid vaseline, moxifloxacin eye ointment, 1% mercury oxide, cryotherapy, argon laser (7), topical botulinum toxin application (9), 50% tea tree oil (10), and single application of 20% fluorescein on the base of the lashes are effective in the treatment (11). Considering the risk of toxicity with gamma benzene hydrochloride and mercury, 2% pilocarpine hydrochloride drops and liquid vaseline application seem to be an effective, inexpensive, and easy-to-use treatment modality. It should be remembered that pilocarpine hydrochloride does not have any effect on the eggs, and it only paralyzes the parasite. The application of vaseline (petrolatum) along with pilocarpine hydrochloride at the base of the eyelashes 2 to 3 times a day can be considered as an alternative treatment particularly in children as it does not result in eye irritation. The treatment should be continued for 8-10 days, the patient should be reexamined after 7-8 days, and other treatment alternatives should be considered if the given treatment does not provide the appropriate results. It should be remembered that vaseline hinders respiration of the parasite and suffocates it, and it has no fatal effect on the eggs; hence, it might be insufficient for complete eradication. Although there are studies suggesting that ivermectin, an anthelmintic drug, is orally used, its side effects limit its wide-

spread use. However, it can be used in resistant cases. There is a contribution of a study from Turkey, reporting that eyelid treatment with diluted vinegar can be useful in the treatment of PP through its keratolytic effect (12). Today, the mechanical removal of the eggs is still a treatment option (13). It has been reported in literature that moxifloxacin and mechanical cleaning are practiced and are effective (14). It has also been reported that only 4% of pilocarpine hydrochloride is effective without mechanical removal (8). The use of fusidic acid, fluorometalon, and tetrazolin drops is reported to be effective after mechanical removal (15). Sundu et al. (16) reported a case of blepharitis related to PP and its treatment using an argon laser. We treated our patient with meticulous application of pilocarpine hydrochloride and liquid petrolatum over the lid margin and eyelashes. We also attempted mechanical removal. It is also important to mention that in addition to treatment, other family members and contact people should be examined and if necessary treated. It should be considered that PP can coexist with other venereal diseases in adult patients, and the possibility of sexual abuse must be investigated, particularly in children. Since it is known that the life span of an adult parasite is less than one month and it cannot survive more than 24–48 hours outside of the human body, clothes and bedding should either kept in air-tight plastic bags for several days, or washed at temperatures above 55°C. In literature, PP has been reported even in an infant aged nine months (17), and it should be considered for the differential diagnosis in cases of blepharitis, particularly those who are resistant to treatment. Eyelids should be carefully examined under a biomicroscope independently of pruritus, hyperemia, and irritation.

CONCLUSION

Pthirus pubis infestations do not occur only in people who live in unfavorable and overcrowded conditions with poor hygiene, but is also observed in people with a high socioeconomic status and in all age groups.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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Psychoda albipennis'in Neden Olduğu Bir Ürogenital Miyaz

Urogenital Myiasis Caused by *Psychoda albipennis*

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ÖZ

Miyazis ülkemizde bilinen ürogenital parazitoz nedenlerinden biridir. Ürogenital miyazis etkeni olarak tanımlanmış sinek türlerinden biri *Psychoda albipennis*'tir. Bu olguda, idrar yaparken yanma bulantı, kusma, karın ağrısı ve idrarından hareketli larva düşürme şikayetiyle polikliniğimize başvuran 28 yaşındaki bir kadın hasta sunulmuştur. Alınan idrar numunesinde larva makroskobik ve mikroskobik olarak incelenmiştir. Bunun sonucu olarak hastaya *P. albipennis* dördüncü dönem larvalarına bağlı gelişen ürogenital miyaz tanısı konulmuştur. Antibiyotik ve üriner antiseptiklerle hastanın şikayetleri sonlanmıştır. Ürogenital yakınması olan hastalarda miyaz akılda tutulması gereken önemli bir tanıdır.
Anahtar sözcükler: *Psychoda albipennis*, ürogenital, miyaz, insan, diptera
Geliş Tarihi: 05.07.2017 **Kabul Tarihi:** 28.12.2017

ABSTRACT

Myiasis is one of the reasons for urogenital parasitosis in our country. *Psychoda albipennis* is a fly that leads to urogenital myiasis. In this case, a 28-year-old female with complaints of dysuria, nausea, vomiting, abdominal pain, and dropping larvae with urine was referred to our hospital. Larvae in the urine sample were macroscopically and microscopically examined. Subsequently, the patient was diagnosed with urogenital myiasis due to *P. albipennis* fourth phase larvae. The symptoms were relieved with antibiotic and urinal antiseptic treatments. A diagnosis of urogenital myiasis should be considered in patients with urogenital complaints.
Keywords: *Psychoda albipennis*, urogenital, miyaz, human, diptera
Received: 05.07.2017 **Accepted:** 28.12.2017

