Mehmet Akif Ersoy Üniversitesi

Sağlık Bilimleri Enstitüsü Dergisi

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BURDUR MEHMET AKİF ERSOY ÜNİVERSİTESİ

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I- Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi Genel Bilgiler

Mehmet Akif Ersoy Üniversitesi (MAKÜ) Sağlık Bilimleri Enstitüsü Dergisi, Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü'nün yayın organıdır. Derginin kısaltılmış adı "MAKÜ Sag. Bil. Enst. Derg" dir. Yılda 2 kez yayınlanır. MAKÜ Sağlık Bilimleri Enstitüsü Dergisi sağlık bilimleri, (veteriner, tıp, diş hekimliği, hemşirelik ve spor bilimleri) alanlarında temel ve klinik hakemli bilim yazılarının yayınlandığı hakem-denetimli bir dergidir. Derginin dili İngilizce'dir. Dergiye gönderilen yazıların başka herhangi bir dergide yayınlanmamış, yayına kabul edilmemiş ya da yayınlanmak üzere değerlendirme aşamasında olmaması gerekir. Bu kural bilimsel toplantılarda sunulan ve özeti yayınlanan bildiriler için geçerli değildir. Ancak, bu gibi durumlarda bildirinin sunulduğu toplantının adı, tarihi ve yeri bildirilmelidir. Makalelerin formatı "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http:/www.icmje.org/)" kurallarına göre düzenlenmelidir.

Gönderilen yazılar yayın kuruluna ulaştıktan sonra öncelikle, yazım kurallarına uygunluğu yönünden değerlendirilir; sonucu yazara dört hafta içinde bildirilir. Yazının, gerek teknik özellikleri gerekse genel kapsamı açısından derginin genel yayın ilkelerine uygun bulunmaması durumunda yazı reddedilir. Ya da, gerekirse, yazar(lar)ın yazıyı yazım kurallarına uygun biçimde yeniden göndermeleri istenebilir. Yeniden gönderilen yazılar benzer bir teknik incelemenin ardından yazım kurallarına uygun ise danışman denetimi sürecine alınır. Yazı, editör ve yardımcı editörler ile yazının başlık sayfasını görmeyen en az iki danışmana gönderilerek incelenir. Yazı, yayın kurulunun belirlediği ve bilimsel içerik ve yazım kuralları açısından değerlendirilir. Editör ve yardımcı editörler gerek gördüğünde makaleyi üçüncü bir danışmana gönderebilir. Hakem belirleme yetkisi tamamen editör ve yardımcı editörler ve yayın kuruluna aittir. Danışmanlar belirlenirken derginin uluslararası yayın danışma kurulundan isimler seçilebileceği gibi yazının konusuna göre ihtiyaç duyulduğunda yurt içinden veya yurt dışından bağımsız danışmanlar da belirlenebilir. Daha sonra, danışman raporları dikkate alınarak ve gerekirse yazar(lar)la tekrar iletişim kurularak yayın kurulunca son redaksiyon yapılır. Yazıların kabulüne editör karar verir.

Editör yayın koşullarına uymayan yazıları; düzeltmek üzere yazarına geri gönderme, biçimce düzenleme veya reddetme yetkisine sahiptir. Yazılarını geri çekmek isteyen yazarlar bunu yazılı olarak editöre bildirmek durumundadır. Editör görülen lüzum halinde bazı makaleler hakkında yayın yürütme kurulunun görüşüne başvurur. Bu değerlendirme süreci dergiye gönderilen yazı türlerinden araştırma yazılarını, olgu sunumlarını ve özgün yazıları kapsar. Diğer yazı türlerindeki yazılar doğrudan yayın kurulunca değerlendirilir. Dergiye gönderilen yazılar yayınlansın ya da yayınlanmasın geri gönderilmez. Tüm yazarlar bilimsel katkı ve sorumluluklarını ve çıkar çatışması olmadığını bildiren toplu imza ile yayına katılmalıdır. Araştırmalara yapılan kısmi de olsa nakdi ya da ayni yardımların hangi kurum, kuruluş, ilaç-gereç firmalarınca yapıldığı dip not olarak bildirilmelidir. Dergide yayınlanan yazılar için herhangi bir ücret ya da karşılık ödenmez.

Yayın kurulu yazar(lar)ın dergiye gönderdikleri yazıları değerlendirme süreci tamamlanmadan başka bir dergiye göndermeyeceklerini taahhüt ettiklerini kabul eder. İnsanlar ve hayvanlar üzerinde yapılan deneysel araştırmaların bildirildiği yazıların gereç ve yöntem bölümünde, bu araştırmanın yapıldığı gönüllü ya da hastalara uygulanan işlemler anlatıldıktan sonra kendilerinin onaylarının alındığını (informed consent) gösterir bir cümle bulunmalıdır. Yazar(lar), bu tür araştırmalarda, uluslararası alanda kabul edilen kılavuzlara (2002 yılında revize edilen 1975 Helsinki Deklarasyonu- http://www.wma.net/e/policy/b3.htm, Guide for the care and use of laboratory animals - www.nap.edu/catalog/5140.html), T.C. Sağlık Bakanlığı tarafından getirilen, 29 Ocak 1993 tarih ve 21480 sayılı Resmi gazetede yayınlanan "İlaç Araştırmaları Hakkında Yönetmelik" ve daha sonra yayınlanan diğer yönetmeliklerde belirtilen hükümlere uyulduğunu belirtmeli ve kurumdan aldıkları Etik Kurul Onayı'nın bir kopyasını göndermelidir. Metin içinde standart kısaltmalar kullanılır, bunlar ilk geçtikleri yerde açık olarak yazılır. İlaç adları kullanımında ilaçların jenerik adları Türkçe okunuşlarıyla yazılır. Ölçüm birimleri metrik sisteme uygun olarak verilir; örneğin, "mg" olarak yazılır, nokta kullanılmaz; ek alırsa („) ile ayrılır. Laboratuar ölçümleri Uluslararası Sistem (US; Systéme International: SI) birimleri ile bildirilir.

Bilimsel sorumluluk

Makalelerin tüm bilimsel sorumluluğu yazarlara aittir. Gönderilen makalede belirtilen yazarların çalışmaya belirli bir oranda katkısının olması gereklidir. Yazarların isim sıralaması ortak verilen bir karar olmalıdır. Sorumlu yazar, yazar sıralamasını "Yazar Sorumluluk ve Yayım Hakkı Devir Formu'nu" doldurarak tüm yazarlar adına kabul etmiş sayılır. Yazarların tümünün ismi makale başlığının altındaki bölümde yer almalıdır.

Yayın Ücretleri

Bu dergide yayın tamamen ücretsizdir. Yayın ücreti, başvuru ücreti, makale işleme ücreti ve bir figürün, rakamın veya tamamlayıcı verinin uzunluğuna göre ek ücret ödenmesi gerekmez. İçerik öğeleri (Editörler, Düzeltmeler, İlaveler, Geri Çekmeler, Mektuplar, Yorumlar vb.) tamamen ücretsizdir.

Etik sorumluluk

Makalelerin etik kurallara uygunluğu yazarların sorumluluğundadır. Hayvanlar üzerinde yapılan deneysel çalışmalarda, çalışma protokolünün çalışmanın yapıldığı kurumdaki hayvan deneyleri etik kurulu tarafından onaylandığı belirtilmelidir. Yazarlar etik kurul onayını makale ile birlikte göndermelidir. Eğer makalede daha önce yayımlanmış alıntı yazı, tablo, resim vs. var ise yazarlar; yayım hakkı sahibi ve yazarlarından yazılı izin alarak bu durumu makalede belirtmek zorundadır. Makalenin değerlendirilmesi aşamasında yayın kurulunun gerek görmesi halinde, makale ile ilgili araştırma verilerinin ve/veya etik kurul onayı belgesinin sunulması yazarlardan talep edilebilir.

İntihal politikası

Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi'ne (MAKÜ Sag. Bil. Enst. Derg.) Gönderilen yazılar intihal açısından değerlendirilir. Her gönderilen makale, iThenticate ve Turnitin yazılımı ile intihal için kontrol edilir. Makalenin benzerlik oranı %20'nin üzerinde ise, revize edilmesi için ilgili yazara geri gönderilir. Eğer makalenin yayınlanmasından sonra intihal kanıtlanırsa, bu makale derhal web sitesinden kaldırılır ve ilgili yazarlara makalelerinin MAKÜ Sag. Bil. Enst. Derg.'de yayınlanmasının uygun olmadığı bildirilecektir.

II- Dergiye Gönderilecek Yazı Türleri ve Özellikleri

a) Araştırma Makaleleri: Bu yazılar daha önce yayınlanmamış özgün araştırma verilerinin değerlendirildiği net anlam taşıyan bilimsel çalışmaları kapsar. Araştırma makaleleri "Öz, Giriş, Gereç ve Yöntem, Bulgular, Tartışma ve Kaynaklar" bölümlerinden oluşmalıdır. Dergide yayınlanmak üzere gönderilen araştırma makaleleri kapak sayfası hariç en fazla 20 sayfa olmalıdır. Araştırma makalelerinde kullanılacak tablo, çizim ve resim sayısı toplam 10'u geçmemelidir. Yazarlar gerek duydukları takdirde "Tartışma" bölümünden sonra "Teşekkür" bölümü açarak gerekli açıklamaları yapabilirler.

b) Derleme Makaleleri: Derleme makaleleri dergi editör/yayın kurulu tarafından "çağrılı derlemeler" başlığı altında oluşturulan alnında katkı sağlama potansiyeli olan yazıları içerir. Kaynakça bölümü en fazla 30 kaynakçadan oluşturulmalıdır. Derlemelerde kullanılacak tablo, çizim ve resim sayısı toplam 10'u geçmemelidir. Kapak sayfası hariç en fazla 20 sayfa olarak hazırlanmalıdır. Derlemelerde mutlaka "Öz, Giriş, Sonuç ve Kaynaklar" bölümleri bulunmalıdır.

c) Olgu Sunumları: Yazarların, herhangi planlanmış bir araştırmaya dayanmayan ancak karşılaştıkları yeni veya ender gözlemlenen olguların ele alındığı, bilimsel değere sahip bilgileri içeren eserlerdir. Bu eserlerde gereksiz uzatmaları önlemek amacıyla en fazla 15 kaynak kullanılmalı ve bu kaynakların güncel olmasına özen gösterilmelidir. Kapak sayfası hariç en fazla 5 sayfa olmalı; "Öz, Giriş, Olgu, Tartışma ve Kaynaklar" bölümlerinden oluşmalıdır.

d) Kısa Araştırma Raporu: Dar kapsamlı ele alınmış (sınırlı sayıda örneğin analiz edildiği çalışmalar vb.) ancak önemli ve yeni bilgiler sunan bilimsel araştırmaya dayalı makalelerdir. Kısa bildiriler araştırma makalesi formatında hazırlanmalı ve kapak sayfası hariç en fazla 10 sayfa olmalıdır. Bu eserlerde kullanılacak tablo ve şekil sayısı beşi geçmemelidir.

e) Özel Bölümler:

1. Editöre mektuplar: Dergide yayınlanan yazılara ilişkin değerlendirme ve eleştirileri içeren yazılardır. Mümkün olduğunca eleştirilen yazının yazar(lar)ınca verilen yanıtlar ile birlikte yayınlanır. Editöre mektuplar 3 sayfayı geçemez.

2. Toplantı haberleri/izlenimleri: Derginin yayın alanıyla ilgili konularda yapılmış ya da yapılacak olan bilimsel toplantıları tanıtıcı yazılardır. 1 sayfayı geçemez.

3. Dergi haberleri: Derginin yayın alanıyla ilgili konularda yayınlanmakta olan bilimsel dergileri tanıtıcı yazılardır; 1 sayfayı geçemez.

4. Web siteleri tanıtımı: Derginin yayın alanıyla ilgili konulardaki web sitelerini tanıtıcı yazılardır; 1 sayfayı geçemez.

5. Kitap/tez tanıtımı: Derginin yayın alanıyla ilgili konularda yayınlanmış bulunan kitapları/tezleri tanıtan yazılardır; 3 sayfayı geçemez.

III- Makalelerin Düzenlenmesi

Dergiye gönderilecek yazılar türlerine göre, başlık sayfası, İngilizce ve Türkçe özetler, ana metin, kaynaklar, tablo/şekil/resim bölümlerini içerir. Dergiye yayınlanması için gönderilen makalelerde aşağıdaki biçimsel esaslara uyulmalıdır: Yazı Microsoft Word programında Times New Roman yazı stilinde 12 punto büyüklüğünde, siyah renkte, 1,5 satır aralığında hazırlanmalıdır. Kenarlardan 2,5 cm boşluk bırakılmalıdır. Her sayfaya satır numarası eklenmelidir.

Anatomik terimler Latincede yazıldığı gibi kullanılmalıdır. Günlük tıp diline yerleşmiş terimler ise okundukları gibi Türkçe yazım kurallarına uygun olarak yazılmalıdır. İngilizce veya başka bir yabancı dildeki şekli ile yazılan terimler tırnak içinde belirtilmelidir. Yazının başlık sayfasında, yazının Türkçe ve İngilizce başlığı ve sayfa üstünde kullanılmak üzere boşluklar da dahil 40 karakteri aşmayacak şekilde Türkçe ve İngilizce kısa başlık önerisi bulunmalı. Çalışmaların yapıldığı klinik, anabilim dalı/bilim dalı, enstitü ve kuruluşun adı belirtilmelidir.

a) Başlık Sayfası: Gönderilen makalenin kategorisini, başlığını (Türkçe-İngilizce ve sadece ilk sözcüğün baş harfi büyük), yazarların adlarını (sadece baş harfleri büyük yazılır), çalıştıkları kurumları (rakamla dipnot olarak belirtilmeli), yazışmaların yapılacağı sorumlu yazarın adı, açık adresi, telefon ve faks numaraları ile e-posta adresini içermelidir. Sorumlu yazar yıldız (*) ile belirtilir. Makale daha önce bilimsel bir toplantıda sunulmuş ise toplantının adı, tarihi ve yeri belirtilerek yazılmalıdır.

b) Ana Metin Bölümü: Yazının ana metni Öz ve Anahtar Kelimeler, Giriş, Gereç ve Yöntem, Bulgular ve Tartışma başlıkları içinde düzenlenir. Özler ve anahtar sözcükler: Türkçe ve İngilizce olmak üzere iki dilde yazılır ve yazının başlığını da içerir.

Öz 200 kelimeyi geçmemeli, çalışmanın ana noktaları olan amacını, hayvan ve örnek popülasyonunu, metodunu ve önemli sonuçlarını, çalışmadan elde edilen çıkarımı klinik olarak uygulanabilirliğini içermelidir. Yayını okumadan okuyucular için anlaşılır olmalıdır ve özet içinde kaynaklara atıf yapılmamalıdır. Türkçe ve İngilizce özetler ayrı sayfalarda yazılmalı ve özetlerin sonunda her iki dilden en az 3, en çok 5 anahtar sözcük yer almalıdır. Anahtar kelimeler Index Medicus Medical Subject Headings (MeSH)'e uygun olmalıdır. Anahtar kelimeler için www.nlm.nih.gov/mesh/MBrowser.html adresine başvurulmalıdır.

Giriş bölümünde yazının dayandığı temel bilgilere ve gerekçelere kısaca değinildikten sonra, son paragrafında amaç açık bir anlatımla yer alır. Gereç ve yöntem bölümü gerekirse araştırma/hasta/denek grubu, araçlar, uygulama ve istatistik değerlendirme gibi alt başlıklara göre düzenlenebilir. Bu bölüm çalışmaya katılmayan birisinin de rahatlıkla anlayabileceği açıklıkta yazılmalıdır. Bulgular bölümü çalışmanın sonuçlarını özetler ve temel bulgular gerekirse tablo ve şekillerle desteklenir. Tartışma bölümünde çalışmanın bulguları ilgili yurt içi ve yurt dışı çalışmaların sonuçları bağlamında tartışılır; genel bir gözden geçirmeyi değil, özgün bulguların tartışılmasını içerir. Yayın sisteme yüklenirken ana metin bölümü ana dosya olarak yüklenmelidir.

c) Teşekkür: Yazarlar çalışmalarında vermek istedikleri ek bilgiler ile katkı sağlayan destekçi kurumlara ve/veya şahıslara teşekkür yazılarını bu bölümde belirtebilirler.

d) Kaynaklar: Kaynaklar listesi alfabetik sıraya göre yazılmalıdır. Sadece yayınlanmış veya yayına kabul edilmiş kaynaklar yer almalıdır. Kabul edilmiş ancak henüz yayınlanmamış kaynaklar için "baskıda" ifadesi kullanılmalıdır. Yazarlar kaynaklar listesinde bulunan bütün kaynakların metin içinde kullanılmış olduğunu kontrol etmelidirler.

Yayındaki bütün kaynaklar kullanılmalıdır. Makale içinde referans kullanma şekline örnekler.

Metin içinde doğrudan atıf yapılırken yazar veya yazarların soyadından sonra parantez içinde kaynağın yayın yılı belirtilmelidir.

Örnekler: Bell (2005) tarafından; Nielsen ve Engberg (2006) tarafından; Doyle ve ark. (2007) tarafından

Cümlenin sonunda atıf yapıldığında ise yazar ismi ve yayın yılı parantez içinde belirtilmelidir.

Örnekler: ...bildirilmiştir (Bell, 2005); ....bildirilmiştir (Nielsen ve Engberg, 2006); .....bildirilmiştir (Doyle ve ark., 2007).

Birden çok kaynağa atıf yapılması durumunda kronolojik sıralama yapılmalıdır.

Örnekler: ….bildirilmiştir (Bell, 2005; Nielsen ve Engberg, 2006; Doyle ve ark., 2007).

Aynı yazarın aynı yıl yayınları söz konusu ise her biri "a" harfinden başlayarak küçük harflerle işaretlenmelidir.

Örnek: …. (Bell, 2005a; Bell, 2005b; Bell, 2005c …). Atıf yapılırken aşırı kaynak kullanımından kaçınılmalıdır.

Kaynaklar listesinin düzenlenmesi:

Mendeley programı kullanan yazarlar aşağıda linki verilen dergi format stilini kullanarak çalışmalarını düzenleyebilir:
https://csl.mendeley.com/styles/529990351/makusagbilensderg

Kaynaklar listesinde yazar isimleri ve yayın yılı koyu harflerle yazılmalıdır. Kaynak listesi şu şekilde hazırlanmalıdır:

i) Kaynak makale ise

Yazarların soyadları ve adlarının ilk harfi yazılmalıdır. Devamında sırasıyla makalenin yayın yılı, makalenin adı, yayınlandığı derginin açık adı, cilt, sayı ve sayfa numaraları belirtilmelidir.

Örnekler:

Cohen, N.D., Vontur, C.A., Rakestraw, P.C., 2000. Risk factors for enterolithiasis among horses in Texas. Journal of the American Veterinary Medical Association 216, 1787-1794.

Rajmohan, S., Dodd, C.E., Waites, W.M., 2002. Enzymes from isolates of *Pseudomonas fluorescens* involved in food spoilage. Journal of Applied Microbiology 93, 205-213.

Ono, K., Yamamoto, K., 1999. Contamination of meat with *Campylobacter jejuni* in Saitama, Japan. International Journal of Food Microbiology 47, 211-219.

Yayınlanmak üzere kabul edilen ve DOI numarası bulunan, ancak henüz basılmamış makaleler için; makale künyesinin sonunda DOI numarası belirtilmelidir.

McGregor, B.A., Butler, K.L., 2014. The value of visual fleece assessment in addition to objective measurements in identifying Angora goats of greater clean mohair production. Small Ruminant Research, in press (DOI: 10.1016/j.smallrumres.2014.04.001).

ii) Kaynak kitap ise

Yazarların (veya editörün) soyadları ve adlarının ilk harfi yazılmalıdır. Devamında sırasıyla kitabın yayın yılı, adı, yayınevi veya yayınlayan kuruluş ve yayınlandığı yer belirtilmelidir. Kaynak, kitaptan bir bölüm ise bölüm yazarlarının isminden sonra sırasıyla kitabın yayın yılı, bölümün adı, editörün soy ismi ve adının ilk harfi, bölümün alındığı kitabın adı, yayınevi veya kuruluş, yayınlandığı yer, bölümün sayfa numaraları yazılmalıdır.

Örnekler:

Combs, G.F., 1992. The Vitamins: Fundamental Aspects in Nutrition and Health. Academic Press, San Diego.

Concannon, P.W., 1986. Physiology and Endocrinology of Cannine Pregnancy. In: Marrow, D.A. (Ed.), Current Therapy in Theriogenology. Philadelphia, W.B. Saunders Company, pp. 491-497.

Perkins, J.B., Pero, J., 2002. Vitamin biosynthesis. In: Sonenshein, A., Hoch, J., Losick, R. (Eds.), Bacillus subtilis and Its Closest Relatives: from Genes to Cells. ASM Press, Washington D.C., pp. 271-286.

Kramer, J.M., Gilbert, R.J., 1989. Bacillus cereus. In: Doyle, M.P. (Ed.), Foodborne Bacterial Pathogens. Marcel Dekker, New York, pp. 22-70.

iii) Kaynak bir tez ise

Tezi yazan kişinin soyadı ve adının ilk harfi koyu olarak yazılmalı, kabul edildiği yıl, tezin başlığı, tezin cinsi (yüksek lisans veya doktora), üniversitesi ve enstitüsü belirtilmelidir.

Örnek:

Bacınoğlu, S., 2002. Boğa spermasında farklı eritme süreleri ve eritme sonrasında oluşturulan soğuk şoklarının spermatolojik özelliklere etkisi. Doktora Tezi, İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü, İstanbul.

iv) Kaynak internette bulunan bir web sitesi ise

Yazarların soyadları ve adının ilk harfi (Yazar adı yoksa web sitesinin veya kaynağın adı) yazılır. Daha sonra sırasıyla yılı, makalenin adı, varsa yayıncı, internet adresi ve erişim tarihi belirtilir.

Örnekler:

FDA, 2001. Effect of the use of antimicrobials in food-producing animals on pathogen load. Systematic review of the published literature. http://www.fda.gov/cvm/antimicrobial/PathRpt.pdf (Erişim 14.12.2001)

Cleveland, C.W., Peterson, D.S., Latimer, K.S., 2005. An Overview of Canine Babesiosis. Clinical Pathology. College of Veterinary Medicine, The University of Georgia: http://www.vet.uga.edu/vpp/clerk/Cleveland (Erişim 17.12.2005).

Thierry, F., 2006. Contagious equine metritis: a review. Equine Reproductive Infections: http://www.equinereproinfections.com (Erişim 07.07.2006].

FSAI, 2008. Report of the Implementation Group on Folic Acid Food Fortification to the Department of Health and Children. Food Safety Authority of Ireland: http://www.fsai.ie/assets/0/86/204/cc3c2261-7dc8-4225-bf79-9a47fbc2287b.pdf (Erişim 20.06.2008)

v) Kaynak bilimsel toplantıda sunulmuş bir bildiri ise

Yazarların soyadı ve adının baş harfinden sonra sırasıyla toplantının yılı, bildirinin başlığı, toplantının adı, toplantı yeri, bildiri kitabındaki sayfa no yazılmalıdır.

Örnekler:

Cardinali, R., Rebollar, P.G., Mugnai, C., Dal Bosco, A., Cuadrado, M., Castellini, C., 2008. Pasture availability and genotype effects in rabbits: 2. development of gastro-intestinal tract and immune function of the vermiphorm appendix. In: Proc. 9th World Rabbit Congress, Verona, Italy, 1159-1164.

Mauget, R., Legendre, X., Comizzoli, P., 1998. Assisted reproductive technology in sika deer: a program to preserve endangered deer subspecies. In: Proc. 4th Int. Deer Biology Congress, Kaspovar, 185-186.

e) Tablolar: Kullanım sırasına göre numaralandırılmalı, kısa başlıklarla ifade edilmeli ve metin içinde tablo numarası verilerek (örneğin Tablo 1) atıfta bulunulmalıdır. Tablo başlıkları tablonun üst bölümüne yazılmalıdır. Tabloda kullanılan kısaltmalar ve gerekli açıklamalar tablo altında verilmelidir.

f) Şekil ve Resimler: Metinde kullanılan fotoğraflar, grafikler ve çizimler metin içinde şekil adı ile kullanılmalıdır. Şekiller kullanım sırasına göre numaralandırmalı ve kısa başlıklarla ifade edilmeli, metin içinde şekil numarası verilerek (örneğin Şekil 1) atıfta bulunulmalıdır. Şekil başlıkları şekillerin altında yer almalıdır. Şekillerde istenilen noktaya dikkat çekmek amacıyla; üzerlerine işaret konulmalı ve başlıklardan sonra yer alacak olan şekil altı notta kullanılan işaretler belirtilerek gerekli açıklamalar yapılmalıdır.

IV- Makale Süreci (Kör hakemlik)

Makale başvurusu yalnızca online olarak http://dergipark.gov.tr/maeusabed adresi üzerinden kabul edilmektedir. Sorumlu yazar, makale ile birlikte göndereceği tüm dosyaları yukarıdaki internet adresinde bulunan yeni makale gönder ikonunu tıklayarak sisteme ekleyebilir. Yazarlar dergiye gönderi yapmadan önce kayıt olmalıdır. Kaydolduktan sonra, ana sayfadaki Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi ikonuna tıklayarak; yazım kurallarına göre düzenlenmiş bilimsel çalışmayı dergi panelindeki Makale Gönder kısmından 4 basamaklı (başlarken, yükleme, kaynaklar, önizleme&gönder) gönderi işlemini yapabilir. Gönderilen makalede ön değerlendirme aşaması sırasında yazar künyeleri, çalışmanın yapıldığı kurum, etik kurul ya da özel izin adres bilgileri gibi tanıtıcı bilgiler içermemelidir. Ön değerlendirmeden (bilimsel nitelik, dil, yazım kuralları kontrolü, İntihal kontrolü iThenticate ve Turnitin programı,) geçen bilimsel çalışmaların hakem ataması yapılır. Sorumlu yazar makalenin hangi aşamada olduğunu sistem panelindeki Süreçteki Makaleler kısmından takip edebilir. Atanan hakemlere, kör hakemlik kuralları çerçevesinde çalışmanın tam metni, şekil, tablo, grafik ve resimleri sistem üzerinden yüklenerek e-posta aracılığıyla makale değerlendirme talebi gönderilir. Hakemler e-posta aracılığıyla gönderilen linke tıklayarak talebi kabul ya da reddederler. Kabul eden hakemler, kararlarını sistem üzerinden en fazla 1 ay içinde sebeplerle birlikte yüklemelidirler. Hakemin önerdiği düzeltme var ise tekrar yazara gönderilir. İstenilen düzeltmeler 1 ay içinde tamamlanıp gönderilmediği takdirde makale otomatik olarak iptal edilecektir. Editör, makalelerin yayın değerliliği ve hakemlerin görüşlerine dayanarak yayına kabul veya red kararını verir. İstenilen düzeltmeler yapıldıktan sonra makale yazar tarafından sisteme tekrar yüklenir. Derginin gizlilik bildiriminde belirtildiği gibi, yazarların kimlik bilgileri ve e-posta adresleri hiçbir şekilde başka amaçlar için kullanılmayacaktır.

Bu dergi; bilimsel araştırmaları halka ücretsiz sunmanın bilginin küresel paylaşımını artıracağı ilkesini benimseyerek, içeriğine anında açık erişim sağlamaktadır.

Mehmet Akif Ersoy University Journal of Health Sciences Institute
INSTRUCTIONS TO AUTHORS

I- Mehmet Akif Ersoy University Journal of Health Sciences Institute General Information

Mehmet Akif Ersoy University Journal of Health Sciences Intitute (MAKU J. Health Sci. Inst.) is the publication of Mehmet Akif Ersoy University Health Sciences Institute. It is published two times annualy. The journal is a peer-reviewed scientific journal in which basic and clinical scientific articles in the field of medical sciences (veterinary, medicine, dentistry, nursing and sports sciences) are published. The language of the journal is English. Papers submitted to the journal should not have been previously published, accepted for publication or be in the process of evaluation for publication in any other journal. This rule does not apply to articles presented as bulletins in scientific meetings and whose summaries are published. In such cases, however, the name, date and place of the meeting in which the paper was presented should be notified. The format of the article should be in accordance with the rules of "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http:/www.icmje.org/)".

On receipt of the paper by the Editorial Board, the paper is evaluated for compliance with the format rules and the authors are informed about the result in four weeks. In the event that the paper is not found to comply with the general publication principles of the journal from the standpoint of either technical characteristics or general scope, the paper is rejected. Alternatively, the author(s) may be asked to re-submit the paper in accordance with the writing requirements. Papers resubmitted are passed through a similar technical examination and, if found to comply with the rules, are passed on for peer review. The paper is sent, without the title, to two reviewers selected by the board, who then assess the paper for scientific content and format compliance. When necessary the Editorial Advisory Board can send the paper to third reviewers. The selection of reviewers is ultimately at the discretion of the editor, associate Editors and/or the editorial board. The appropriate reviewers can be selected from journal's international database of reviewers listing or, if needed; independent reviewers can be determined from inland or abroad. Thereafter the Editorial Advisory Board carries out the final editing, taking the reports of the reviewers into consideration, and, when necessary, communicating with the author(s).

The Editor gives the final decision about the acceptance of the manuscript. The Editorial Board is authorized to publish the paper, return it for correction, or reject it. The assessment process involves research articles, case reports and original articles submitted to the journal. Other types of articles are evaluated directly by the Board. Papers submitted to the journal will not be returned whether they are published or not. The Editor and the Editorial Board have the right to reject, to require additional revision or to revise the format of manuscripts which do not follow the rules. The authors should inform the editorial board if they decide to withdraw the manuscript. The editor may consult editorial executive board about a manuscript if (s) he deems necessary. All the authors should submit a collectively signed statement that there is no conflict of interest regarding scientific contribution or responsibility. The association, establishment, and medication-material supply firms which have given financial, even partial, or material support to the research should be mentioned in a footnote. No fee or compensation will be paid for articles published in the journal.

The Editorial Board assumes that the author(s) are obliged not to submit the paper to another journal before completion of the assessment process. In the "method" section of articles concerned with experimental research on humans or animals, a sentence showing that the informed consent of patients and volunteers has been obtained following a detailed explanation of the interventions carried out on them. In such studies, authors should clearly state the compliance with internationally accepted guidelines (1975 Helsinki declaration revised in 2002 http://www.wma.net/e/policy/b3.htm, Guide for the care and use of laboratory animals-www.nap.edu/catalog/5140.html) issued by the Republic of Turkey Ministry of Health and published in the Official Journal dated 29 January 1993 number 21480 "Regulations Concerning Drug Research", and other more recently published rules laid out in governing statutes. They should forward a copy of the Ethic Committee Approval received from the relevant institution. Standard abbreviations used in the text are written in full when first mentioned. In the use of drugs, the generic names should be written in their Turkish pronunciation spelling

form. Measurement units are given according to the metric system; e.g. written as “mg”, no punctuation is used, in the case of extensions (,,) is used as a separator. Laboratory measurements are reported in International System Units (US; Systeme Internationale; SI).

Scientific responsibility

All scientific responsibility of the articles belongs to the authors. The authors of the submitted article must have a specific contribution to the work. Authors' name ordering should be a joint decision. Corresponding author is considered to accept the author sorting by filling in "Author Responsibility and Publication Transfer Form" on behalf of all authors. All of the authors should be listed under the title of article.

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The authors are responsible for their compliance with the ethical rules. In experimental studies on animals, it should be noted that the study protocol has been approved by the animal experiment ethics committee at the institution where the study was conducted. Authors should submit the ethics committee's approval with the article. If there are previously published text, tables, pictures, etc. in the article, the authors have to get written permission from the copyright holder and the authors should specify and indicate the used material in the manuscript. In the course of the manuscript evaluation, the authors may be requested to submit the research data and / or the ethics committee approval document if deemed necessary.

Plagiarism policy

Manuscripts submitted to Mehmet Akif Ersoy University Journal of Health Sciences Institute is evaluated in terms of plagiarism. Every submitted article is checked for plagiarism through iThenticate and Turnitin software. When Smilarity Index of the article is above %20, it is sent back to the corresponding author to revise it. If plagiarism is proved after publication of the article, that article will be immediately removed from the website and the concerned authors will be considered ineligible for publication of their articles in Mehmet Akif Ersoy University Journal of Health Sciences Institute.

II- Types and Characteristics of Papers to be Submitted to the Journal

a) Research Articles: These articles are prepared in full accordance with the writing style definitions given below, in which previously unpublished original research data are evaluated. The main text section of the research articles should include (Title, Introduction Materials and Methods, Results, Discussion and Conclusion) sections and (excluding title page, bibliography, tables/figures/pictures) should not exceed 20 pages. If some parts of the research data given in these articles have previously been discussed in another paper, this must be notified without fail when sending the paper and, in addition, reference should be made to the relevant paper within the bibliography.

b) Review Articles: Review Articles should cover subjects falling within the scope of the journal which are of active current interest. They may be submitted or invited. Invited reviews will normally be solicited by the Review's Editor, but suggestions for appropriate review topics may be sent to editor.

c) Case Reports: These are articles which present and discuss the characteristics of one or more cases which have special features and scientific importance from the clinical evaluation, observation or other standpoint. Case presentations include the title page, summary, main text (includes introduction, case and discussion), bibliography,

table/figure/picture sections; subtitles in the main text are organised according to the text content. Abstracts of the case presentations should have 150 words. The main text (excluding title page, bibliography, table/figure/picture) should not exceed 10 pages.

d) Brief Reports: These are articles in which original ideas dealing with important theoretical or practical problems related to a specific subject are presented and discussed. Original articles include a title page, summary,

main text, bibliography, table/figure/picture sections; subtitles in the main text are organised according to the text content. The main text of original articles (excluding title page, bibliography, table/figure/picture) should not exceed 10 pages.

e) Special Sections:

1. Letters to the Editor: These articles include evaluation and criticisms of articles published in the journal. These are published together with the responses of the author(s) of the paper concerned where possible. Letters to the Editor may not exceed 5 pages.

2. Meeting news/notes: These articles introduce scientific meetings held or to be held on subjects within the scope of the journal. The paper may not exceed 1 page.

3. Journal news: These articles introduce scientific journals being published within the scope of the journal. The paper may not exceed 1 page.

4. Introduction of websites: These articles introduce websites relevant to the scope of the journal. These articles may not exceed 1 page.

5. Book/Thesis Section: These articles introduce books/theses published on subjects related to the scope of the journal and may not exceed 3 pages.

III- Preparation of Manuscripts

Papers to be submitted to the journal include the sections of title page, abstract, main text, references and tables/figures/pictures. Articles submitted for publication in the journal should follow the following formal principles: The text should be prepared in Microsoft Word program in Times New Roman font style with a font size of 12 font, black and 1.5 line. All side of the paper, page margins should be as 2.5 cm. Line numbers should be added to the beginning of the page.

Anatomical terms should be used as written in Latin. Running title (not exceed 40 characters) of the manuscript should add to title page. The name of the clinic, department / science, institute and institution should be stated.

a) Title Page: should contain the category, the title (only first letter capital), the names of the authors (only the first letters capital), the institution (s) where they work (indicated with numbered footnotes), corresponding author (address, phone, fax numbers and e-mail address). Corresponding author is indicated by an asterisk (*). If the article was previously presented at a scientific meeting, the name, date and place of the meeting must be stated.

b) Main Text: The main text of the paper is organised under the subtitles of Abstract and Keywords, Introduction, Materials and Methods, Results and Discussion.

Abstract and Keywords: This is written in two languages, Turkish and English, and also includes the title of the paper. The abstract is consists of 200 words. The abstract should bring out the main points of the manuscript and should include the following information: objective, the animals or sample population involved, design, the materials and methods used, the main results, a brief conclusion and clinical relevance, where applicable. They should be comprehensible to readers before they have read the paper, and abbreviations and reference citations should be avoided. At the end of the abstract, at least 3, at most 5 keywords in both languages are included.

In the introduction, following a brief statement of basic information and justifications which constitute the basis of the paper, the objective is clearly given in the last paragraph. If necessary, the "method" section may be organised according to sub-titles such as research/patient/ test group, instruments, application and statistical analysis. This section should be written with clarity so that a person not involved in the study may easily understand. Results summarize the findings of the study and, when necessary, basic findings are supported with tables and figures. In the discussion section, the findings of the study are discussed in the light of relevant national and international studies; this section includes discussion of original findings, not a general review.

c) Acknowledgements: When considered necessary, author(s) may add brief acknowledgements in a few sentences to those whose contributions to the paper are not at author level but deserve to be mentioned. Here, the contributions of those acknowledged (e.g. financial or equipment aid, technical support etc) are clearly stated (e.g. "scientific counseling", "editing of the draft", "data collection", "participation in clinical research" etc).

d) Bibliographic References:

All citations in the text should refer to: the year of publication of the reference should be indicated in parentheses after the surname of the author or authors.