GİRİŞ

Miyaz Yunanca bir kelime olan ve sinek anlamına gelen "myia" kelimesinden gelmektedir. Insecta sınıfına bağlı Diptera takımına ait sinek türlerinin larva ve yumurtalarının, insan ve omurgalı hayvan dokularında patolojik lezyonlara yol açması miyazis olarak tanımlanmaktadır (1, 2). İnsanlarda görülen miyazis olgularına, hijyen koşul ve davranışlarının düşük seviyede olduğu toplumlar, tropik ve subtropik iklim bölgelerinde daha sık rastlanmaktadır (3). Miyaz etkeni sinekler, larva ve yumurtalarının gelişmeleri için çöp ve lağım suları gibi organik atıkların bulunduğu nemli ortamlar ve çürümekte olan hayvan dokularını tercih etmektedir. Bazı durumlarda hayvan ve insan vücudunda açık yara ve kronik yangı bölgeleri gibi üreyebileceği uygun alanlara larva ve yumurtalarını bırakmaktadırlar. Bu zeminde gelişen enfestasyonlar fakültatif miyaz olarak adlandırılmaktadır (4, 5). Larvaların genital ve üriner kanal gibi boşluklara yerleşmesi ile enfestasyon gelişebilir. İnsanlarda ürogenital miyaz etkeni sinek türlerinden biri ise *P. albipennis*'tir (6). Psychodidae ailesi, Psychodinae alt ailesinde olan bu türün erginleri, küçük (1,5-2 mm) sineklerdir. Özellikle tuvalet ve banyo gibi nemli alanlarda yaşarlar.Dört larva dönemi vardır. Larvalar silindirik görünümlü, beyaz-gri renkli, üzerleri soluk kısa tüylü veya pulludur, bazen kenarları dişlidir. Son segmentte solu-

Bu olgu, sözlü bildiri olarak 25-29 Eylül 2017 tarihlerinde Eskişehir'de gerçekleştirilmiş olan 20. Ulusal Parazitoloji Kongresi'nde sunulmuştur.
This case was presented at the 20th National Parasitology Congress held in Eskişehir on 25-29 September 2017 as an oral statement.

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num tüpü ve ucunda bir çift stigma bulunur, etrafı uzun tüylüdür (7, 8). Bu çalışmamızda, bir kadın hastada *P. albipennis*'e bağlı oluşan ürogenital miyazis olgusu sunulmuştur.

OLGU SUNUMU

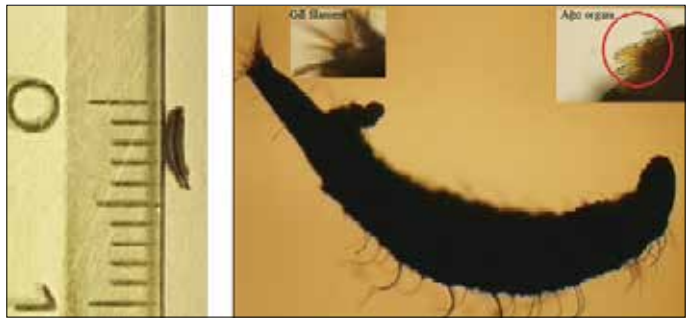
Yirmi sekiz yaşında kadın hasta yaklaşık iki haftadır halsizlik, kasıklarda ağrı, sık idrara çıkma, bulantı, kusma ve idrarda hareketli parça düşürme şikayeti ile enfeksiyon hastalıkları polikliniğimize başvurdu. İl merkezinde ikamet eden hastamızın yakın dönemde kırsal alana seyahat öyküsü vardı. Bu dönemde hijyen şartları iyi olmayan alanlarda bulunduğu anamnezden öğrenildi. Hastanın eşi benzer şikayetler açısında sorgulandı bir özellik saptanmadı. Fizik muayenede suprapubik hassasiyet dışında diğer sistemler doğal olarak değerlendirildi. Alınan idrar örneğinin mikroskobisinde lökosit yoktu,her sahada bir veya iki eritrosit vardı. İdrar kültüründe üreme olmadı. Evde idrarını biriktirmesi söylenen hastanın idrarında dört adet larva olduğu tespit edildi. Larvalar 4-8 mm arası ölçülerde arka sifon bölgesine doğru kıllarla kaplı olduğu makroskopik olarak görüldü. Larvalar %70'lik etil alkol içine alınarak üniversitemiz parazitoloji laboratuvarına incelemeye gönderildi, *P. albipennis*'in dördüncü dönem larvası olarak değerlendirildi. Larvaların atılımını kolaylaştırması için hastaya bol sıvı alması önerildi. İdrar yolu antiseptiği kullandırılan hastanın şikayetleri geriledi, larva düşürmesi sonlandı.

TARTIŞMA

P. albipennis, özellikle tropikal, subtropikal ve sıcak ılıman iklimin hakim olduğu bölgelerde ve ülkemizi de içine alan Palaeartic bölgede görülmektedir. Ürogenital miyaz olguları fakültatif tarzda olup, olguların daha çok hijyen koşulları ile ilişkili olduğu bildirilmiştir (8, 9). Üriner sistemin son kısmı olan üretra çıkış deliği yakınına bırakılan larva idrar yollarına girer. Daha sonra yukarı doğru çıkarak, gittiği yerde miyazis olarak isimlendirilen ve doku kaybı ile karakterize lezyona sebep olur (5). Literatür ile uyumlu olarak olgumuz kötü hijyen koşullarına maruz kalmıştır ve ılıman bir bölgede yaşamaktadır.

P. albipennis dördüncü dönem larvaları beyaz-gri renkte, ortalama 3-5 mm boyunda hafif yassı görünümde kurtçuklardır. Kenarları dişçikli olabilen larvaların üzeri kısa tüyler veya pullarla kaplıdır. Vücut dorsalinde yer alan plak sayısı değişken olup, genellikle geriye doğru yer alan 7-8 halka dikkati çekmektedir. Dipten uca doğru incelen sifonun uç kısmında etrafında kıllar bulunan bir çift stigma vardır (4). Bizim olgumuzda elde edilen larvaların boyu 4 mm, sifonun etrafında kıllar izlenmekteydi. Olgumuzdan elde edilen larvanın görüntüleri Resim 1'de gösterilmiştir.

Fannia species, Lucilia sericata, Chrysomya bezziana, Eristalis tenax ve *Megaselia scalaris*'e ait larvalar dünyanın değişik ülkelerinde ürogenital miyazise sebep olmaktadır (10-14). Ülkemizde Güven ve ark. (4) tarafından Eskişehir'de üriner girişim geçirmiş 50 yaşında bir kadın hastada *P. albipennis*'e ait üriner miyazis olgusu bildirilmiştir. Ayrıca, Kırşehir'de 29 yaşında erkek, Siirt'te 20 yaşında kadın, Sakarya'da 21 yaşında kadın, Trabzon'da 29 yaşında erkek olguda *P. albipennis* dördüncü dönem larvaları ile oluşan üriner miyazis olguları bildirilmiştir (9, 15-17). Olgumuz 28 yaşında kadın hasta olup *P. albipennis* dördüncü dönem larvaları ile oluşan üriner miyazise sahipti.



Resim 1. Olgumuz idrarından elde edilen *Psychoda albipennis* larvasının makroskobik ve mikroskobik görünümü

Ürogenital miyazisli hastalarda disüri, pollaküri, hematüri, yan ağrısı, bulantı ve kusma gibi yakınmalar sıklıkla görülmektedir. Bu yakınmaların larvanın üriner sistem dokusunda oluşturduğu yangısal reaksiyonlara bağlı olarak geliştiği bilinmektedir (1-4). Hastada bu yakınmaların tamamına ek olarak pelvik ağrı ve basınç hissi de mevcuttu. Hastanın üriner sistem direkt muayenesi normal olup, idrar tetkiklerinde mikroskobik hematüri dışında bir bulgu yoktu ve ultrason bulguları normaldi.

Üriner miyazis tedavisinde çeşitli tedavi şekilleri mevcut olup enfestasyonun lokalizasyonu ve semptomların derecesine göre tedavi şekli değişmektedir. Larvaların doğrudan doku üzerinden toplanması, hasarlanmış dokuya antiseptik uygulanması, antiparaziter ilaçlar verilmesi ve dokuda oluşan hasar dolayısı ile oluşabilecek sekonder bakteriyel enfeksiyonların gelişiminin antibiyotiklerle önlenmesi önerilmektedir (4, 7, 9, 15). Olgumuzda hastanın şikayetlerini azaltmak için idrar yolu antiseptiği uygulandı ve hastaya bol sıvı verildi. Hastanın takiplerinde şikayeti olmadı.

SONUÇ

P. albipennis'e bağlı üriner miyazis nadir görülen bir hastalıktır. Hastalığın tanısında anamnez ve risk faktörlerinin araştırılması oldukça önemlidir. Sıcak yaz aylarında, nemli ortamlarda ve kötü hijyen koşullarında görülme oranı artmakta olup ülkemizde de görülmektedir. Tedavide bol sıvı alınması, üriner sistem antiseptiği kullanılabilir. Korunmada hijyen en önde gelen etkendir.

Hasta Onamı: Yazılı hasta onamı bu olguya katılan hastadan alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir – A.R.Ş., E.K., U.Ö.; Tasarım – S.N., A.R.Ş.; Denetleme – S.G., E.K.; Veri Toplanması ve/veya İşlemesi – U.Ö., A.R.Ş.; Analiz ve/veya Yorum – A.R.Ş., S.G., E.K.; Literatür Taraması – S.N., U.Ö.; Yazıyı Yazan – A.R.Ş., S.N.; Eleştirel İnceleme – E.K., S.G.

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Informed Consent: Written informed consent was obtained from patient who participated in this case.

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Author contributions: Consept – A.R.Ş., E.K., U.Ö.; Design – S.N., A.R.Ş.; Supervision – S.G., E.K.; Funding – U.Ö., A.R.Ş.; Materials – A.R.Ş.,

S.G., E.K.; Data Collection and/or Processing – S.N., U.Ö.; Analysis and/or Interpretation – A.R.Ş., S.G., E.K.; Literature Review – S.N., U.Ö.; Writer – A.R.Ş., S.N.; Critical Review – E.K., S.G.

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Bir Kedide (*Felis catus*) *Felicola subrostratus* (Burmeister, 1838) (Phthiraptera: Ischnocera) Olgusu

A Case of *Felicola subrostratus* (Burmeister, 1838) (Phthiraptera: Ischnocera) on a Cat (*Felis catus*)

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Cite this article as: Dik B. A Case of *Felicola subrostratus* (Burmeister, 1838) (Phthiraptera: Ischnocera) on a Cat (*Felis catus*). Turkiye Parazitol Derg 2018; 42:96-100.