Examples: Bell (2005), Nielsen and Engberg (2006), Doyle et al. (2007) were indicated that.....

The name of the author and the year of publication should be stated in parentheses at the end of the sentence.

Examples: ...were detected as 23% of the samples (Bell, 2005); ....were detected as 23% of the samples (Nielsen and Engberg, 2006); ...were detected as 23% of the samples (Doyle et al., 2007).

In case of more than one reference, references should be arranged chronologically.

Examples: ....were reported that... (Bell, 2005; Nielsen and Engberg, 2006; Doyle et al., 2007).

More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

Examples: (Bell, 2005a; Bell, 2005b; Bell, 2005c …)

The authors can use below formatted style link in mendeley:

http://csl.mendeley.com/styles/529990351/sagbilensderg

References should be written in alphabetical order. Reference style, the authors' names and year of publication should be written in bold. Source list should be prepared as follows:

i) Examples of journal articles:

Cohen, N.D., Vontur, C.A., Rakestraw, P.C., 2000. Risk factors for enterolithiasis among horses in Texas. Journal of the American Veterinary Medical Association 216, 1787-1794.

Rajmohan, S., Dodd, C.E., Waites, W.M., 2002. Enzymes from isolates of *Pseudomonas fluorescens* involved in food spoilage. Journal of Applied Microbiology 93, 205-213.

Ono, K., Yamamoto, K., 1999. Contamination of meat with *Campylobacter jejuni* in Saitama, Japan. International Journal of Food Microbiology 47, 211-219.

For articles that are accepted for publication and have a DOI number but not yet published; DOI number must be specified at the end of the article.

McGregor, B.A., Butler, K.L., 2014. The value of visual fleece assessment in addition to objective measurements in identifying Angora goats of greater clean mohair production. Small Ruminant Research, in press (DOI: 10.1016/j.smallrumres.2014.04.001).

ii) Books:

Combs, G.F., 1992. The Vitamins: Fundamental Aspects in Nutrition and Health. Academic Press, San Diego.

Concannon, P.W., 1986. Physiology and Endocrinology of Cannine Pregnancy. In: Marrow, D.A. (Ed.), Current Therapy in Theriogenology. Philadelphia, W.B. Saunders Company, pp. 491-497.

Perkins J.B., Pero, J., 2002. Vitamin biosynthesis. In: Sonenshein, A., Hoch, J., Losick, R. (Eds.), Bacillus subtilis and Its Closest Relatives: from Genes to Cells. ASM Press, Washington D.C., pp. 271-286.

Kramer, J.M., Gilbert, R.J., 1989. Bacillus cereus. In: Doyle, M.P. (Ed.), Foodborne Bacterial Pathogens. Marcel Dekker, New York, pp. 22-70.

iii) Thesis:

Bacınoğlu, S., 2002. Boğa spermasında farklı eritme süreleri ve eritme sonrasında oluşturulan soğuk şoklarının spermatolojik özelliklere etkisi. Doktora Tezi, İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü, İstanbul.

iv) Web site or author is an institution:

FDA, 2001. Effect of the use of antimicrobials in food-producing animals on pathogen load. Systematic review of the published literature. http://www.fda.gov/cvm/antimicrobial/PathRpt.pdf (Accessed: 14.12.2001)

Cleveland, C.W., Peterson, D.S., Latimer, K.S., 2005. An Overview of Canine Babesiosis. Clinical Pathology. College of Veterinary Medicine, The University of Georgia: http://www.vet.uga.edu/vpp/clerk/Cleveland (Accessed: 17.12.2005).

Thierry, F., 2006. Contagious equine metritis: a review. Equine Reproductive Infections: http://www.equinereproinfections.com (Accessed: 07.07.2006).

FSAI, 2008. Report of the Implementation Group on Folic Acid Food Fortification to the Department of Health and Children. Food Safety Authority of Ireland:http://www.fsai.ie/assets/0/86/204/cc3c2261-7dc8-4225-bf79-9a47fbc2287b.pdf (Accessed: 20.06.2008).

v) Paper presented at a scientific meeting

Cardinali, R., Rebollar, P.G., Mugnai, C., Dal Bosco, A., Cuadrado, M., Castellini, C., 2008. Pasture availability and genotype effects in rabbits: 2. development of gastro-intestinal tract and immune function of the vermiphorm appendix. In: Proc. 9th World Rabbit Congress, Verona, Italy, 1159-1164.

Mauget, R., Legendre, X., Comizzoli, P., 1998. Assisted reproductive technology in sika deer: a program to preserve endangered deer subspecies. In: Proc. 4th Int. Deer Biology Congress, Kaspovar, 185-186.

e) Tables: Each table is printed on a separate page and numbered according to the sequence of referral within the text (Table 1). Each table has a title and, when necessary, explanations are given under the table (e.g. abbreviations given in the table). Each table should be understandable without need for referral to the text. Each table should be referred to in the text..

f) Figures and Pictures: Figures should be numbered according to the order of use and should be expressed with short titles.Figures should be numbered in the text (Figure 1). Letters, numbers and symbols within the figure should be clear and readable when downsized for printing.Each figure should be referred to in the text..

IV- Submission of Articles (Blind Peer-Review)

The article submission is only accepted online via 'http://dergipark.gov.tr/maeusabed' The Corresponding authors, all the files can be added to the system by clicking the submit new article icon at the above address. Authors must register on Dergipark system before submitting a manuscript. After signing up, clicking Mehmet Akif Ersoy University Journal of Health Sciences icons on the main page, the manuscript written according to the guide for authors is submitted in 4 steps (start, submission, reference, preview & submit). The submitted manuscript must not contain any identifying information, such as author information, institution, ethics committee or special permit address, during the preliminary evaluation phase. The manuscript that pass the preliminary evaluation (paper scientific qualification, language, conformity to Guide for author and checking plagiarism via

iThenticate and Turnitin program,) are assigned to the Reviewers. The corresponding author can follow the article evaluation process from the section on the Articles in the Process. According to the blind peer-review rules, the main text, tables, graphics and pictures of the manuscript are uploaded via the system and sent to the appointed reviewers for an article evaluation request via e-mail. The reviewers accept or reject the request by clicking on the link sent via e-mail. The reviewers who accept it have to upload their decisions together with the reasons within a maximum of 1 month via the system. If the correction requested by the Reviewer is sent back to the author. If the requested corrections are not completed within 1 month, the article will be automatically canceled. After the desired corrections are made, the article is uploaded back to the system by the author. The editor makes decisions to accept or reject papers based on their opinion of the papers' publication worthiness and reviewers' comments. As stated in the privacy statement, authors' identity information and e-mail addresses will not be used for any other purpose.

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Olgu Sunumları / Case Reports

MAKU J. Health Sci. Inst. 2024, 12(1): 1-14.
doi: 10.24998/maeusabed.1392677

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http://dergipark.gov.tr/maeusabed

Researh Article / Araştırma Makalesi

Prevalence and Pattern of Antibiotic Susceptibility of Gram-negative Bacteria Isolated from Pediatric Blood Culture

Pediatrik Kan Kültüründen İzole Edilen Gram Negatif Bakterilerin Prevalansı ve Antibiyotik Duyarlılık Paterni

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Abstract: It was aimed to evaluate the antibiotic susceptibilities of Gram-negative bacteria isolated from blood samples taken from pediatric patients. The samples were evaluated with the Bactec 9120 automation system bacteria were identified by the Gram-Negative ID panel using the Vitek 2 Compact (Biomerieux France) device performed with the AST N090 panel, and the results were evaluated according to The Clinical and Laboratory Standards Institute (CLSI) recommendations. Antibiotic resistance results: Ceftriaxone was the most resistant antibiotic (71.4%). *Salmonella spp*. it was mostly resistant to levofloxacin and ciprofloxacin (100%). While *E. coli* strains were the most resistant to ticarcillin and piperacillin (71.4%), the most effective antibiotics against this bacterium were imipenem and meropenem (100%). Resistance rates to all tested antibiotics were significantly higher in ESBL-producing *Klebsiella spp* and *E coli* strains than in non-ESBL-producing strains ($p<0.05$). Considering this information, it is vital to evaluate the current resistance profiles in the application of empirical treatment in premature and newborn patients.

Keywords: Child , Blood culture, Gram-negative, Antibiotic resistance, Vitek 2..

Öz: Pediatrik hastalardan alınan kan örneklerinden izole edilen Gram negatif bakterilerin antibiyotik duyarlılıklarının değerlendirilmesi amaçlandı. Örnekler Bactec 9120 otomasyon sistemi ile değerlendirildi. AST N090 paneli ile gerçekleştirilen Vitek 2 Compact (Biomerieux Fransa) cihazı kullanılarak Gram-Negatif ID paneli ile bakteriler tanımlandı ve sonuçlar Klinik ve Laboratuvar Standartları Enstitüsü (CLSI) tavsiyelerine göre değerlendirildi. Antibiyotik direnci sonuçları: Seftriakson en dirençli antibiyotik (%71,4) oldu. *Salmonella spp*. çoğunlukla levofloksasin ve siprofloksasine (%100) dirençliydi. *E. coli* suşları tikarsilin ve piperasilin'e en dirençli (%71,4) iken, bu bakteriye karşı en etkili antibiyotikler imipenem ve meropenem (%100) oldu. Test edilen tüm antibiyotiklere karşı direnç oranları, ESBL üreten *Klebsiella spp* ve *E coli* suşlarında, ESBL üretmeyen suşlara göre anlamlı derecede yüksekti ($p<0,05$). Bu bilgiler göz önüne alındığında prematüre ve yenidoğan hastalarda ampirik tedavinin uygulanmasında mevcut direnç profillerinin değerlendirilmesi hayati önem taşımaktadır.

Anahtar Kelimeler: Çocuk, Kan kültürü, Gram negatif, Antibiyotik direnci, Vitek 2..

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Introduction

Increasing antimicrobial resistance in bacteria continues to be an important health problem in our country as well as all over the world. Accordingly, in addition to the increase in mortality and morbidity, the increase in the cost of treatment is also growing day by day. Gram Negative Bacteria (GNB) are especially important in nosocomial infections, and these bacteria are often isolated from community-acquired infections (Jain et al., 2021). With the spread of broad-spectrum antibiotics in recent years, the development of antibiotic resistance has increased and this resistance is transferred between bacterial species through genes. Therefore, the choice of antibiotics is important. Antibiotic resistance follow-up should be done regularly in the relevant

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center to determine the ideal treatment option. In empirical antibiotic selection, the change in antibiotic resistance patterns should be evaluated locally (He et al., 2019; Meng et al., 2022). The results of antibiotic susceptibility may vary from region to region, from hospital to hospital, and even between units of the same hospital. In addition, the rates change over the years according to the principles of antibiotic use. Therefore, regional antibiotic resistance patterns should be determined by performing susceptibility tests at regular intervals (Prestinaci et al, 2015). Gram-negative bacteria are one of the most important causes of hospital and community-acquired infections. Enterobacteriaceae (*Escherichia coli, Citrobacter, Klebsiella, Serratia, Proteus, Morganella, Providencia, and Enterobacter species, Pseudomonas aeruginosa, Acinetobacter* species, *Stenotrophomonas maltophilia*) are gram-negative nosocomial agents commonly encountered in children (Gajdács et al., 2020). Most infections caused by these organisms occur in neonatal and pediatric intensive care unit patients. Underlying diseases such as malignancy, immunosuppressive diseases, burns, prematurity, intravascular and/or central nervous system catheter, mechanical ventilation, and urinary catheterization are the main risk factors for developing these organism infections. Due to multidrug resistance among GNB, the number of antibiotics that can be used in treatment is gradually decreasing, the development of resistance sometimes creates problems during treatment, and almost incurable infections occur (Atay et al., 2019; de Oliveira Costa et al., 2015).

This study, aimed to evaluate antibiotic sensitivity against Gram-negative bacteria isolated from blood samples.

Materials and Methods

Study criteria

Blood samples taken from pediatric patients hospitalized in Diyarbakır Children's Hospital were analyzed. Study criteria; it was determined that the isolates grew easily on media such as blood agar and EMB, were Gram-negative and did not have colonization, contamination, or relapse disease.

Reproductive and Results Evaluation

Blood culture bottles [BACTECTM PLUS+ Aerobic/F and BACTECTM PEDS PLUS/F blood culture bottles (aerobic and pediatric bottles)] taken from the clinics were placed in the BACTEC 9120 automatic system. After the bottles with positive signals were removed from the device, they have inoculated on blood agar and EMB (Eosin Methylene Blue) media. All media were evaluated after incubation at 35°C for 18-24 hours. Colony morphology and reproductive characteristics were examined. Gram staining was done. To identify these bacteria and ensure antibiotic sensitivity, 3.0 ml of saline was first transferred from the dispenser to the tubes. Similar colonies were selected from fresh plates (medium) and suspended in ID (Identification) tubes. ID tubes were mixed with vortex and left in the Mcfarland device Those of the suspended ID tubes adjusted according to Mcfarland 0.5-0.63 were placed in the cassette and pipetted 145 µl from the ID tube to the AST (Antibiotic Susceptibility Test) tube. Then, the ID and AST cards were placed in the prepared tubes, and the cassette was identified with the Gram-negative ID panel in the Vitek 2 Compact (Biomerieux France) device in accordance with the manufacturer's instructions, and antibiotic susceptibility was tested with the AST N090 panel. Then, antibiotic susceptibility results in accordance with CLSI (Clinical and Laboratory Standards Institute) criteria were recorded using Vitek 2 device software with different options. These data were transferred to SPSS Statistics 17.0 program and evaluated statistically.

Data analysis

The data obtained in this study were expressed as frequencies and percentages, and statistical analyzes of the data were used to compare the difference in antibiotic susceptibility between

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ESBL-positive and ESBL-negative and other resistant strains, Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS Inc., Chicago). IL, USA) using the $\chi 2$ test. The level of significance was accepted as $p<0.05$ in all statistical analyses.

Ethical consideration

This study received approval from the non-invasive research ethics committee (Date: 03.10.2022, Decision No: HRU/22.19.34, Session No: 19). Consent forms were obtained from the relatives of the patients included in the study it was carried out at Diyarbakır Children's Hospital.

Results

In the study, 23 *Klebsiella spp*., 21 *Acinetobacter spp*., 15 *Salmonella spp*., 14 *E. coli*, 8 *Enterobacter spp*.,6 *Sphingomonas spp*., 4 *Pseudomonas spp*., 3 *Serratia spp*., 3 *Burkholderia spp*., 2 *Stenotrophomonas maltophilia*, 1 Proteus mirabilis, and 1 Pantoea agglomerans, a total of 101 strains were analyzed. Distribution of these bacteria according to clinics and other demographic information is given in Table 1.

Table 1: Distribution of bacteria by clinics

CLINICS	PİC	GİC	HEM	PED	İNT	NN	OC	EME	ONC.	TOTAL
BACTERIA										
Klebsiella spp.	4	3	1	8	1	4	1	0	1	**23**
Acinetobacter spp.	13	0	0	3	2	1	1	1	0	**21**
Salmonella spp.	0	0	2	3	3	0	7	0	0	**15**
E. coli	4	2	0	3	2	3	0	0	0	**14**
Serratia spp.	1	0	0	0	0	2	0	0	0	**3**
E. cloacae	1	0	0	1	1	4	1	0	0	**8**
S. paucimobilis	0	0	0	1	0	3	2	0	0	**6**
Burkholderia spp.	0	0	0	2	1	0	0	0	0	**3**
Pseudomonas spp.	2	0	0	0	1	0	0	0	1	**4**
S. maltophilia	1	1	0	0	0	0	0	0	0	**2**
Proteus mirabilis	0	1	0	0	0	0	0	0	0	**1**
Pantoea agglomerans	0	0	0	0	0	1	0	0	0	**1**
TOTAL (n / %)	**26/25,8**	**7/6,9**	**3/2,9**	**21/20,8**	**11/10,9**	**18/17,9**	**12/11,8**	**1**	**2**	**101/100**

PIC: Premature Intensive Care, **GIC:** General Intensive Care, **HEM:** Hematology, **PED:** Pediatrics, **INT:** Intania (İnfection), **NN:** Neonatal, **OC:** Older Child, **EME:** Emergency**, ONC:** Oncology, **T:** Total.

In our study, 26 (25.8%) isolates were from the premature intensive care unit, 21 (20.8%) from pediatric clinics, 18 (17.9%) from the neonatal service, and 12 (11.8%) from the old children's service. 11 (10.9%) were recruited from the infection service, 7 (6.6%) from the general intensive care service, 3 (2.9%) from the hematology service, 2 (2%) from the oncology service, and 1 from the emergency Table 2. 12 (11.9%) girls and 39 (38.6%) boys, totally 51 (50.5%) of our patients whose blood cultures were taken are 0-3 months old, 9 (8.9%) A total of 32 (31.7%) 4-60 months old, 5 (4.9%) girls, 4 (4%) boys, 23 girls (22.8%) boys 9 (8.9%) were in the 5-10 age group, 5 (4.9%) girls, 4 (4%) boys, a total of 9 (8.9%) 11-18 in the age group.

Klebsiella spp. when the susceptibilities of the strains to antibiotics were examined, resistance developed against Cefepime, Ceftriaxone, and Ceftazidime at a rate of 56.5%, except Ticarcillin and Piperacillin, which were naturally resistant (100%). No resistance developed against Colistin, Tigecycline, Amikacin, Meropenem, Imipenem. Of the 23 examined Klebsiella spp. 13 of the strains were found to be ESBL positive. When the antibiotic resistance patterns of ESBL positive and ESBL negative *Klebsiella spp* strains were examined, it was

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seen that ESBL negative Klebsiella strains were naturally resistant to all antibiotics except Ticarcillin and Piperacillin. ESBL-positive *Klebsiella* strains were found to be resistant to Ampicillin/Sulbactam with the highest rate of 61.5% Table 3.

Table 2: Distribution of bacteria by age/gender characteristics.