ÖZ

Bu olgu sunumu Kocaeli'de özel bir veteriner kliniğine getirilen 2 yaşında bir sokak kedisinde (*Felis catus*) tespit edilen *Felicola subrostratus* (Burmeister, 1838) (Phthiraptera: Ischnocera) hakkında bilgi vermek amacıyla hazırlanmıştır. Yapılan dış parazit muayenesinde kedide şiddetli bit enfestasyonu gözlenmiştir. Bitlerin bir kısmı pensle toplanarak içinde %70 alkol bulunan bir tüpe konmuş ve Selçuk Üniversitesi Veteriner Fakültesi Veterinerlik Parazitolojisi Anabilim Dalı'na gönderilmiştir. Mikroskobik incelemede bitler *F. subrostratus* (Burmeister, 1838) olarak teşhis edilmiştir. Bu türün Türkiye'deki kedilerde görüldüğü bilinmekle birlikte, bu konuda yapılmış herhangi bir çalışmaya veya makaleye rastlanmamıştır. Bu nedenle, bu makalede, hem bu konuda çalışanları, hem de veteriner hekimleri bilgilendirmek amacıyla *F. subrostratus* hakkında ayrıntılı bilgi verilmiştir.

Anahtar sözcükler: Bit, çiğneyici bit, Türkiye
Geliş Tarihi: 25.10.2017 **Kabul Tarihi:** 04.12.2017

ABSTRACT

We present this case report to provide information about *Felicola subrostratus* (Burmeister, 1838) (Phthiraptera: Ischnocera) detected on a 2-year-old stray cat (*Felis catus*) brought for treatment to a veterinary clinic in Kocaeli, Turkey. Macroscopically, severe louse infestation was detected on the cat. Some of the lice on the cat were collected using forceps and preserved in 70% ethanol. Then, they were sent to Department of Parasitology, Veterinary Faculty, Selçuk University in Konya for identification. Samples were examined under a microscope and identified as *F. subrostratus* (Burmeister, 1838). *F. subrostratus* has been known to be detected on cats in Turkey, but no study is found about this species. For this reason, in this case report, *F. subrostratus* was studied to further educate veterinarians and parasitologists in the country.

Keywords: Louse, Chewing lice, Turkey
Received: 25.10.2017 **Accepted:** 04.12.2017

GİRİŞ

Felicola subrostratus evcil kedilerin tüylerini yiyerek beslenen daimi bir parazittir ve 1838 yılında *Trichodectes subrostratus* olarak tanımlanmıştır (1). Bu tür Phthiraptera takımı, Ischnocera alt takımı, Trichodectidae ailesi *Felicola* cinsinde yer alır. Genel olarak evcil kedilerde görülür ve temas yoluyla bir konaktan diğerine bulaşır. Konak seçiciliği olmasına rağmen, evcil kedilerin yanı sıra; Afrika yaban kedisi (*Felis silvestris lybica*), Avrupa Yaban kedisi (*Felis silvestris silvestris*), Doru Vaşak (*Lynx rufus*), Afrika Misk kedisi (*Viverra civetta*), Madagaskar Kahverengi-kuyruklu Firavun Faresi (*Salanoia concolor*) ve Beyaz-kuyruklu Firavun Faresi'nde (*Ichneumia albicauda*) de görüldüğü bildirilmiştir (2-4).

Bu makale Uluslararası katılımlı 20. Ulusal Parazitoloji Kongresi'nde (25-29 Eylül 2017, Eskişehir, Türkiye, Poster No 18, Sayfa 438) poster sunusu olarak sunulmuştur.
This paper was presented as poster presentation in 20. National Parasitology Congress (25-29 September, 2018, Eskişehir, Turkey, Poster no. 18, page 438)