	AGE/GENDER								
BACTERIA	**0-3 Month**		**4-60 Month**		**5-10 Years**		**11-18 Years**		**TOTAL/ (%)**
	K	E	K	E	K	E	K	E	
Klebsiella spp.	3	10	3	5	1	-	1	-	23 / 22,7
Acinetobacter spp.	4	12	2	3	-	-	-	-	21 / 20,8
Salmonella spp.	-	-	-	3	2	3	4	3	15 / 14,8
E. coli	2	5	4	3	-	-	-	-	14 / 13,9
Serratia spp.	-	2	-	1	-	-	-	-	3 / 3
Enterobacter cloacae	-	5	-	2	1	-	-	-	8 / 7,9
Sphingomonas paucimobilis	1	2	-	1	1	1	-	-	6 / 5,9
Burkholderia spp.	-	-	-	3	-	-	-	-	3 / 3
Pseudomonas spp.	1	1	-	1	-	-	-	1	4 / 4
Stenotrophomonas maltophilia	1	1	-	-	-	-	-	-	2 / 2
Proteus mirabilis	-	-	-	1	-	-	-	-	1 / 1
Pantoea agglomerans	-	1	-	-	-	-	-	-	1 / 1
TOTAL (n / %)	12	39	9	23	5	4	5	4	101 /100

Acinetobacter spp. When the susceptibility of the strains to antibiotics is examined, the most resistant antibiotic is CRO with 71.4%. CL, TGC, and CN seem to be the least resistant antibiotics with 4.8% Table 4.

Salmonella spp. when we look at the susceptibility of the strains to antibiotics, it is seen that they are 100% resistant to LEV and CIP, 2 (13.3%) strains are resistant to TC and PIP, and there is no resistance in all the remaining strains. In ESBL-producing Klebsiella spp strains, resistance rates against all tested antibiotics were found to be significantly higher than in non-Klebsiella spp-producing strains ($p<0.05$). (Table 4). When we look at the susceptibility of *Enterobacter cloacea* strains to antibiotics, they are naturally resistant (100%) and resistant to 25% CPZ/SUL PIP, TC, CRO, and CAZ except for TE, SAM, CIP, LEV, IPN, TOB, CN, AK, MEM and there is no resistance against FEP Table 4.

Considering the antibiotic susceptibility of *E. coli* strains, it is seen that the highest resistance against TK and PIP is 71.4%, followed by CAZ with 64.3%. It is seen that the least resistant strains are against LEV, CL, CIP, and TOB with 7.1%, while there is no resistance against AK, TGC, MEM, and IPN. Antibiotic susceptibility of ESBL-positive *E. coli* strains was investigated. It has been determined that it is resistant to TK and PIP at most 100%. Then 87.5% SAM and 50% SXT and TE were resistant. When the susceptibility of ESBL-negative *E. coli* strains to antibiotics was examined, it was found that the highest rate was 33.3% resistant to TC, PIP, and TE. In ESBL-producing *E. coli* strains, resistance rates against all tested antibiotics were found to be significantly higher than in non-ESBL-producing strains ($p<0.05$) Table 5.

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Tablo 3. *Klebsiella spp.,* Resistance rates of *Klebsiella* ESBL positive*, Klebsiella* ESBL Negative strains to various antibiotics.

Klebsiella spp							**ESBL positive** ***Klebsiella spp***						**ESBL negative** ***Klebsiella spp***					
Antibiotic	S		I		R		S		I		R		S		I		R	
	n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
TK	0	0	0	0	23	100*	0	0	0	0	13	100*	0	0	0	0	10	100*
PIP	0	0	0	0	23	100*	0	0	0	0	13	100*	0	0	0	0	10	100*
SXT	16	69,6	0	0	7	30,4	6	46,2	0	0	7	53,8	10	100	0	0	0	0
CL	23	100	0	0	0	0	13	100	0	0	0	0	10	100	0	0	0	0
TGC	23	100	0	0	0	0	13	100	0	0	0	0	10	100	0	0	0	0
TE	21	91,3	0	0	2	8,7	11	84,6	0	0	2	15,4	10	100	0	0	0	0
LEV	22	95,7	0	0	1	4,3	11	84,6	0	0	2	15,4	10	100	0	0	0	0
CIP	22	95,7	0	0	1	4,3	11	84,6	0	0	2	15,4	10	100	0	0	0	0
TOP	18	78,3	1	4,3	4	17,4	8	61,5	1	7,7	4	30,8	10	100	0	0	0	0
GN	19	82,6	0	0	4	17,4	9	69,2	0	0	4	30,8	10	100	0	0	0	0
AK	20	87	3	13	0	0	10	76,9	3	23,1	0	0	10	100	0	0	0	0
MEM	23	100	0	0	0	0	13	100	0	0	0	0	10	100	0	0	0	0
İPN	23	100	0	0	0	0	13	100	0	0	0	0	10	100	0	0	0	0
FEP	10	43,5	0	0	13	56,5	0	0	0	0	13	100	10	100	0	0	0	0
CPZ/SUL	18	78,3	1	4,3	4	17,4	9	69,2	2	15,4	2	15,4	10	100	0	0	0	0
CRO	10	43,5	0	0	13	56,5	0	0	0	0	13	100	10	100	0	0	0	0
CAZ	10	47,8	0	0	13	56,5	0	0	0	0	13	100	10	100	0	0	0	0
PTZ	16	69,6	2	8,7	2	21,7	7	53,8	1	7,7	5	38,5	9	90	1	10	0	0
SAM	11	47,8	3	13	9	39,2	3	23,1	2	15,4	8	61,5	8	80	1	10	1	10
TOTAL	n: 23/100						n: 13/100						n: 10/100					

p<0.01 (SD±) ; * : Intrinsically Resistant

(n: Strain number, S: Susceptible, I: Intermediate, R: Resistant, TC: Ticarcillin, PIP: Piperacillin, SXT: Sulphamethox-Trimethoprim, CL: Colistin, TGC: Tigecycline, TE: Tetracycline, LEV: Levofloxacin, CIP : Ciprofloxacin, TOB: Tobramycin, CN: Gentamicin, AK: Amikacin, MEM: Meropenem, IPN: Imipenem, FEP: Cefepime, CTX: Cefotaxime, CPZ/SUL: Cefoperazone/Sulbactam, CRO: Ceftriaxone, CAZ: Ceftazidime, PTZ-Taz-Piperacillin : Ampicillin-Sulbactam, SAM : Ampicillin/Sulbactam).

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Tablo 4. Various antibiotics resistance rates of *Acinetobacter spp., Salmonella spp., Enterobacter cloacae* strains.

	Acinetobacter spp						***Salmonella spp***						***Enterobacter cloacae***					
Antibiotic	S		I		R		S		I		R		S		I		R	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
TK	8	38,1	0	0	13	61,9	13	86,7	0	0	2	13,3	6	75	0	0	2	25
PIP	7	33,3	1	4,8	13	61,9	13	86,7	0	0	2	13,3	6	75	0	0	2	25
SXT	9	42,9	0	0	12	57,1	15	100	0	0	0	0	7	87,5	0	0	1	12,5
CL	20	95,2	0	0	1	4,8	15	100	0	0	0	0	7	87,5	0	0	1	12,5
TGC	23	100	0	0	1	4,8	15	100	0	0	0	0	7	87,5	0	0	1	12,5
TE	10	47,6	1	4,8	10	47,6	15	100	0	0	0	0	7	87,5	1	12,5	0	0
LEV	9	42,6	7	33,3	5	23,8	0	0	0	0	15	100	8	100	0	0	0	0
CIP	8	38,1	2	9,5	11	52,4	0	0	0	0	15	100	8	100	0	0	0	0
TOP	10	47,6	7	33,3	4	19,1	15	100	0	0	0	0	8	100	0	0	0	0
GN	18	85,7	2	9,5	1	4,8	15	100	0	0	0	0	8	100	0	0	0	0
AK	19	90,5	0	0	2	9,5	15	100	0	0	0	0	8	100	0	0	0	0
MEM	10	47,6	0	0	11	52,4	15	100	0	0	0	0	8	100	0	0	0	0
İPN	10	47,6	0	0	11	52,4	15	100	0	0	0	0	8	100	0	0	0	0
FEP	8	38,1	0	0	13	61,9	15	100	0	0	0	0	8	100	0	0	0	0
CPZ/SUL	8	38,1	1	4,8	12	57,1	15	100	0	0	0	0	6	75	0	0	2	25
CRO	5	23,8	1	4,8	15	71,4	15	100	0	0	0	0	6	75	0	0	2	25
CAZ	6	28,6	1	4,8	14	66,6	15	100	0	0	0	0	6	75	0	0	2	25
PTZ	7	33,3	1	4,8	13	61,9	15	100	0	0	0	0	6	75	1	12,5	1	12,5
SAM	10	47,6	1	4,8	10	47,6	15	100	0	0	0	0	0	0	0	0	8	100*
TOTAL	n: 21/100						n: 15/100						n: 8/100					

(n: Strain number, S: Susceptible, I: Intermediate, R: Resistant, TC: Ticarcillin, PIP: Piperacillin, SXT: Trimethoprim /Sulfamethoxazole -, CL: Colistin, TGC: Tigecycline, TE: Tetracycline, LEV: Levofloxacin, CIP: Ciprofloxacin, TOB: Tobramycin, CN: Gentamicin, AK: Amikacin, MEM: Meropenem, IPN: Imipenem, FEP: Cefepime, CTX: Cefotaxime, CPZ/SUL: Cefoperazone/Sulbactam, CRO: Ceftriaxone, CAZ: Ceftazidime, PTZ-Taz-Piperacillin: Ampicillin-Sulbactam, SAM : Ampicillin/Sulbactam).

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Tablo 5: Resistance rates of *E coli., E coli* ESBL positive, *E coli* Negative strains to various antibiotics.

E coli							**ESBL positive *E. coli***						**ESBL negative *E. coli***					
Antibiotic	S		I		R		S		I		R		S		I		R	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
TK	4	28,6	0	0	10	71,4	0	0	0	0	8	100	4	66,7	0	0	2	33,3
PIP	4	28,6	0	0	10	71,4	0	0	0	0	8	100	4	66,7	0	0	2	33,3
SXT	10	71,4	0	0	4	28,6	4	50	0	0	4	50	6	100	0	0	0	0
CL	13	92,9	0	0	1	7,1	8	100	0	0	0	0	5	83,4	0	0	1	16,7
TGC	14	100	0	0	0	0	8	100	0	0	0	0	6	100	0	0	0	0
TE	8	57,1	0	0	6	42,9	4	50	0	0	4	50	4	66,7	0	0	2	33,3
LEV	13	92,9	0	0	1	7,1	7	87,5	0	0	1	12,5	6	100	0	0	0	0
CIP	13	92,9	0	0	1	7,1	7	87,5	0	0	1	12,5	6	100	0	0	0	0
TOP	13	92,9	0	0	1	7,1	7	87,5	0	0	1	12,5	6	100	0	0	0	0
GN	11	78,6	1	7,1	2	14,3	6	75	0	0	2	25	5	83,3	1	16,7	0	0
AK	13	92,9	1	7,1	0	0	7	87,5	1	12,5	0	0	6	100	0	0	0	0
MEM	14	100	0	0	0	0	8	100	0	0	0	0	6	100	0	0	0	0
İPN	14	100	0	0	0	0	8	100	0	0	0	0	6	100	0	0	0	0
FEP	6	42,9	0	0	8	57,1	0	0	0	0	8	100	6	100	0	0	0	0
CPZ/SUL	6	42,9	6	42,9	2	14,2	1	12,5	5	62,5	2	25	5	83,3	1	16,7	0	0
CRO	6	42,9	0	0	8	57,1	0	0	0	0	8	100	6	100	0	0	0	0
CAZ	5	35,7	0	0	9	64,3	0	0	0	0	8	100	5	83,3	0	0	1	16,7
PTZ	11	78,6	0	0	3	21,4	5	62,5	0	0	3	37,5	6	100	0	0	0	0
SAM	6	42,9	0	0	8	57,1	1	12,5	0	0	7	87,5	5	83,3	0	0	1	16,7
TOTAL	n: 14/100						n: 8/100						n: 6/100					

(n: Strain number, S: Susceptible, I: Intermediate, R: Resistant, TC: Ticarcillin, PIP: Piperacillin, SXT: Sulphamethox-Trimethoprim, CL: Colistin, TGC: Tigecycline, TE: Tetracycline, LEV: Levofloxacin, CIP: Ciprofloxacin, TOB: Tobramycin, CN: Gentamicin, AK: Amikacin, MEM: Meropenem, IPN: Imipenem, FEP: Cefepime, CTX: Cefotaxime, CPZ/SUL: Cefoperazone/Sulbactam, CRO: Ceftriaxone, CAZ: Ceftazidime, PTZ-Taz-Piperacillin tazobactem, Ampicillin-Sulbactam, SAM : Ampicillin/Sulbactam).*: The bacterium that is naturally resistant to these antibiotics is *P. aeruginosa.* The susceptible bacterium is *P. luteola.*

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Tablo 6: Resistance rates of *Sphingomonas paucim, Pseudomonas spp., Serratia spp* strains to various antibiotics.

Sphingomonas paucim							***Pseudomonas spp***						***Serratia spp***					
Antibiotic	S		I		R		S		I		R		S		I		R	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
TK	5	83,3	1	16,7	0	0	4	100	0	0	0	0	3	100	0	0	0	0
PIP	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
SXT	6	100	0	0	0	0	1	25	0	0	3	75*	0	0	0	0	0	0
CL	2	33,3	0	0	4	66,7	3	75	0	0	1	25	2	66,7	0	0	3	100*
TGC	6	100	0	0	0	0	1	25	0	0	3	75	3	100	1	33,3	0	0
TE	6	100	0	0	0	0	1	25	0	0	3	75	3	100	0	0	0	0
LEV	4	66,7	2	33,3	0	0	4	100	0	0	0	0	3	100	0	0	0	0
CIP	5	83,3	0	0	1	16,7	4	100	0	0	0	0	3	100	0	0	0	0
TOP	5	83,3	0	0	1	16,7	4	100	0	0	0	0	3	100	0	0	0	0
GN	6	100	0	0	0	0	3	75	1	25	0	0	3	100	0	0	0	0
AK	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
MEM	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
İPN	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
FEP	5	83,3	0	0	1	16,7	4	100	0	0	0	0	3	100	0	0	0	0
CPZ/SUL	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
CRO	5	83,3	0	0	1	16,7	1	25	0	0	3	75*	3	100	0	0	0	0
CAZ	5	83,3	0	0	1	16,7	4	100	0	0	0	0	3	100	0	0	0	0
PTZ	6	100	0	0	0	0	4	100	0	0	0	0	3	100	0	0	0	0
SAM	6	100	0	0	0	0	1	25	0	0	3	75*	1	33,3	0	0	2	66,7
TOTAL	n: 6/100						n: 4/100						n: 3/100					

*: Intrinsically Resistant. (n: Strain number, S: Susceptible, I: Intermediate, R: Resistant, TC: Ticarcillin, PIP: Piperacillin, SXT: Sulphamethox-Trimethoprim, CL: Colistin, TGC: Tigecycline, TE: Tetracycline, LEV: Levofloxacin, CIP : Ciprofloxacin, TOB: Tobramycin, CN: Gentamicin, AK: Amikacin, MEM: Meropenem, IPN: Imipenem, FEP: Cefepime, CTX: Cefotaxime, CPZ/SUL: Cefoperazone/Sulbactam, CRO: Ceftriaxone, CAZ: Ceftazidime, PTZ-Taz-Piperacillin : Ampicillin-Sulbactam, SAM : Ampicillin/Sulbactam).

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When we look at the susceptibility of *Sphingomonas paucimobilis* strains to the given antibiotics, resistance to CL was found at a rate of 66.7%. It is seen that there is no resistance against other antibiotics such as LEV, SAM, TK, CN, PIP, SXT, TGC, TE, AK, MEM, IPN, CPZ/SUL, PTZ, and PTZ, *Pseudomonas spp.* When we look at the susceptibility of the strains to antibiotics, it was found that 75% of them were resistant to TGC and TE. However, there is no resistance against other antibiotics such as TOB, CAZ, NEM, TK, PIP, LEV, CIP, CN, AK, IPN, FEP, CPZ/SUL, CAZ, and PTZ *Serratia spp.* When we look at the susceptibility of the strains to antibiotics, it is seen that 66.7% are resistant to SAM, except for colistin, which is naturally resistant (100%), and no resistance has developed against the remaining antibiotics. There was no significant difference in the resistance rates against all tested antibiotics for 3 bacteria ($p>0.05$) Table 6.

Only SXT and LEV were studied in the antibiotic susceptibility of *Stenotrophomonas maltophilia* strain and no resistance was detected against either antibiotic. In our study, 1 *Proteus mirabilis* and 1 *Pantoea agglomerans* were isolated. When we examine the sensitivity of Pantoea agglomerans to antibiotics, it is seen that it is resistant to TK and CL and sensitive to other antibiotics. Proteus mirabilis was resistant to TK, PIP, CL (naturally resistant to colistin), FEP, CAZ, SAM, TGC, TE, TOB, CN, and CRO. In the examination of ESBL distributions, 56.5% of Klebsiella spp and 57.1% of E. coli were found positive (Table 7).

Table 7. ESBL Distributions.