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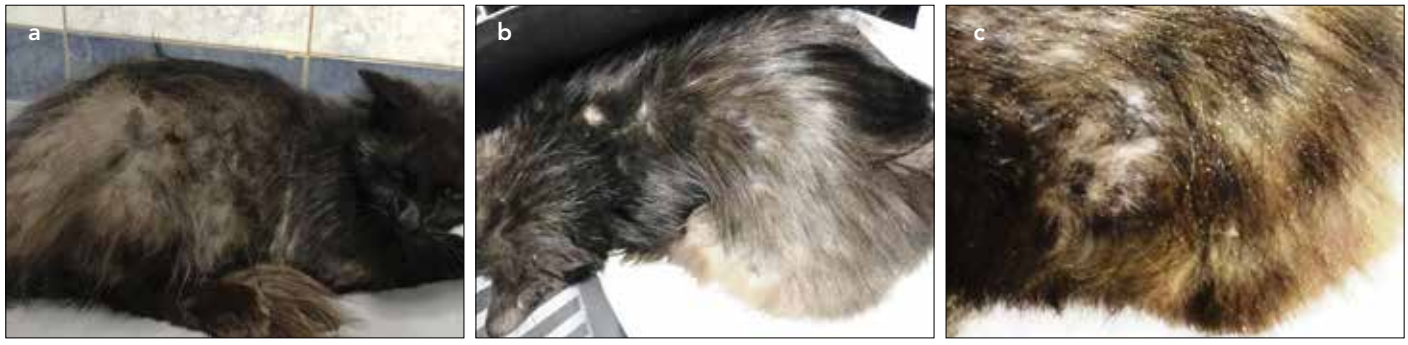
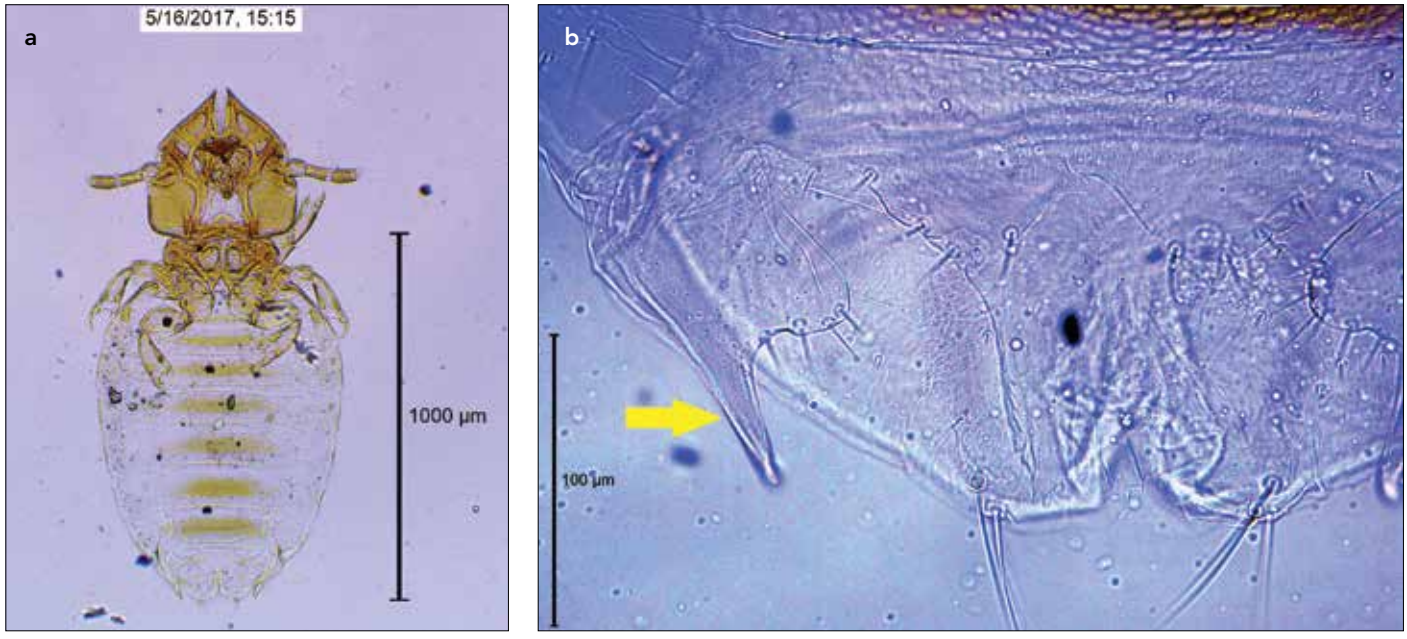


Resim 1. a-c. *Felicola subrostratus* ile enfeste kedi, orijinal



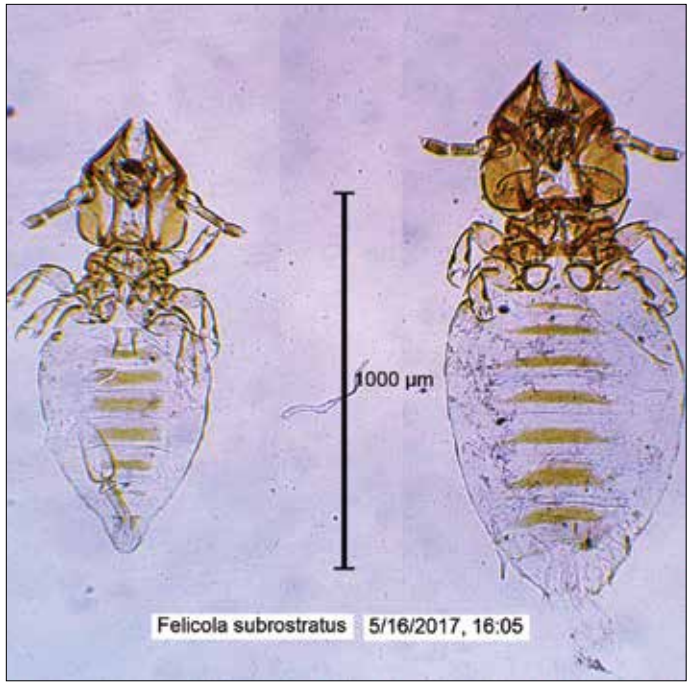
Resim 2. a, b. (a) *Felicola subrostratus*, dişi, orijinal. (b) *Felicola subrostratus*, dişi, gonopofiz (okla işaretli), orijinal

F. subrostratus kozmopolit bir yayılışa sahiptir, ABD, Avrupa, Güney Afrika, Kanada, Avustralya, Hindistan, Pakistan, Brezilya, İsrail ve Macaristan'daki kedilerde değişik oranlarda görüldüğü belirtilmiştir (4-10).

Capári ve ark. (9) Batı Macaristan'da inceledikleri 82 kedinin sadece birisinde *F. subrostratus*'a rastlamıştır. İsrail'de, Jerusalem'de yapılan bir araştırmada ise 340 sokak kedisinin 49'unun (%14,4) *F.subrostratus* ile enfeste olduğu kaydedilmiştir (10). Brezilya'nın Rio de Janerio şehrinde 2002-2004 yılları arasında yapılan bir çalışmada, *F. subrostratus*'un yaygınlığının yıllara göre %4,3 ile %39,4 arasında değiştiği tespit edilmiştir (11).

F. subrostratus'un biyolojisi iyi bilinmemektedir. Dişi, yumurtaları konağın kıllarına yapıştırır. Birkaç saat ile birkaç gün arası değişen sürede yumurtadan nimf çıkar. Üç nimf dönemi vardır ve nimf dönemi yaklaşık 2-3 haftada tamamlanır. Enfestasyonun yaz aylarına oranla kışın daha yaygın olduğu düşünülmektedir. *F. subrostratus* genel olarak klinik belirtiye neden olmaz, ancak çok sayıda olduklarında ağırlık kaybı ve zayıflama görülür. Tedavisinde pretrinler, avermektinler, fipronil ve imidacloprid kullanılabilir (12, 13). Selamectin *F. subrostratus*'a karşı yüksek etkili bulunmuştur (14).

F. subrostratus'un Türkiye'deki kedilerde görüldüğü belirtilmekle birlikte (15, 16), nerede görüldüğü, yaygınlık durumunun ne

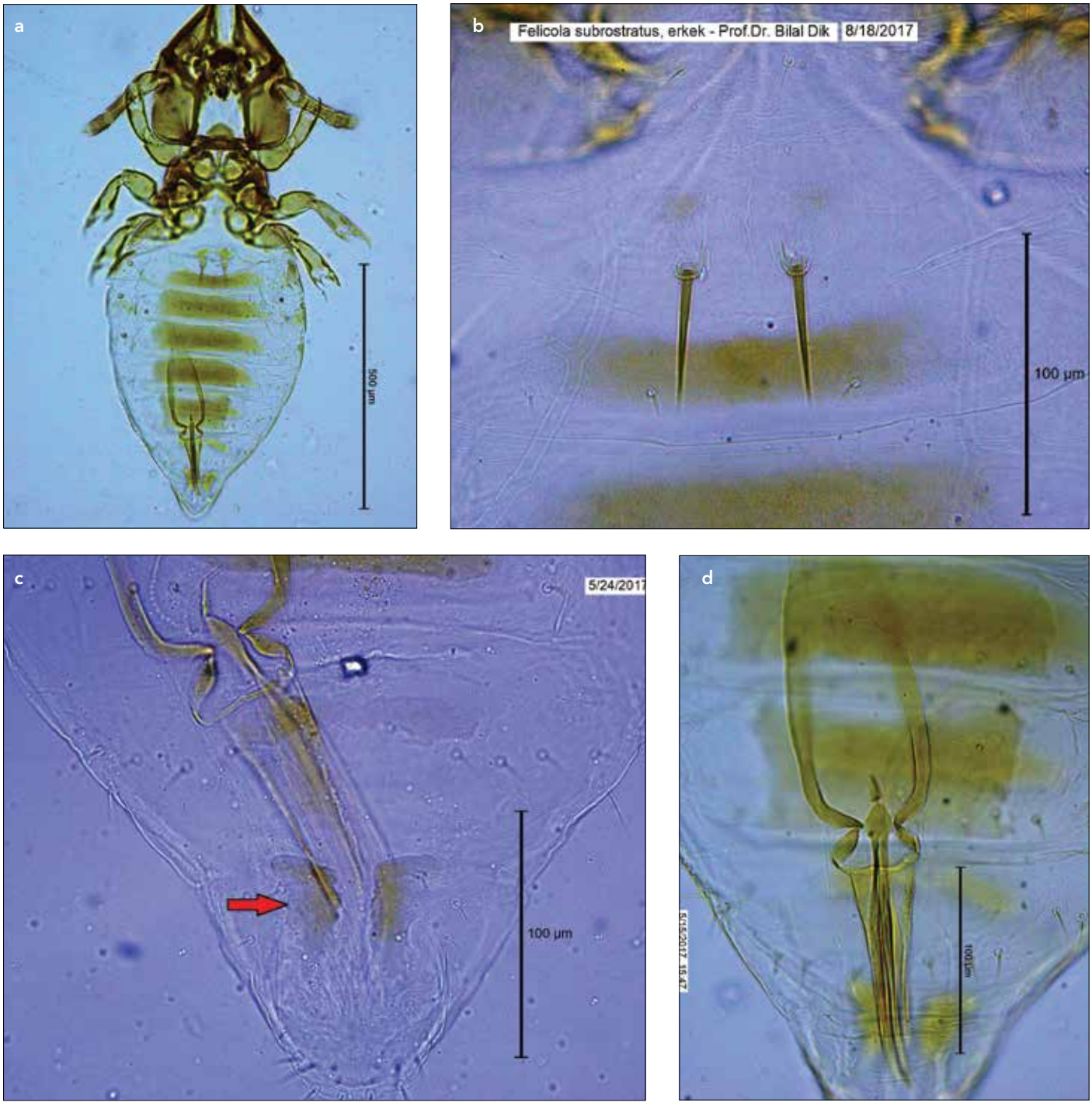


Resim 3. *Felicola subrostratus*, erkek (solda), dişi (sağda), orijinal

olduğu veya diğer özellikleri ile ilgili ayrıntılı bir bilgiye veya makaleye rastlanmamıştır. Bu nedenle, *F. subrostratus*'un Türkiye'deki varlığını bildirmek, morfolojik ve diğer özellikleri hakkında ayrıntılı bilgi vermek ve bu konuda çalışanları bilgilendirmek amacıyla bu makale hazırlanmıştır.