	ESBL (+)		**ESBL (-)**		**TOTAL**	
	n	**%**	**n**	**%**	**n**	**%**
Klebsiella spp.	13	56,5	10	43,5	23	100
E. coli	8	57,1	6	42,9	14	100
TOTAL	21	56,8	16	43,2	37	100

Discussion

Antibiotics, which seem to be our most important weapon in the fight against microorganisms, cause problems from time to time. Because the intensive (sometimes unnecessary) use of antibiotics, especially in the hospital environment, has led to an increase in resistant microorganisms. Most of the microorganisms resistant to antibiotics are bacteria resistant to various disinfectants, antiseptic agents, and external environmental conditions. For this reason, it settles in various parts of the hospital, especially in the intensive care units, causing outbreaks from time to time (Dhingra et al., 2020; van Dijk et al., 2022). While gram-positive microorganisms came to the fore as the causative agent of hospital infections, nosocomial infections caused by gram-negative bacteria started to draw attention after 1970. Today, depending on the centers, gram-positive bacteria come to the fore in some centers, and infection with gram-negative bacteria takes the first place in some centers. The situation of the centers, the patient population, and the antibiotics used are effective in this (Maugeri et al., 2019). Antibiotic resistance patterns may vary constantly between hospitals. It is essential to reveal resistance patterns, especially to guide the clinician (Rhomberg et al., 2004). Gram-negative nosocomial agents frequently encountered in the pediatric population are *Enterobacteriaceae* (*Escherichia coli, Klebsiella, Serratia, Proteus*, and *Enterobacter spp.*), *Pseudomonas aeruginosa*, *Acinetobacter spp., Stenotrophomonas maltophilia, Burkholderia cepacia,* and *Sphingomonas paucimobilis* (Boguniewicz et al., 2021). Most infections caused by these organisms occur in neonatal and pediatric intensive care unit patients. Underlying diseases

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such as malignancy, immunosuppressive diseases, burns, prematurity, intravascular and/or central nervous system catheter, mechanical ventilation and urinary catheterization are the main risk factors for developing these organism infections. Due to multidrug resistance among GNB, the number of antibiotics that can be used in the treatment is gradually decreasing, the development of resistance during treatment sometimes creates problems and almost incurable infections occur (Behzadnia et al., 2014; Oskouie et al., 2013). The first 4 of the most isolated bacteria in our study were *Klebsiella spp.* (22.7%), *Acinetobacter spp.* (20.8%), *Salmonella spp.* (14.8%) and *E. coli* (13.9%). When we look at the distribution of these bacteria by age, *Klebsiella spp., Acinetobacter spp.*, and *E. coli* are more common in children under 5 years of age, while *Salmonella spp.* It has been seen in children over 5 years old. Most of the isolates were obtained from the PIC unit, 26 (25.8%), 21 (20.8%) from the pediatric clinics, and 18 (17.9%) from the NN service. This is due to the dense patient population of these wards, the low average age, and the high number of invasive interventions. Invasive interventions in patients hospitalized in Intensive Care Units pave the way for Acinetobacter strains to colonize and cause infections (Garnacho-Montero et al., 2015; Iosifidis et al., 2017).

In our study, most of the *Acinetobacter* strains, 61.9%, were obtained from patients hospitalized in premature intensive care units. In a study, it was reported that the ward where *Acinetobacter* strains were most frequently isolated was the intensive care unit with 87.7% (Arslan Gülen et al. 2020). In our study, *Acinetobacter* spp. The most resistant antibiotic of the strains was ceftriaxone with 71.4%, followed by ceftazidime with 66.6%, cefepime, piperacillin, and ticarcillin with 61.9%. In a study, the rate of bacterial resistance against ceftriaxone was found to be 99.5% (Al-Tamimi et al. 2022). In another study, a total of 402 *A. baumannii* strains were 20.9% AK, 36.3% MEM, 40.5% IPN, 57.2% CIP, 66.4% PTZ, 69.4% CAZ, 69.7% SAM, 71.1%, CN, and 84.6 CRO, resistance was detected (Gazi H 2007). In our study, it was determined that the most effective antibiotics against Acinetobacter strains were 95.2%, colistin, and tigecycline. The high resistance of *A. baumannii* strains to many antibiotics makes the treatment of *A. baumannii* infections seriously difficult. The reason why the resistance rates are so high may be that although the notifications were made according to CLSI standards, clinics did not take these reports into account. It is thought that the controlled and rational use of broad-spectrum antibiotics currently used in hospitals may lead to the formation of more resistant strains. *Salmonella* is bacteria from the Enterobacteriaceae family that cause different clinical pictures. They can cause asymptomatic gastrointestinal carriage, gastroenteritis, typhoid or paratyphoid, and local organ infections (Nepal et al., 2022). In recent years, increased resistance to antimicrobials in Salmonella serotypes has been reported from many centers. The most important reason for this problem is the widespread use of antibiotics in the empirical treatment of febrile cases (la Tela et al., 2021). In one study, 41.66% salmonella spp. isolated from a total of 460 blood cultures. strains have been shown to be resistant to many antibiotics (Kashosi et al. 2018). In our study; *Salmonella spp.* strains were found to be 100% resistant to LEV and CIP, 2 (13.3%) strains were resistant to TK and PIP, and were susceptible to all the remaining antibiotics. When the literature is examined, the resistance of *Salmonella* strains to quinolones is low, but why the *Salmonella* strains in our study are so resistant should be further investigated. In addition, although it is a promising result that ESBL production was not detected in the tested isolates, it would be appropriate to direct the treatments according to the antibiogram results in order to protect this situation. The incidence of *E. coli*, which is the most common pathogen among urinary system infection agents, is 80-90% (Alanazi et al., 2018).

In our study, *E. coli* strains were mostly formed against PIP and TE with 71.4%, followed by CAZ with 64.3%, CRO, FEP, and SAM with 57.1%. Also, no resistance developed against AK, MEM, and IPN. These results show that multi-drug

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resistance has increased compared to previous studies. Especially the high resistance to cephalosporins draws attention. As in every hospital, our physicians must give conscious antibiotics according to the results of the antibiogram in our hospital. *Enterobacter* strains are among the leading causes of nosocomial infections and cause a wide variety of infections in humans, especially lung, surgical wounds, urinary tract infections, and bacteremia (Annavajhala et al., 2019). In our study, *Enterobacter cloacae* strains were found to be 100% resistant to SAM, to which they are naturally resistant, and no resistance was found against TGC, LEV, CIP, TOP, CN, AK, MEM, IPN, and FEP. The susceptibility rates to the other antibiotics studied were less resistant (12-25%) than the susceptibility rates in the studies. *S. paucimobilis* can cause community and hospital-acquired infections. *S. paucimobilis* can often be seen in people with additional diseases such as immunosuppression, malignancy, and diabetes, as well as in healthy people (Dsouza et al., 2021).

In our study, it was determined that S. paucimobilis strains were resistant to CL 66.7%, CIP, TOP, FEP, CRO, and CAZ 16.7% and were sensitive to other antibiotics studied. *P. aeruginosa* occupies a special place among the nosocomial infectious agents due to its resistance to many antibiotics. The rate of development of resistance to antibiotics varies according to the structure of that hospital, the characteristics of the patients, the spectrum and frequency of invasive interventions in the hospital, and most importantly, the antibiotic use policy (Pachori et al., 2019). Although the clinic of bacteremia due to *P. aeruginosa* is no different from bacteremia caused by other Gram-negative bacteria, mortality rates are higher in these cases (Horcajada et al., 2019).

In our study, *Pseudomonas spp*. strains were resistant to TE and TGC by 75% and CL by 25%, while no resistance was detected against the other antibiotics examined. *P. aeruginosa,* SXT, CRO, and SAM are inherently (100%) resistant. *P. luteola* was sensitive to all antibiotics except CL. Although resistance rates were found to be low in our hospital according to studies, the development of resistance should be followed up periodically. *Serratia spp.* They cause bacteremia, lower respiratory tract, surgical wounds, and skin and soft tissue infections and are responsible for 2% of nosocomial infections. The mortality rate in nosocomial infections originating from Serratia is reported to be 26% (Kim et al., 2015;Al-Tamimi et al., 2022). In our study, *Serratia spp*. SAM resistance was detected in 66.6% of the strains, except CL, which is naturally resistant (100%), and no resistance was observed to other antibiotics studied. *Klebsiella spp.* is gram-negative bacteria that mostly cause opportunistic infections. These microorganisms often show resistance to many antimicrobial agents (Siddiqui et al., 2016). In our study, 23 *Klebsiella spp*. The antibiotic susceptibility of the strain was investigated. Except for TK and PIP, which it is naturally resistant to (100%), resistance developed against FEP, CRO, and CAZ at the rate of 56.5%. Also, no resistance developed to CL, TGC, AK, MEM, and IPN. ESBL positivity was found to be 56.5% in *Klebsiella* strains, and ESBL negative strains were found to be sensitive to all antibiotics. The findings in our study were close to the findings of other studies. *S. maltophilia* is an increasingly important microorganism in hospital infections in recent years. *S. maltophilia* is intrinsically resistant to many antibiotics due to its genes encoding efflux pumps and enzymes that inactivate beta-lactamase, aminoglycoside acetyltransferase, and erythromycin. It is one of the bacteria whose treatment is problematic, since it can show resistance to many antibiotics used today, including carbapenems (Adegoke et al., 2017). In our study, 2 strains of *Stenotrophomonas maltophilia* were isolated. The antibiotic susceptibilities of these 2 strains were studied only for SXT and LEV, and no resistance was found to either antibiotic. In our study, 1 *Proteus mirabilis* and 1 *Pantoea agglomerans* were isolated. When we examine the sensitivity of *Pantoea agglomerans* to antibiotics, it is seen that it is resistant to TK and CL and sensitive to other antibiotics. *Proteus mirabilis* was resistant to TK, PIP, TGC, TE, TOB, CN, FEP, CRO, CAZ, and SAM, and sensitive to

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other antibiotics, except for colistin, to which it is naturally resistant.

ESBL-producing bacteria can be identified by showing resistance to CTX, CRO, CAZ, and aztreonam in routine susceptibility tests. The presence of ESBL in microorganisms causing infections is important in determining the treatment strategy (Castanheira et al., 2021). In our study, resistance patterns of ESBL positive and ESBL negative *Klebsiella* and *E. coli* strains were investigated. ESBL-negative *Klebsiella* strains were found to be sensitive to all antibiotics except TE and PIP, to which they were naturally resistant ESBL-positive *Klebsiella* strains were 61.5% SAM, 53.8% SXT, 38.5% PTZ, 30.8% TOB and GN, 15.4% TE, LEV, CIP and It was found to be resistant to CPZ/SUL. No resistance developed to MEM, IPN, CL, AK, and TGC. ESBL negative *E.coli* strains were 33.3% TK, PIP, and TE, 16.7% were resistant to CL, SAM, and CAZ, sensitive to other antibiotics, ESBL positive *E.coli* strains were 100% TK and PIP. , 87.5% SAM, 50% SXT and TE, 37.5% PTZ, 25% GN and CPZ/SUL, 12.5% LEV, CIP and TOB were found to be resistant. All ESBL-positive *Klebsiella and E. coli* strains were 100% resistant to CRO, FEP, and CAZ. Inadequate implementation of some basic rules, such as the high rate of ESBL in *E.coli* and *Klebsiella* strains isolated in our hospital, the high use of broad-spectrum antibiotics, the lack of attention to hand hygiene by healthcare professionals who are closely involved in the care and treatment of patients, and the isolation of patients infected with ESBL-producing strains may be associated with ESBL-producing microorganisms have often been found to be resistant to other antibiotics. Since treatment options are limited in infections caused by these resistant microorganisms, it is important to monitor the resistance profile and determine whether the isolated microorganisms produce ESBL. Especially *E. coli* and *Klebsiella spp*. ESBL positivity rates should be monitored regularly, and the use of broad-spectrum beta-lactam antibiotics should be decided by considering its advantages and disadvantages. Regarding colistin, since CLSI does not provide breakpoints for *Enterobacteriaceae* when testing colistin, European Committee on Antimicrobial Susceptibility Testing (EUCAST) MIC breakpoints for colistin could be used. The interpretationwas as follows: ≤2 mg/l susceptible and >2 mg//resistant (European Committee on Antimicrobial Susceptibility., 2015).

Conclusion

Our study showed that isolated Gram-negative bacteria showed high rates of antimicrobial resistance and multi-resistance in some strains. This high resistance in our hospital was mostly detected against cephalosporins, penicillins, cotrimoxazole, and quinolone group antimicrobials at rates ranging from 50% to 100%. In addition to these antimicrobials, up to 52%, carbapenem resistance was detected in Acinetobacter strains. These determined resistance rates are in dimensions that cannot be ignored. It is important to know these resistance mechanisms and to prevent their spread. When the findings in our study were evaluated, it showed that carbapenems and aminoglycosides are the most effective antimicrobials for resistant strains of GNB, except for Acinetobacter species. Colistin is considered the last-line drug for MDR Gram-negative bacteria and its susceptibility shoula be checked microbroth dilution method. Epidemiological studies to determine the characteristics of resistance are useful in guiding the clinician in empirical treatment. Considering the high resistance to antibiotics, it is necessary to reconsider antibiotic use habits in our hospital, determine rational antibiotic use policies and strictly follow these rules. Antibiotics should be used considering these data and in line with the recommendations of infection control committees. To prevent the spread of resistance, to strictly comply with hospital infection control measures, and comply with sterilization and disinfection rules, chronic patients should be followed especially in premature intensive care and pediatric intensive care units and in clinics where resistant strains are more common. To prevent the production of ESBL, first, great care should be

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taken to use antibiotics in the right indication for hospitalized patients; deciding on antibiotic therapy by making a good distinction between infection and colonization, especially in chronic patients with long-term follow-up; Inappropriate and unnecessary use of antibiotics should be avoided.

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Research Article / Araştırma Makalesi

The Effect of Six-week Bodyweight High-intensity Interval Training on the Performance of Young Female Athletes

Altı Haftalık Vücut Ağırlığı ile Uygulanan Yüksek Şiddetli İnterval Antrenmanın Genç Kadın Sporcularda Performans Üzerine Etkisi

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Abstract: This study aimed to assess the impact of high-intensity interval training with bodyweight on the physical performance of young female athletes. Thirteen young female athletes participated in the study. Participants performed HIIT with bodyweight three times a week for six weeks, following five months of standardized training. The study examined participants' aerobic and anaerobic performance, including their countermovement jump (CMJ), 30-meter sprint, change of direction (COD), flexibility, weight, and body mass index (BMI). The study was designed as a single-blind, posttest-only, single-group repeated measurement study. All analyses were conducted with a 95% confidence interval, and a significance level was accepted as $\alpha = 0.05$. The effect size (ES) was calculated according to Cohen's effect size. The study revealed statistically significant differences in all outputs except for BMI ($p < 0.05$). Bodyweight HIIT had a large to small effect on the following parameters: VO2max (d = 1.48), Illinois COD test (d = 0.93), 30-meter sprint (d = 0.78), CMJ (d = 0.75), flexibility (d = 0.63), BMI (d = 0.62), peak power (d = 0.61), weight loss (d = 0.58), mean power (d = 0.55). The study results indicated that HIIT with bodyweight could improve the performance of young female athletes.

Keywords: Athletic Performance, Exercise Program, High-Intensity Intermittent Exercises, Young Female.

Öz: Çalışma, vücut ağırlığı ile uygulanan yüksek şiddetli interval antrenmanın (HIIT) genç kadın sporcuların fiziksel performansı üzerindeki etkisini değerlendirmeyi amaçladı. Çalışmaya on üç genç kadın sporcu katıldı. Katılımcılar, beş aylık standardize antrenmanı takiben, altı hafta boyunca haftada üç kez vücut ağırlığıyla HIIT gerçekleştirdi. Çalışma, katılımcıların aktif sıçrama (CMJ), 30 m koşu, yön değiştirme (COD), esneklik, ağırlık ve vücut kütle indeksi (VKİ) dahil aerobik ve anerobik performanslarını inceledi. Çalışma tek kör, sadece son test, tek grup tekrarlı ölçümler olarak tasarlandı. Tüm analizler %95 güven aralığı ile yürütüldü ve anlamlılık seviyesi $\alpha = 0,05$ olarak kabul edildi. Etki büyüklüğü (EB) Cohen'in etki büyüklüğüne göre hesaplandı. Çalışma, VKİ hariç tüm çıktılarda istatistiksel olarak anlamlı farklılıklar ortaya çıkardı ($p < 0,05$). Vücut ağırlığı ile uygulanan HIIT aşağıdaki parametreler üzerinde büyükten küçüğe etki gösterdi: $VO2_{max}$ (EB= 1,48), Illinois COD testi (d= 0,93), 30 m koşu (d= 0,78), CMJ (d= 0,75), esneklik (d= 0,63), VKİ (d= 0,62), zirve güç (d= 0,61), kilo kaybı (d= 0,58), ortalama güç (d= 0,55). Vücut ağırlığı ile uygulanan HIIT, genç kadın sporcularda performansı arttırabilir.

Anahtar Kelimeler: Atletik Performans, Egzersiz Programı, Yüksek Şiddetli İnterval Antrenman, Genç Kadın.

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Introduction

Endurance can be defined as the ability to resist fatigue or maintain a sport-specific task. Athletes' endurance level may affect the sport-related actions performed during the competition (Helgerud et al., 2001). For example, researchers observed significant improvements in football players (n = 19) following aerobic endurance training. These improvements included a 100% increase in linear sprint performance, a 6.7% improvement in running economy, a 24% enhancement in actions involving a ball, and a 20% increase in the covered distance (Helgerud et al., 2001). Similarly, it was reported that basketball players (n = 24) improved their chest pass skills (ES = 0.25) and shuttle sprint time with the ball (ES = 0.56) after endurance training (Aschendorf et al., 2019). In addition, these results were evaluated in relation to other team sports. The researchers stated that endurance performance could have an impact on sports-specific complex skills (Bishop and Girard, 2013). On the other hand, endurance performance can also contribute to developing motor skills. In one study, it was found that anaerobic endurance had a positive correlation with strength (r = 0.05), countermovement jump (r = 0.49), and squat jump (r = 0.55) performance (Alemdaroğlu, 2012). Similarly, researchers reported a strong correlation (r = 0.74 - 0.96, $p < 0.001$) between anaerobic endurance and swimming sport-specific sprint ability (Hawley and Williams, 1991). The findings of these studies showed that endurance performance is an essential athletic performance component that needs to be developed.

High-intensity interval training (HIIT) is one of the training methods preferred by coaches to increase endurance performance. HIIT is based on the principle of combining fast-paced activities performed by high oxygen consumption with low-intensity rests (Gibala et al., 2012). In addition, HIIT is divided into running-centered and resistance-centered (Kilpatrick et al., 2014). While running-centered HIIT is defined as aerobic HIIT, resistance-centered HIIT is expressed as bodyweight HIIT (Kilpatrick et al., 2014). Many studies have investigated the effect of HIIT on motor skills (Alonso-Fernández et al., 2017; Martínez-Rodríguez et al., 2021), team sports (Aschendorf et al., 2019; Rowan et al., 2012), and different age groups (Engel et al., 2018; Stern et al., 2023). Previous studies stated that HIIT positively affects various performance components, age groups, and athletes (Aschendorf et al., 2019; Engel et al., 2018; Martínez-Rodríguez et al., 2021; Rowan et al., 2012; Stern et al., 2023). Although previous studies claimed that HIIT is an important method to increase athletic performance, there were controversial results regarding the effect of HIIT on gender (Engel et al., 2018). Many studies reported that HIIT positively affects the male population (Hannan et al., 2018). However, the researchers stated that the effect of HIIT on the male population was evaluated 5.5 times more than the female population (Hannan et al., 2018). Another systematic review and meta-analysis declared insufficient studies to interpret HIIT regarding gender (Engel et al., 2018). In addition, the researchers noted that the female athlete population is a highly unexplored group in exercise science and recommended that future studies be conducted on the female population (Engel et al., 2018). Other researchers reported similar recommendations (Astorino et al., 2012). Researchers emphasized that the effect of HIIT applied for more than three weeks on the performance of female athletes should be investigated (Astorino et al., 2012). HIIT is a basic method for athletic performance, and its effect on female athletes is still controversial. Therefore, evaluating the impact of HIIT on female athletes' performance should need for the subject area, coaches, and practitioners.