OLGU

Kocaeli, Sapanca civarlarında bulunan ve tedavi amacıyla Pasteur Veteriner Kliniği'ne getirilen 2 yaşında, siyah tekir sokak kedisinin klinik muayenesi yapılmış, yemesi, içmesi ve ateşinin normal, fakat tüy kalitesinin mat ve kötü olduğu gözlenmiştir. Tüylerinde kırılganlık ve kaşıntısı olan kedinin yapılan dış parazit muayenesinde bitlerle aşırı derecede enfeste olduğu gözlenmiştir (Resim 1a, b, c). Bitlerin bir kısmı pensle toplanarak, içinde %70 alkol bulunan bir tüpe konulmuş ve Selçuk Üniversitesi Veteriner Fakültesi Veterinerlik Parazitolojisi Anabilim Dalı'na gönderilmiştir. Mikroskobik inceleme sonucu bitlerin *F. subrostratus* olduğu saptanmıştır. Kedinin üzerinden toplanan 100'den fazla örneğin büyük bir kısmının dişi olduğu,



Resim 4. a-d. (a) *Felicola subrostratus*, erkek, orijinal. (b) *Felicola subrostratus*, erkek, I. tergit, orijinal. (c) *Felicola subrostratus*, erkek, 8. tergit, sclerit (okla işaretli), orijinal. (d) *Felicola subrostratus*, erkek genitalia, orijinal

erkek ve nimf sayısının oldukça az olduğu tespit edilmiş, ayrıca kıllara yapışık çok sayıda yumurtaya rastlanmıştır.

Morfolojik Özellikleri: Bu çalışmada toplanan *F. subrostratus* örneklerine ait bazı ölçümler Tablo 1'de verilmiştir. Bu tabloda da görüleceği üzere, dişinin ortalama büyüklüğü 1,36 mm, erkeğin ki ise 1,10 mm'dir.

Dişi (Resim 2a, b, 3)
Baş beşgenimsi olup, erkeğe oranla daha geniştir (Resim 2a, 3). Preantennal bölge üçgen, post-antennal bölge dörtgen şeklindedir. Marginal carina ortada dar ve derin bir yarıkla ayrılmıştır. Mandibula ve hipofarinksin sitophore sclerite'i iyi kitinleşmiştir. Anten 3 segmentlidir, ilk segment diğerlerine oranla daha kalın ve kısa, ikinci ve üçüncü segmentler ise birbirine yakın uzunluk ve kalınlıktadır.

Toraks kısa ve dar olup, önden arkaya doğru genişlemiştir. Genişliği uzunluğunun iki katına yakındır. Bacaklar kısadır ve tek tırnakla sonlanmıştır. Tırnakların karşısında kuvvetli spinler vardır.

Abdomen oval ve geniştir. Abdominal segmentler lateralde iyi kitinleşmemiştir. Tergal levhalar sadece ortada ince, yatay bir çizgi şeklinde iyi kitinize olmuşlardır. Tergal levhalar posterior segmentlere doğru giderek kalınlaşmış ve lateralde incelerek öne doğru kıvrılmıştır. Sadece 2-4. segmentlerde stigma mevcuttur. Tergitlerde birer sıra kısa seta bulunur. Gonopophyse iç kısmında gelişmiş bir loba sahiptir (Resim 2b).

Erkek (Resim 3, 4a, b, c, d)
Genel olarak dişiye benzemekle birlikte, ondan daha küçük ve daha dardır (Resim 3, 4a). İkinci anten segmenti diğerlerinden daha uzuncadır. Abdomen arkaya doğru daralmış ve nispeten sivri olarak sonlanmıştır. Tergal levhalar dişiye oranla daha iyi gelişmiştir. I. tergitte, medialde iki adet kuvvetli seta vardır (Resim 4b). VIII. tergitte, ortada, birbirinden ayrı, anterior uçları dışa doğru bükülmüş, uzunlamasına iki seklerit bulunur (Resim 4c).

Genitalia Resim 10'daki gibidir. Bazal levha anteriora doğru daralır, paramerler ve aedeagus uzun ve sivri olarak sonlanır.