This study may offer an original approach to the literature in terms of evaluating female athletes, a group that has yet to be discovered in exercise science. The main aim of the study was to evaluate the effect of bodyweight HIIT versus standardized training on the physical performance of young female athletes and to compare training methods. We hypothesized that HIIT would increase physical performance and improve the

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anthropometric characteristics of young female athletes.

Material and Method

Study Design

While the study was designed according to a similar study protocol (Twist et al., 2022), the current study was based on the design of single-blind, posttest-only, single-group repeated measurement. Before the study, the participants received the same training five days a week for five months, and none of them participated in different training. Details of this training are given in Appendix 1. Pretest measurements were not taken as the inclusion criteria homogenized the participants. Posttest measurements were taken three days after participants followed a standard training protocol three days a week for six weeks. Participants were informed regarding the performance tests to reduce the learning effect, and each participant performed the performance tests at least once. Countermovement jump, Illinois agility test, and 30-meter sprint performance were measured on the first day, while anthropometric, flexibility, and yo-yo intermittent endurance test I performance were measured on the second. Participants were evaluated at the same times on both test days. To avoid fatigue, the rest periods after each test were left to the participant's preference, and the tests were continued when all participants declared that they were ready for the next test. Before tests, a standard warm-up was done for 15 minutes, and no stimulant use (e.g., caffeine, smoke, supplement) was allowed during the trial. After the measurements, the participants were given three days of rest. Then, the same participants performed HIIT thrice a week for six weeks, and posttest measurements were measured again. While one researcher included the study process, the other included the analysis process. The researcher who performed the performance tests was blinded to the study analyses, while the researcher who conducted the analysis was blinded to the intervention process. The flow diagram of the study process is given in Figure 1. The Reporting of Evaluations with Nonrandomized Designs (TREND) checklist was used to improve the reporting quality in the study. Detailed information on the checklist is given in Appendix-2. Open access to the working process documents was provided through the Open Science Framework (OSF).

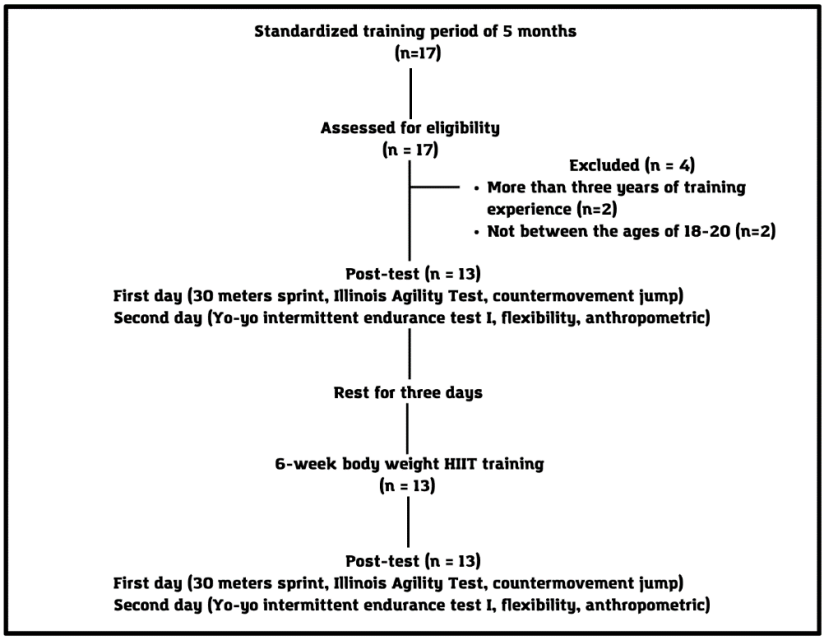

Figure 1. Flow diagram of the study process.

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Participants

The purposive sampling method was preferred to determine the study's sample type. Seventeen participants were evaluated for eligibility. Four participants were excluded because they did not meet the inclusion criteria (Figure 1). Thirteen young female athletes who met the following criteria were included in the study; (i) young female athletes with a maximum of three years of training experience, (ii) between the ages of 18-20, (iii) without any injury in the last six months, (ii) healthy young female athletes.

G*Power (Duesseldorf University, Germany) package program was used to determine the sample size. Most researchers agree that HIIT positively affects different motor abilities. In addition, a very large effect on many motor abilities, such as anaerobic power, aerobic power, and strength, was reported in reference studies (Bauer et al., 2022; Martínez-Rodríguez et al., 2021). Therefore, a two-way hypothesis was established to identify the study's sample size, and power analysis was performed at the large effect level ($\alpha = 0.05$, $\beta = 0.80$, and effect size = 0.85). The power analysis results indicated that a minimum of 13 participants should be included in the study. As a result, 13 young female athletes who met the inclusion criteria, received the same training for five months and were preparing for the sports science exam of universities were included in the study. Detailed information on the anthropometric characteristics of the participants is given in Table 1.

Table 1. Anthropometric and physical characteristics of the participants (Mean ± SD).

Age (y)	Height (cm)	Body Mass (kg)	BMI
18.8± 0.8	167±4.84	61.5±8.73	22±2.23

Note. Y: Years; cm: Centimeter; kg: Kilogram; BMI: Body mass index.

Before starting the study, the advantages and disadvantages of the training protocol were communicated to the participants verbally and in writing. However, participants were not given details about the experimental and control conditions. Moreover, the participants were assured that they could leave the research without being penalized for any reason. All protocols necessary for the study were designed following the Declaration of Helsinki, which allows the ethical use of human subjects. This research was approved by local ethical committee (Approval No: 2022/9).

Procedure

Vertical Jump Performance: The vertical jump test was performed with a standardized protocol on the participants through the countermovement jump test (CMJ) (Martínez-Rodríguez et al., 2021). The CMJ performance of the participants was measured with a Takei jump meter. Participants were asked to use their arms, jump as high as possible, and fall onto the jump meter pad. The obtained data were also used to calculate the anaerobic peak and mean power. The formula PP= 60.7 × (jump height [cm]) + 45.3 × (body mass [kg]) − 2055 was used for peak power. The formula (21.2 x jump height (cm)) + (23.0 x body mass (kg)) – 1393 was preferred for mean power.

Linear Sprint Performance: In this study, the sprint performance of the participants was evaluated with the 30-meter sprint test. Two pairs of timing gate devices (the Newtest Powertimer 300, Finland, accuracy 1000Hz) were used to assess the 30-meter sprint performance. Timing gates were positioned 1 meter above the ground. When the participants felt ready on the hardwood floor, they started the test. Each participant's starting positions were standardized, and the athletes began the test 0.5 meters behind the timing gate.

Change of Direction Performance: The Illinois agility test was used to determine young female athletes' change of direction (COD) performance (Quezada-Muñoz et al., 2021). The test field was designed with four funnels arranged vertically at 3.3 meters distance and four corner funnels

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arranged around these funnels at five meters horizontally and 10 meters perpendicular. Athletes started testing 0.5 meters behind the timing gates when they felt ready. Participants were informed of the change of direction in the Illinois agility test. During the trial, participants changed direction and sprinted at 10-meter intervals. Test times were measured via timing gates (the Newtest Powertimer 300, Finland, accuracy 1000Hz). Timing gates were placed at a height of 1 meter from the ground.

Anthropometry measurements: This study used height and body weight measurements to evaluate anthropometric characteristics. While body weight was measured with a smart scale (Aprilla ABS 10809), a tape measure was used for height measurement. From these data, the body mass index values of the participants were determined according to the Body weight [kg] / Body Height [cm] ^ 2 formula. Anthropometric measurements were made in the morning hours. Participants were instructed to adopt an upright posture for height measurement, while kilograms were measured with T-shirts and shorts.

Flexibility Performance: The sit and reach test was preferred to evaluate the hamstring flexibility of the participants. Participants stretched their soles flat on the test bench on a bench with a length of 35 cm, a width of 45 cm, and a height of 32 cm. Participants leaned forward as far as possible without bending their knees and arms. The value at the last point reached is recorded. If the given instructions were not followed, the test was repeated.

Aerobic Endurance Performance: While many field tests measured VO_{2max}, Yo-yo Intermittent Endurance Test I, preferred in similar populations, was used in this study (Rowan et al., 2012). The participants tried to stay within the determined area until they heard the beep within the 20-meter area. The test of the participant who made three mistakes was terminated. Participants cut eating at least 3 hours before the test so that endurance performance was not affected. VO_{2max} value was calculated according to the following formula on the running distance of the participants; VO_{2max} (ml/min/kg) = distance run (m) × 0.0084 + 36.4.

Table 2. Six week HIIT programming with bodyweight resistance exercise.

Exercises	Training Intensity	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
		Reps x Work (sec) x Rest (sec)					
Jumping Lunges	As fast as possible	8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Burpee with Star		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Mountain Climbers		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Jumping Squat		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Knee Tucks		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Explosive Surfer		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Knee Push-Up		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10
Push-Up		8x20x10	8x20x10	8x20x10	10x20x10	10x20x10	10x20x10

Note. sec: Second.

Training Program

The training protocol consisted of bodyweight HIIT for six weeks. The program design was adapted according to the protocol of a similar study (Mcrae et al., 2012). Participants performed the training protocol three days a week for six weeks. A 48-hour rest period was given between training sessions. The training includes eight exercises: push-ups, jumping lunges, burpee with star, jumping squats, knee tucks, explosive surfer, mountain climbers, and knee push-ups. Bodyweight HIIT was performed according to the Tabata protocol, based on the principle of 20 seconds of working and 10 seconds of rest. The

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time total of the bodyweight HIIT was determined as 8 minutes for the first three weeks, and as of the fourth week, the movement was performed for 10 minutes. Each training started with a standardized warm-up of 15 minutes and ended with a 5-minute cool-down activity. The training took about 25 minutes. Detailed information on the training protocol is given in Table 2.

Data Analyses

Statistical analyzes of the study were carried out with Jamovi 1.8.0, R (R Core Team), and G*Power (Duesseldorf University, Germany) package program. Normality distributions were checked with the Shapiro-Wilk test and skewness-kurtosis values. The normality distribution results showed that all data assumed normality except the 30-meter sprint and peak power (Appendix 3). In-group analyses of 30-meter sprint and peak power data were analyzed with the Wilcoxon test. Paired sample T-test was used in the analysis of other dependent variables. The statistical significance level was accepted as $p < 0.05$ in the analyses performed. The rate of change was calculated according to the following formula: ([Bodyweight HIIT value – Standardized five months training values] / Standardized five months training values) x 100. Effect sizes were evaluated according to Cohen's d formula and interpreted according to the specified reference values; (< 0.2) = trivial, (0.2 – 0.6) = small, (0.6 – 1.2) = moderate, (1.2 – 2.0) = large, (2.0 – 4.0) = very large and (> 4.0) = extremely large (Hopkins et al., 2009). The sensitivity analysis was performed to calculate the estimated effect size. The results indicated that the dependent variables' estimated effect level was moderate ($\alpha = 0.05$, $\beta = 0.80$, Total sample size = 13, estimated effect size = 0.86).

Results

A total of 13 moderately active young female athletes participated in this research. All of the participants were included in the pre-test and post-tests. No injury or injury related to the research protocol was encountered during the six-week HIIT protocol. Detailed information about the research results is given in Table 3 and Figure 2.

Table 3. Mean ± SD of biomotor parameters in the intervention group before and after the 6 week of HIIT

Valuable	Pre Test (n = 13)	Post Test (n = 13)	Comparison Within Group (*p*-value)	Percent Change (%)	ES (Cohen' d)	ES (Interpretation)
Body weight (kg)	61.5±8.73	59±7.01	0.002**	4.06 ↓	0.58	Small
VO_{2max} (ml/kg/min)	30.8±4.12	37.2±4.50	0.001**	20.77 ↑	1.48	Large
30 Meters Sprint (sec)	5.54±0.47	5.11±0.44	0.001**	7.90 ↑	0.78	Modarate
Illinois Test (sec)	21.4±1.24	18.9±1.05	0.001**	11.68 ↑	0.93	Modarate
Flexibility (cm)	39.5±5.06	41.6±5.35	0.001**	5.04 ↓	0.63	Modarate
CMJ (cm)	37.6±4.03	41.9±4.93	0.001**	10.26 ↑	0.75	Modarate
Peak Power (watt)	3010±392	3163±350	0.002**	5.08 ↑	0.61	Modarate
Mean Power (watt)	817±191	853±158	0.004**	4.40 ↑	0.55	Small
BMI	22±2.23	21.1±1.80	0.088	4.09 ↓	0.62	Modarate

Note. **: $p < 0.01$; ES: Effect size; sec: Second; BMI: Body mass index; kg: kilogram; max: Maximum.

Effect of bodyweight HIIT on weight loss and body mass index

The HIIT applied with strength exercises at the end of 6 weeks created a statistically significant difference in the weight loss of young female athletes ($p = 0.002$). It was determined that this training protocol had a minor effect on the weight loss of young women, while a 4% change in weight loss of the participants was achieved (d = 0.58). However, the HIIT had a greater effect on the

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participant's body mass index, which was not statistically significant ($p = 0.08$, d = 0.62).

Effect of bodyweight HIIT on vertical jump performance

The vertical jump performance of the participants increased by 10% in the post-test. This performance increase was considered statistically significant ($p < 0.001$). The study's results showed that the HIIT with resistance exercises moderately affected CMJ performance (d = 0.75).

Effect of bodyweight HIIT on change of direction speed performance

COD performance results indicated a statistically significant difference ($p < 0.001$). The HIIT increased the COD performance of young female athletes by 11% and was found to have a moderate effect (d = 0.93). Similar results were observed in the sprint performance of young female athletes. While there was an approximately 8% increase in 30-meter sprint performance, a statistically significant difference was determined with a moderate effect ($p < 0.001$, d = 0.78).

Effect of bodyweight HIIT on aerobic endurance performance

The HIIT with resistance exercises had the greatest effect on the VO_{2max} values of young female athletes (d = 1.48). While six weeks of HIIT provided a 20% improvement in endurance performance, the analysis results showed a statistically significant difference ($p < 0.001$).

Effect of bodyweight HIIT on anaerobic endurance and flexibility performance

On the other hand, a statistically significant difference was found for anaerobic power values ($p = 0.002$, $p = 0.004$). The HIIT allowed a moderate effect on the peak power of young female athletes (d = 0.61), while it had a minor impact on the average power values (d = 0.55). The 6-week HIIT moderately affected flexibility, which was considered statistically significant ($p < 0.001$, d = 0.63).

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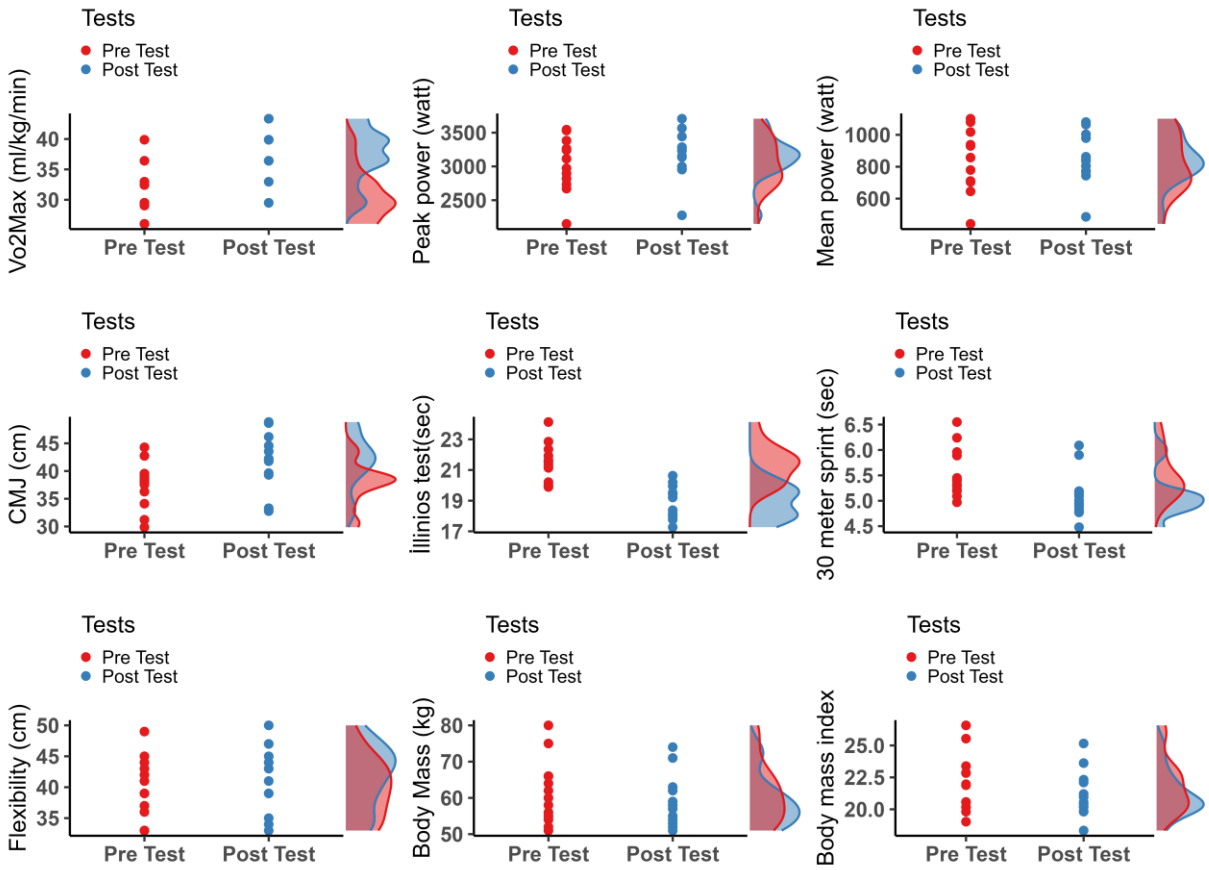

Figure 2. The effect of six week bodyweight HIIT on young female athletes.

Discussion

This study examined the effect of bodyweight HIIT for six weeks on athletic performance in young female athletes. The results showed that bodyweight HIIT positively affected athletic performance at various levels. While body weight and mean power were below the expected effect size, other athletic performance components' effect sizes had at least 80% power.

Bodyweight HIIT improved the VO_{2max} levels of young female athletes (d = 1.48). The improvement in VO_{2max} observed in this study agreed with previous studies that performed a similar HIIT protocol in active women and team athlete females (Alonso-Fernández et al., 2017; Mcrae et al., 2012). Alonso-Fernández et al. (2017) reported that after eight weeks of HIIT combined with functional exercises, the VO_{2max} levels of young female handball players improved by 6.19% and that the combined HIIT provided a moderate (d = 0.78) effect on VO_{2max}. Similarly, in a study involving 22 active women, aerobics and strength training were combined, and the study results indicated an 8% increase in the VO_{2max} level of active women ($p < 0.05$) (Mcrae et al., 2012). The rise in VO_{2max} levels with the bodyweight HIIT is explained by some mechanism (Astorino et al., 2012; Gibala et al., 2012). It is stated that bodyweight HIIT can provide an increase in peroxisome proliferator-activated receptor alpha (PGC)-1α activity. This receptor protein can trigger the adenosine triphosphate (ATP) production mechanism and allow mitochondrial biogenesis (Gibala et al., 2012). In addition, bodyweight HIIT can enhance VO_{2max} levels by improving cardiac function or O_2 pulse (Astorino et al., 2012). These mechanisms may contribute to enhancing the VO_{2max} level in young female

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athletes. The study's results also showed that peak power (d = 0.61) and mean power (d = 0.55) could be improved with Bodyweight HIIT (d = 0.55). Improving anaerobic performance with bodyweight HIIT is based on increasing the ability to move at high blood lactate concentrations, improving lactate buffering capacity, and stimulating supraspinal nervous system adaptations (Kinnunen et al., 2019; Laursen and Jenkins, 2002; Sporis et al., 2008).

On the other hand, bodyweight HIIT can contribute to body composition by providing 24-hour energy consumption and increasing calorie burn in individuals (Andreato et al., 2019; Falcone et al., 2015; Skelly et al., 2014). Researchers observed that HIIT versus continuous moderate-intensity training had similar oxygen consumption ($p > 0.05$) (Skelly et al., 2014). A similar study investigated the effects of HIIT, aerobic, and resistance training on calorie consumption (Falcone et al., 2015). Study results showed that resistance and HIIT increased calorie consumption compared to the others ($p < 0.05$) (Falcone et al., 2015). These results may explain the improvements in participants' weight loss and BMI levels.

Bodyweight HIIT had a moderately positive effect on the 30-meter sprint (d = 0.78), countermovement jump (d = 0.75), and COD (d = 0.93) performances of young female athletes at the end of 6 weeks. Discussions on these study findings have continued in the literature. Although some researchers claim that HIIT can affect sprint, vertical jump, and COD performance, others state that HIIT does not affect these abilities (Aschendorf et al., 2019; Engel et al., 2018). Some physiological mechanisms can explain these controversial results. Endurance training, such as HIIT training, stimulates mitochondrial biogenesis through intracellular metabolic reactions initiated by the activating protein kinase (AMPK) enzyme within the cell (Akın et al., 2018). In addition, this training also inhibits the mammalian target of the rapamycin protein complex (mTOR) enzyme, which effectively enhances the neuromuscular system and improves strength, speed, and agility performance (Nader, 2006). According to this information, it is concluded that there is an inverse relationship between the development of movement patterns that require high intensity and adaptations to endurance training. However, developing parallel endurance and strength parameters is possible with appropriate training design. Both endurance and strength-based abilities can be created simultaneously by combining strength and endurance exercises that incorporate appropriate loads (Baar, 2014; Petre et al., 2018; Wong et al., 2010). This situation is explained by concurrent training adaptations (Gravelle & Blessing, 2000; Hawley, 2009; Nader, 2006). In this study, the selection of body-weight HIIT training over running-based HIIT training may account for the performance improvements observed in test protocols that require explosiveness. In similar protocols, improvements were observed in participants' vertical jump, speed, and agility performances. It was also stated that endurance adaptations did not inhibit neuromuscular adaptations (Petre et al., 2018; Wong et al., 2010). Studies reported that these motor skills could be improved when appropriate loads are combined with endurance and resistance exercises (Baar, 2014; Petré et al., 2018), and this mechanism has been explained by concurrent training adaptations (Hawley and Williams, 1991). This study's preference for Bodyweight HIIT may explain the increase in COD, sprint, and jump performance. In previous studies, improvement in the vertical jump, speed, and COD performances of participants was observed, and it was stated that endurance adaptations did not inhibit neuromuscular adaptations (Petré et al., 2018; Wong et al., 2010).

This study had some limitations. The study includes young female athletes between the ages of 18-20. Additionally, young female athletes did not have elite training experience. Therefore, there is a need for the study to be studied with female athletes in different age groups.

As a result, bodyweight HIIT can improve young female athletes' endurance performance and body composition. However, it should not be forgotten

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that as long as calorie deficit is created, both HIIT and continuous moderate-intensity training have similar effects on long-term fat loss and both are an important tool for body composition. In this case, HIIT can be considered a time-efficient alternative for managing weight loss. In addition, bodyweight HIIT can improve young female athletes' strength-based motor skills, such as COD, linear sprinting, and jumping. Field professionals, practitioners, and coaches may choose bodyweight HIIT over the long-term to improve their female athletes' athletic performance. Bodyweight HIIT, which is a safe and effective training method, should be progressively optimized according to the training period. While acknowledging the necessity for additional studies employing diverse approaches, including our own methodology, we contend that the proposal outlined in this study offers a straightforward approach to structuring and organizing bodyweight HIIT sessions. This study discussed possible mechanisms of how HIIT improves aerobic and anaerobic performance. However, the relationship between existing mechanisms and body weight HIIT needs to be supported by empirical evidence. Therefore, the effect of bodyweight HIIT training on biomarkers can be investigated. In this way, HIIT training can be comprehensively evaluated regarding possible mechanisms.

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Research Article / Araştırma Makalesi

Investigation of Adiponectin, Leptin and Ghrelin Levels and Evaluation of Metabolic Profiles in the Periparturient Period in Romanov Sheep

Romanov Koyunlarında Geçiş Döneminde Adiponektin, Leptin ve Ghrelin Düzeylerinin Araştırılması ve Metabolik Profillerinin Değerlendirilmesi

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Abstract: The periparturient period is very important especially in terms of pregnancy-related herd-based diseases. In this period, especially for early diagnosis of subclinical diseases, a metabolic profile test is used. In the periparturient period, important changes occur in adipose tissue. Blood samples were collected from 16 Romanov sheep in the periparturient in serum tubes on the 21st, 14th, 7th, and postpartum days, and 7th, 14th, and 21st days after delivery. Metabolic profile and Adiponectin, Leptin and Ghrelin parameters evaluated from the blood samples. In the periparturient period, ELISA analyzes of TNF-α were performed for inflammatory evaluation. As a result of the analyzes, Prenatal increase in NEFA concentrations, postpartum decrease in cholesterol concentrations, postpartum increase and decrease in AST concentrations, postpartum increase in GGT concentrations, prenatal and postnatal increases in total protein concentrations, postpartum increase in BUN and creatinine concentrations, postpartum decrease in magnesium concentrations, Prenatal increase in adiponectin concentrations and postpartum decrease, postpartum decrease in leptin concentrations and prenatal increase in ghrelin concentrations occurred. With the results obtained, it was concluded that the evaluation of metabolic profile and adipose tissue is important in the diagnosis of diseases in the periparturient period.

Keywords: Adiponectin, Ghrelin, Leptin, Metabolic profile, Periparturient period.

Öz: Periparturient dönem, doğumdan önceki 3 hafta ve doğumdan sonraki 3 hafta olmak üzere toplam 1,5 ayı kapsar. Periparturient dönem özellikle gebeliğe bağlı sürü kaynaklı hastalıklar açısından çok önemlidir. Bu dönemde özellikle subklinik hastalıkların erken teşhisi için metabolik profil testi kullanılmaktadır. Periparturient dönemde yağ dokusunda önemli değişiklikler meydana gelir. Çalışma materyali olarak periparturient dönemdeki 16 Romanov koyunundan doğum öncesi 21., 14., 7. ve doğum sonrası 7., 14. ve 21. günlerde serum tüplerine kan örnekleri alındı. Kan örneklerinden metabolik profil Adiponektin, Leptin ve Ghrelin parametreleri değerlendirilmişitir. Periparturient dönemde enflamatuar değerlendirme için TNF-α ELISA analizleri yapıldı. Analizler sonucunda NEFA konsantrasyonlarında prenatal artış, kolesterol konsantrasyonlarında postpartum düşüş, AST konsantrasyonlarında postpartum artış ve düşüş, GGT konsantrasyonlarında postpartum artış, total protein konsantrasyonlarında prenatal ve postnatal artış, BUN ve kreatinin konsantrasyonlarında postpartum artış, magnezyum konsantrasyonlarında postpartum düşüş, adiponektin konsantrasyonlarında prenatal artış ve postpartum düşüş, leptin konsantrasyonlarında postpartum düşüş ve ghrelin konsantrasyonlarında prenatal artış meydana geldi. Elde edilen sonuçlar ile periparturient dönemdeki hastalıkların tanısında metabolik profil ve yağ dokusunun değerlendirilmesinin önemli olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Adiponektin, Ghrelin, Leptin, Metabolik profil, Periparturient dönem.

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Introduction

Romanov sheep are known as one of the most productive breeds. This short-tailed sheep breed was first bred in the Yaroslavl region of Russia. It has been reported that Romanov sheep are characterized by an extremely long season of sexual activity and early sexual maturity, which is used by breeders to shorten the mating and thus production interval and increase annual selection progress (Vostry et al., 2018).

Due to the high incidence of disease during transition period of sheep.and the increase in technologies that facilitate behavioural monitoring, researchers have become increasingly interested in investigating the later health and performance relationships of postnatal nutrition, rest, and social behaviour (Sepúlveda-Varas et al., 2012).

In developed countries, metabolic profile testing is applied as the most important criterion, with the control of metabolic diseases and the increase in yield expectation from animals. With this tests, the needs and yields of animals are regulated from the dry period to the end of lactation (Aslan et al., 1993). Evaluation of metabolic profile is considered a reliable tool by veterinarians to evaluate nutrient-productivity relationships (Chalmeh et al., 2017).

Periparturient period (PPD); is defined as the last 3 weeks of pregnancy (3 weeks before birth) and the first 3 weeks after delivery, a total of 1.5 months (Arslan et al., 2012). The three weeks before birth is called the dry period, and the first three-week period after birth is called the lactation period (Tunç ve ark., 2017). The peripartum period; covers three periods: prenatal (prepartum), birth (partum), and postpartum (postpartum). Physiological, metabolic, and physical changes occur to adapt to the transition from pregnancy to motherhood, pregnancy, birth, and breastfeeding (Sepúlveda-Varas et al., 2012). In the PPD, in addition to major changes in the placenta, breast, liver, adipose tissue, muscle tissue, and gastrointestinal system in ruminants, weakening of the immune system and some metabolic and hormonal changes occur (Merhan and Özcan, 2010). Farm animals that become ill shortly after birth are more likely to die young and are less productive throughout their lives (Sepúlveda-Varas et al., 2012).

In many species, changes occur in the energy balance and adipose tissue during pregnancy and lactation (Uyanık et al., 2009). It has been reported that the function of adipose tissue is to provide energy in the form of fatty acids to other organs, especially in the first week after birth, when dietary intake cannot meet the high requirements needed for the rapid increase in milk production (Rukkwamsuk et al., 1998).

Adiponectin is primarily secreted by adipose tissue but is also expressed in cardiomyocytes and skeletal muscles (Kabara et al., 2014). Data obtained from clinical studies support the role of hypoadiponectinemia in the development of obesity-related metabolic and cardiovascular diseases, liver diseases, and some types of cancer (Altıner et al., 2016). Leptin is mainly secreted by adipose tissue and is a hormone found in both primary and secondary lymphoid organs and has an important metabolic and immunomodulatory role (Matarese et al., 2005). The primary role of leptin in metabolic homeostasis is to provide hypothalamus information about body fat amount, thereby modulating central nervous system (CNS) functions that regulate late food intake and energy balance (Proloa et al., 1998). Ghrelin, an acylated peptide consisting of 28 amino acids, has been identified as an endogenous ligand of the growth hormone secretagogue receptor (GHS-R). Ghrelin acts through its receptor, GHS-R. Recently, it has been shown that the GHS-R exhibits a high signal of constitutive activity between meals, with efficacy of approximately 50%, providing the endpoint for food intake between meals (Popovic, 2006).

In this study, it was aimed to evaluate the levels of non-esterified fatty acids (NEFA), beta-hydroxybutyric acid (BHBA), Adiponectin, Leptin, and Ghrelin secreted from the digestive

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system, especially mobilized from adipose tissues during the transition period in sheep breeding, and to recommend the use of metabolic profile testing more widely in sheep. It is thought that it will make an important and innovative contribution to the literature for the pathogenesis of the transition period in sheep.

Material and Method

Ethical Statement

The study protocol was approved by the Animal Ethics Committee for the University of Siirt, (2018/03/05).

Animal Material

The material of the study was started with 20 Romanov breeds aged between 1-4 years of age in Siirt Goat Application and Research Center, which became pregnant beforehand, but was completed with 16 sheep since embryonic death occurred in 4 (four) of the pregnant ewes at the 4th week of pregnancy. All of the animals included in the study were fed in the same housing environment and with the same ration (lentil straw in the morning and evening and 400gr of concentrate feed daily). Clinical examinations of the animals used in the study (body temperature, number of pulsations and respirations, lymph nodes, tracheal palpation, lung auscultation, and percussion) were made in detail.

Collection and Evaluation of Samples

BHBA, NEFA, glucose, albumin, calcium, phosphorus, magnesium, Total protein, BUN, creatinine, cholesterol, triglyceride, GGT, AST, Tumor necrosis factor (TNF-α), adiponectin, leptin, and ghrelin levels were evaluated. Serum samples were taken from the sheep between 11:30 and 14:30 on the 21st, 14th, and 7th days before birth, and at the time of birth and on the 7th, 14th, and 21st days after birth.

Measurement of glucose, triglyceride, calcium, cholesterol, creatinine, albumin, phosphorus, magnesium, AST, GGT, TP, BUN, NEFA, and BHBA values from serum samples was analyzed with an automatic biochemistry analyzer (Randox RX Monaco model sn:5180t240c50485ma) in Burdur Mehmet Akif Ersoy University Veterinary Faculty Animal Hospital Laboratory.

Tumor necrosis factor (TNF-α), Adiponectin, Leptin, and Ghrelin values were measured by ELISA (Enzyme-Linked Immunosorbent Assay) method with commercial kits specific to the species [TNF-α; Sheep Tumor Necrosis Factor (TNF/TNFA/TNFSF2) ELISA Kit (CAT: KTE 110003, Abbkine, China), Adiponectin; Sheep Adiponectin (ADIPOQ) ELISA Kit (CAT: KTE110067, Abbkine, China), Leptin; Sheep Leptin (LEP) ELISA Kit (CAT: KTE110050, Abbkine, China), Ghrelin; Sheep GHRL ELISA Kit (CAT: KTE110062, Abbkine, China)].

Statistical Evaluation

MINITAB program was used for statistical analysis of the data. The distribution of the obtained data was checked by performing a normality test first, and descriptive statistics values were obtained. Repeated Measurements Analysis of Variance (One-Way ANOVA) and Tukey test were used to determine possible differences in the measurement values evaluated on different days for each pair parameter.

Results

Laboratory Findings

Biochemical Findings

In the study, average serum BHBA, NEFA, glucose, cholesterol, triglyceride, AST, GGT, total protein, albumin, BUN, creatinine, calcium, phosphorus, and magnesium concentrations and statistical evaluations of these parameters are shown in Table 1.

No significant difference was found for serum BHBA, glucose, triglyceride, albumin, calcium, and phosphorus concentrations between prenatal, birth, and postpartum days.

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Table 1. Mean serum biochemical values ± standard deviations of animals included in the study (n:16).

Parameters	Prepartum 21st day	Prepartum 14th day	Prepartum 7th day	At Parturition	Postpartum 7th day	Postpartum 14th day	Postpartum 21st day
BHBA (mmol/L)	0.717± 0.553 ^{A}	0.602± 0.498 ^{A}	0.771± 0.827 ^{A}	0.791± 0.720 ^{A}	0.4194± 0.1345 ^{A}	0.4519± 0.1336 ^{A}	0.4813± 0.1202 ^{A}
NEFA (mmol/L)	0.636± 0.518 ^{BC}	0.5388±0.3702 ^{BC}	1.126± 0.978 ^{AB}	1.271± 0.810 ^{A}	0.4156± 0.2452 ^{C}	0.4250± 0.2145 ^{C}	0.564± 0.437 ^{BC}
Glucose (mg/dL)	77.82± 17.46 ^{A}	83.21± 13.14 ^{A}	87.57± 27.92 ^{A}	76.45± 22.33 ^{A}	81.98± 9.95 ^{A}	81.48± 6.82 ^{A}	83.70± 6.11 ^{A}
Cholesterol (mg/dL)	89.92± 9.86 ^{A}	89.50± 15.54 ^{A}	90.01± 19.92 ^{A}	75.73± 10.63 ^{AB}	75.73± 12.73 ^{AB}	70.95± 12.63 ^{B}	78.34± 10.48 ^{AB}
Triglyceride (mg/dL)	32.96± 14.89 ^{A}	42.01± 12.99 ^{A}	39.50± 19.50 ^{A}	45.10± 39.91 ^{A}	33.60± 28.99 ^{A}	46.2± 40.2 ^{A}	41.30± 33.40 ^{A}
AST (U/L)	29.49± 5.52 ^{B}	28.59± 5.87 ^{B}	35.04± 8.11 ^{B}	43.400± 3.704 ^{B}	79.2± 49.4 ^{A}	97.2± 53.8 ^{A}	33.25± 8.56 ^{B}
GGT (U/L)	59.88± 10.84 ^{C}	61.69± 11.48 ^{C}	64.75± 9.97 ^{BC}	60.75± 10.11 ^{C}	80.38± 22.73 ^{AB}	94.19± 25.39 ^{A}	90.50± 21.16 ^{A}
Total Protein (g/dL)	7.071± 0.504 ^{C}	6.761± 0.521 ^{C}	7.883± 0.723 ^{B}	8.098± 0.683 ^{AB}	8.312± 0.492 ^{AB}	8.575± 0.513 ^{A}	8.309^{AB}± 0.588
Albumin (g/dL)	3.6713± 0.2586 ^{A}	4.309± 2.329 ^{A}	3.7756± 0.3563 ^{A}	3.7563± 0.2560 ^{A}	3.6300± 0.3161 ^{A}	3.7125± 0.2982 ^{A}	3.6812± 0.2486 ^{A}
BUN (mg/dL)	30.38 ± 6.56 ^{B}	26.00± 5.49 ^{B}	30.75± 9.42 ^{B}	43.63± 17.76 ^{A}	25.38± 8.82 ^{B}	28.13± 8.90 ^{B}	33.25± 8.56 ^{AB}
Creatinine (mg/dL)	1.2569 ± 0.1759 ^{B}	1.2069± 0.1701 ^{B}	1.1969± 0.2223 ^{B}	1.5113± 0.2153 ^{A}	1.1406± 0.1611 ^{B}	1.2212± 0.1565 ^{B}	1.1900± 0.1887 ^{B}
Calcium (mg/dL)	12.779 ± 1.583 ^{A}	12.600± 0.964 ^{A}	12.476± 1.504 ^{A}	12.248± 1.731 ^{A}	13.177± 1.381 ^{A}	13.444± 1.339 ^{A}	13.256± 1.124 ^{A}
Phosphorus (mg/dL)	8.775± 2.219 ^{A}	9.463± 2.389 ^{A}	9.869± 2.600 ^{A}	9.106± 1.917 ^{A}	9.494± 2.382 ^{A}	10.362± 2.886 ^{A}	9.262± 2.983 ^{A}
Magnesium (mg/dL)	3.2212± 0.2978 ^{AB}	3.4744± 0.1914 ^{AB}	3.4850± 0.3535 ^{AB}	3.590± 0.445 ^{A}	3.252± 0.435 ^{AB}	3.513± 0.480 ^{AB}	3.1813± 0.2386 ^{B}

***A, B, C:** The difference between values with different letters on the same line is statistically significant ($p < 0.05$).