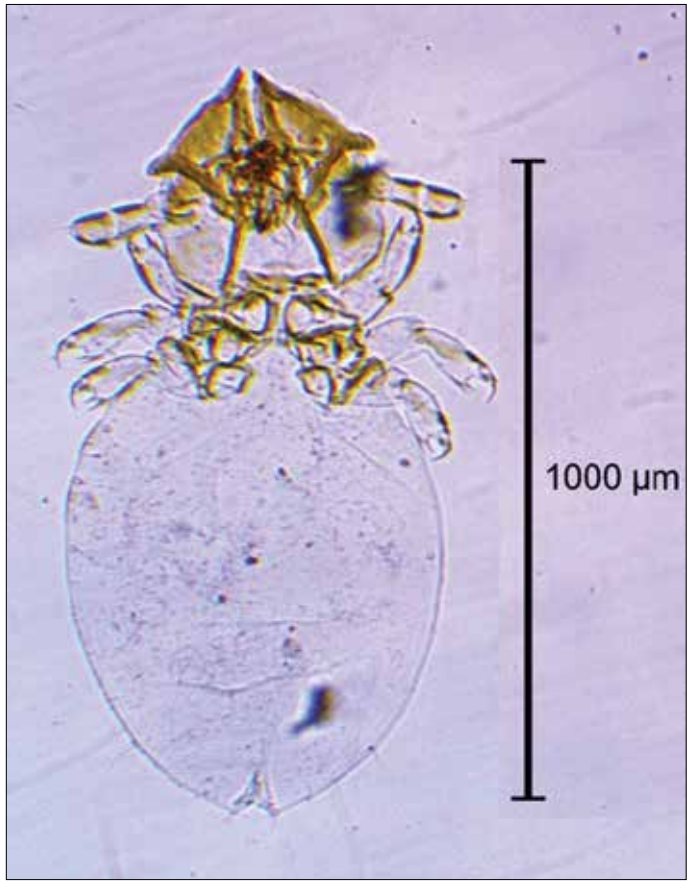
Yumurta silindirik, ön kısmı arkaya oranla daha geniş ve kapaklı olup, 0,5x0,3 mm büyüklüğündedir (Resim 5). Nimf dönemleri ergine benzemekle birlikte, daha küçüktürler ve kitinleşme daha zayıftır. Abdomen segmentleri belirgin değildir (Resim 6). Büyüklükleri nimfin dönemine gore değişmekle birlikte, 1 mm civarında veya daha küçüktür.

TARTIŞMA

F. subrostratus kedi ve kedigillerde görülen, Ischnocera alt takımında yer alan çiğneyici bir bit türüdür ve dünyanın birçok ülkesinde görüldüğüne dair yayınlar bulunmaktadır. Kedilerdeki yaygınlığının %4,3 ile %39,4 arasında değiştiği bildirilmiştir (9, 10). Bu türün Türkiye'de de görüldüğü bildirilmiş olmakla birlikte (15, 16), hangi illerde ve hangi oranlarda görüldüğünü belirten bir kaynağa rastlanmamıştır.

F. subrostratus'un soluk sarı renkte olduğu, dişisinin 1,3 mm, erkeğinin ise 1-1.2 mm büyüklüğünde olduğu bildirilmiştir (17-19). *F. subrostratus*, abdomeninde üç çift stigmanın olması, erkeğin I. tergitinde iyi gelişmiş iki setanın (kıl), 8. tergitin medialinde uzunlamasına iki skleritin bulunması, genital kesede setanın olmaması, genital yapısının farklı oluşu, erkek ve dişide bütün stigmaların aynı büyüklükte olması ile bu cinste yer alan diğer türlerden ayrılır (5). Bu olguda, kediden toplanan bitler mikroskobik olarak incelenmiş, dişinin ortalama büyüklüğünün 1.36, erkeğin büyüklüğünün ise 1,10 mm olduğu gözlenmiştir. Morfolojik özelliklerinin de Bedford'un (5) *F. subrostratus* için belirttiği morfolojik özelliklerle tamamen örtüştüğü belirlenmiştir.

Resim 5. *Felicola subrostratus*, yumurta, orijinal



Resim 6. *Felicola subrostratus*, nimf, orijinal

Tablo 1. *Felicola subrostratus*'a ait bazı morfolojik değerler (mm)

	Dişi (n=5)			Erkek (n=5)		
	En küçük	**En büyük**	**Ortalama**	**En küçük**	**En büyük**	**Ortalama**
Baş uzunluğu	0,37	0,40	0,38	0,32	0,34	0,33
Baş genişliği	0,36	0,39	0,37	0,27	0,28	0,28
Baş indeksi			1,02			1,18
Toraks uzunluğu	0,19	0,23	0,20	0,16	0,18	0,17
Toraks genişliği	0,35	0,36	0,36	0,27	0,28	0,27
Abdomen uzunluğu	0,75	0,81	0,77	0,59	0,66	0,63
Abdomen genişliği	0,59	0,61	0,60	0,41	0,44	0,42
Toplam uzunluk	1,28	1,42	1,36	1,03	1,15	1,10

Türkiye'de Veteriner Entomoloji veya Artropodoloji kitapları ile, derleme makaleler dışında, *F. subrostratus*'un kedilerdeki varlığı, yaygınlığı veya diğer özellikleri ile ilgili herhangi bir makaleye rastlanmamıştır. Bunun üzerine, bu konuda çalışan meslektaşlarımızın bilgilendirilmesi amacıyla bu makalede *F. subrostratus*'un morfolojisi, biyolojisi, epidemiyolojisi ve tedavisi hakkında ayrıntılı bilgi verilmiştir. Bunlara ek olarak, *F. subrostratus*'un değişik gelişme dönemlerine ait fotoğraflar çekilerek, teşhis açısından önemli noktalar bu resimler üzerinde gösterilmiştir.

SONUÇ

F. subrostratus'un Türkiye'de, kedilerdeki yaygınlığının belirlenebilmesi için, değişik bölgelerde yapılacak araştırmalara ihtiyaç vardır. Kedilerin yanı sıra, gerek *F. subrostratus*'un ve gerekse diğer *Felicola* türlerinin diğer kedigillerdeki varlıklarının ve yaygınlıklarının da çalışılması gerekmektedir.

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