Table 2. Mean serum TNF- Alpha. Adinopectin. Leptin and Ghrelin values ± standard deviations of animals included in the study (n:16).

Parameter	*-21th day*	*-21th day*	*-21th day*	*At Parturition*	*7th day*	*14th day*	*21st day*
BHBA (mmol/L)	0.717± 0.553 ^{A}	0.602± 0.498 ^{A}	0.771± 0.827 ^{A}	0.791± 0.720^{A}	0.4194± 0.1345 ^{A}	0.4519± 0.1336 ^{A}	0.4813± 0.1202 ^{A}
NEFA (mmol/l)	0.636± 0.518 $_{BC}$	0.5388±0.3702 ^{BC}	1.126± 0.978 ^{AB}	1.271± 0.810 ^{A}	0.4156± 0.2452 ^{C}	0.4250± 0.2145 ^{C}	0.564± 0.437 ^{BC}
TNF-Alpha (pg/Ml)	40.07 ± 12.68^{A}	34.86 ± 9.82 ^{A}	50.8 ± 47.30 ^{A}	37.47 ± 10.35^{A}	41.18 ± 11.44^{A}	38.09 ± 9.90 ^{A}	42.21 ± 12.81^{A}
Adiponevtin (ug/L)	44.07 ±90.60^{AB}	38.05 ± 8.75 ^{B}	58.2 ± 43.60 ^{A}	37.03 ± 8.83 ^{B}	30.96 ± 7.03 ^{B}	27.68 ± 7.62 ^{B}	25.59 ± 6.25 ^{B}
Leptin (ng/L)	3166 ± 720 ^{AB}	3105 ± 603 ^{AB}	3402 ± 1813^{A}	3432 ± 645 ^{A}	3532 ±496 ^{A}	1869.2 ±338.3 ^{C}	2257 ± 459 ^{BC}
Ghrelin (ng/L)	69.39 ±12.33^{AB}	57.78 ± 9.15 ^{B}	94.6 ±67.70^{A}	68.22 ±11.70^{AB}	75.41 ±17.18^{AB}	69.41 ±9.67^{AB}	75.49 ±19.21^{AB}

∗**A, B, C**: The difference between values with different letters on the same line is statistically significant ($p < 0.05$).

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NEFA concentrations were significantly increased at the time of birth compared to the 21st and 14th days before birth, and a significant decrease occurred on the 7th day after birth. The change in serum NEFA concentrations in the periparturient period was statistically significant (p=0.000).

Serum cholesterol concentrations showed no significant difference between consecutive weeks in the periparturient period. However, there was a significant decrease in the postpartum 14th day compared to the prenatal period (p=0.000).

A significant increase in serum AST concentrations was found at postpartum 7th day and a significant decrease was found at postpartum 21st day. The variation between AST concentrations in the periparturient period was statistically significant (p=0.000).

In the evaluation of serum GGT concentrations, a significant increase occurred on the 7th postnatal day. The variation between serum GGT concentrations in the periparturient period was statistically significant (p=0.000).

Serum total protein concentrations showed a significant increase occurred on the 7th day before birth, and a significant increase occurred on the 14th day after birth compared to the prenatal period. Changes in total protein concentrations in the periparturient period are statistically significant (p=0.000).

It was observed that there was a significant increase in the BUN levels at the time of birth and a significant decrease at the 7th postnatal day compared to the time of birth. Changes in BUN concentrations in the periparturient period are statistically significant (p=0.000).

Serum creatinine concentrations showed a significant increase at the time of birth and a significant decrease on the 7th postpartum day compared to the time of birth (p=0.000).

In the evaluation of serum magnesium concentrations, a significant decrease occurred on the 21st postpartum day compared to the time of birth (p=0.005).

ELISA Findings

In the study, the mean serum TNF-α, Adiponectin, Leptin, Ghrelin concentrations and statistical evaluations of these parameters with the Elisa method are shown in Table 2.

In the evaluation of serum TNF-α concentrations, no significant difference was found between prenatal, birth, and postpartum days (p= 0.450).

Serum adiponectin concentrations were significantly increased at prepartum day 7 and significantly decreased at birth compared to prepartum day 7. The change in serum Adiponectin concentrations in the periparturient period is statistically significant (p=0.000).

Serum leptin concentrations showed a significant decrease on the 14th postpartum day. The change in serum Leptin concentrations during the periparturient period was statistically significant (p= 0.000).

Serum Ghrelin concentrations significantly increase occurred on the 7th day prepartum. The change in serum Ghrelin concentrations in the periparturient period was statistically significant (p=0.028).

Discussion

Prevention of metabolic disorders associated with the periparturient period is an important consideration in the management of ruminant animals (Jones et al., 2018). During the productive lives of sheep, the periparturient period is critical for both animal health and performance. During late pregnancy, sheep are susceptible to serious metabolic diseases (Karagiannis et al., 2014).

Insufficient energy intake causes mobilization of body fats, which increases the concentration of NEFA in the serum, and if the mobilization is excessive, it can cause hepatic lipidosis (Vandehaar et al., 1999). Changes have also been noted in adipose tissue, along with negative energy balance. A study in angora goats stated that serum NEFA concentrations increased in the second week after birth in the periparturient period, and decreased

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continuously in the following weeks, and found that these changes were not statistically significant (Eşki ve ark. 2015). A study conducted on dairy cows reported that blood NEFA level increased at birth, peaked in the first week after birth, and started to decrease after (Yehia and Salem 2015). One study compared the metabolic status of dairy cows in the periparturient period, observed that the NEFA value was significantly higher in cows in the early lactation period than in the late pregnant cows (Djokovic et al., 2013). In Saanen goats, it was reported that serum NEFA concentrations gradually increased 30 days before calving, peaked at birth, after calving gradually decreased until postnatal 35th day, when NEFA reached the lowest level (0.174 mmol/l). In the present study, there was a significant increase in serum NEFA concentrations at the time of birth compared to the 21st and 14th days before birth, and a significant decrease occurred on the 7th day after birth. The increase in NEFA concentrations was thought to be due to the metabolic adaptations that occurred during the transition from late pregnancy to early lactation and the mobilization of fat reserves in the circulation in the form of NEFA to meet the increasing energy demands of lactation.

Small ruminants such as sheep are at risk of ketosis before lambing during late pregnancy, when fetal nutritional demands are highest. BHBA, a ketone substance, is widely used to detect the sheep at risk of developing pregnancy toxemia (Jones et al., 2018). There is a higher BHBA value at the beginning of lactation compared to the last periods of birth and pregnancy in goats (Soares et al., 2018). In Saanen goats, BHBA concentrations increase significantly from 15 days before birth until the 21st day after birth, and then the concentrations decrease (Sadjadian et al., 2013). A study in Makouei sheep reported that the BHBA value increased before birth and decreased after birth (Mohammadi et al., 2016). In the study, no significant difference was found in serum BHBA concentrations during the transition period. Although the changes in BHBA concentrations were not statistically significant, an increase and decrease were observed in parallel with the NEFA concentrations. The increase was attributed to the release of ketone substances by oxidation of fatty acids in the liver to meet the energy needs of sheep entering negative energy balance, especially in the last period of pregnancy and early lactation period.

During the prenatal transition period, most of the maternal glucose supply is used by the near-term fetus, and then after birth, the mammary gland and conditions requiring rapid hepatic changes begin to use the largest portion of the glucose supply. While glucose is regulated under homeostatic controls, a deficiency in dietary carbohydrates or content can lead to inadequate glucose levels (Lager and Jordan, 2012). Boudebza et al. (2016) found that glucose concentrations were significantly higher in the dry period compared to late pregnancy and the beginning of lactation in their study in sheep. One study in Tuj sheep found that serum glucose levels were significantly higher from 1-30 days of lactation to 3 weeks after the dry period. Chalmeh et al. (2017) reported that glucose levels increased before birth, decreased after birth. In the study, no significant difference was found in serum glucose concentrations during the transition period.

In animals other than cattle, it has also been reported that the onset of lactation causes significant changes in hepatic cholesterol metabolism, such as an increase in cholesterol and bile acids in the liver. This adaptation has been suggested to increase the cholesterol level necessary to increase the acid formation and the lipoprotein, cholesterol, and triglyceride levels to support the mammary gland for milk production (Schlegel et al., 2012). Laeger et al. (2013) found no change in cholesterol level during the periparturient period in their study on dairy cows in the periparturient period. Sadjadian et al. (2013) reported that cholesterol decreased during the last two weeks of pregnancy, increased in the first two weeks of lactation, and reached a peak level on the postpartum 42nd day in Saanen goats. Nazifi et al. (2002) observed that serum cholesterol concentrations increased one week before birth

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and remained at their lowest levels 2-3 weeks after birth in sheep. In the present study, no significant difference was found in cholesterol concentrations in the periparturient period between consecutive weeks. However, there was a significant decrease in the postpartum 14th day compared to the prepartum period. It was thought that the decrease may be an indicator of damage to the liver.

Especially in the periparturient period, lipid metabolism is forced to meet the increasing energy demands. Therefore, adipose tissue is mobilized and the liver has to deal with an increased supply of NEFA via oxidation or re-esterification to triglycerides, and fatty liver develops when TG synthesis is increased (Kessler et al., 2014). Boudebza et al. (2016) reported that triglyceride levels were significantly higher in early lactation and dry periods than in the late period of pregnancy in sheep. Celi et al. (2008) observed that the time elapsed after birth did not affect triglyceride concentrations in their study in goats during the periparturient period. Tharwat and Al-Sobayil (2015) reported that there was no significant change in serum triglyceride concentration during the transition period. In the study, parallel to the findings of Celi et al. (2008) and Tharwat and Al-Sobayil (2015), no significant difference was found in serum Triglyceride concentrations during the transition period.

Determination of AST and GGT activities in dairy cows is mostly associated with the fatty liver syndrome, anorexia, and ketosis in dairy cows during early lactation. Increased AST activity in serum is a sensitive indicator of liver damage, even if the damage is subclinical. Seifi et al. (2007) reported that the AST level was measured at the lowest level 22 days before calving and at the highest level 21 days after calving in their study in dairy cows in the transition period. Tharwat and Al-Sobayil (2015) reported that there was a significant increase in the serum AST level from the prepartum 2 weeks to the postpartum 2nd week in their study in goats in the transition period. Soares et al. (2018) found that AST activity in goats during the transition period was relatively higher during the lactation period than during pregnancy. Giuliotti et al. (2014) showed that AST concentrations increased significantly in the postpartum period in their study in Zerasca sheep in the periparturient period. In the study performed, similar to the studies of Soares et al. (2018) and Giuliotti et al. (2014) a significant increase was found at postpartum 7th and 14th days. However, a significant decrease was found on the 21st postpartum day. Since the AST enzyme is not only a liver-specific enzyme, it is also found in muscles, it is not correct to say with certainty whether the increase is related to the liver. For this reason, it would be correct to evaluate especially the CK enzyme. Observation of a parallel increase in GGT level suggested that there may be damage to the liver.

GGT is important as a marker of hepatobiliary system diseases associated with cholestasis and is used in the diagnosis of liver disease (Stojević et al., 2005). Turk et al. (2013) reported that GGT activity increased at birth in their study in cattle. Tharwat et al. (2015) reported that GGT activity in goats decreased significantly only 1 week after birth. Soares et al. (2018) observed an increase in GGT level on the 20th day of lactation in their study in goats. A significant increase occurred in serum GGT concentrations on the 7th postpartum day in the study. It has been concluded that the increase in the GGT enzyme may be the result of damage to the liver.

Serum proteins have generally been used to assess for infections that may occur in the postpartum period and cause a prolonged interval between birth and conception (Piccione et al., 2011). Soares et al. (2018) reported that the total protein value was higher in the last period of pregnancy and the lactation period compared to the birth. In a study on Berari goats, the serum total protein level 14 days before birth showed a significant increase compared to 7 days before birth, the values decreased slightly at birth (day 0), however, the total protein concentration after birth increased from the 7th to the 21st day of birth (Bhoite et al., 2019). They stated that there was a slight increase

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in the amount, but the differences did not significant. Janku et al. (2011) in their study on periparturient goats reported that the TP concentration before and on the day of birth was at the lower limit (or even slightly below) of the physiological range reported in other studies, but began to increase gradually from the 7th day after birth and the highest mean was 71.3 g, measured on the 28th day after birth. Giuliotti et al. (2014) found that the TP value increased significantly in the postpartum period in their study in Zerasca sheep. In the study, there was a significant increase in total protein concentrations on the 7th day before birth, and a significant increase occurred on the 14th day after birth compared to the prenatal period. The increases in total protein concentrations were thought to be due to dehydration.

Decreased albumin levels have been reported as features of liver disease, kidney disease, inflammatory conditions, and malnutrition. It has been shown that serum albumin levels decrease as the severity of fatty liver increases; however, serum levels alone are not an adequate diagnostic tool because albumin can be affected by liver inflammation and other causes of liver disease (Lager and Jordan, 2012). Piccione et al. (2009) reported that albumin increased significantly during the last period of pregnancy and at the end of lactation in their study in sheep. Manat et al. (2016) in their study in Surti goats, reported that the albumin value was the lowest on the postpartum 0th day and reached the highest value on the postpartum 45th day. Tharwat et al (2015) did not find an increase in albumin value after birth in their study on goats. Sadjadian et al. (2013) in their study in Saanen goats, found that albumin was lower in the prepartum period than in the postpartum period and reached the highest level on the 13th and 42nd days postpartum, however, it reached the lowest level 30 days before birth. In this study, unlike other studies, no significant difference was found in serum Albumin concentrations during the transition period.

Turk et al. (2013) found that the concentration of urea in dairy heifers during the transition period was high until the 8th week after birth. Boudebza et al. (2016) reported that the urea concentration in Ouled Djellal sheep was significantly higher in the early lactation period compared to the dry period. Sadjadian et al. (2013) measured the BUN value in Saanen goats at the highest value on the postpartum 21st day and at the lowest value after birth and stated that BUN values were not statistically significant in their study. In the study, it was observed that there was a significant increase in serum BUN concentrations at the time of birth and a significant decrease on the 7th day after birth compared to the time of birth. It was concluded that the increase in BUN concentration was due to the decrease in the glomerular filtration rate due to fluid loss. The decrease in BUN level can be explained by the decrease in feed intake caused by postpartum stress and hormonal changes (Sevinç et al., 1999).

Sevinç et al. (1999) found that although they measured creatinine concentrations within normal limits in the pre and post-partum period in their study in dairy cattle, the values measured in the first 12 hours after birth were high. Piccione et al. (2009) reported that creatinine value increased significantly in the dry period compared to the last periods of pregnancy in sheep. Soares et al. (2018) reported in their study in goats that there was a significant decrease in creatinine after birth and this continued stably throughout lactation. In the study, it was observed that there was a significant increase at the time of birth and a significant decrease on the 7th day after birth compared to the time of birth. It was concluded that the increase in creatinine concentration at the time of birth was due to the decrease in glomerular filtration rate due to fluid loss. The increase in creatinine level at birth can be attributed to the hemodynamic effect of birth stress on the glomerular filtration rate (Sevinç et al., 1999).

The increased demand for Ca by the mammary glands for milk production at the start of lactation draws calcium from the blood and extracellular

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fluids more rapidly, thus depleting the circulating Ca levels of the mother and leading to subclinical or clinical hypocalcemia in periparturient lactating cows and other mammals (Jin et al., 2019). Soares et al. (2018) in their study in goats measured a decrease in total calcium concentration during birth, and values similar to those in pregnancy at the beginning of lactation. Andersen et al. (2005) reported an increase in calcium in the first week of lactation in dairy cattle. Celi et al. (2008) did not record a significant change in calcium levels in late pregnancy and early lactation in their study on goats. Boudebza et al. (2016) reported that the calcium level increased significantly in the late period of pregnancy in Ouled Djellal sheep and there was a decrease in the calcium level in the early period of lactation when compared to the dry period. In the study, similar to the result of Celi et al. (2008), no significant difference was found in serum calcium concentrations during the transition period.

The late stages of pregnancy and early lactation cause changes in both Ca and P metabolism. The increase in bone resorption occurs due to skeletal mineralization of the fetus in late pregnancy and milk production during early lactation. Milk production requires an available source of P, and bone resorption during the first few weeks of lactation is estimated to provide 500 to 600 g of P. Most of the phosphorus mobilized from bone tissue may be a direct result of Ca mobilization for Ca homeostasis in early lactation (Peterson et al., 2005). Tharwat et al. (2015) found that phosphorus concentration increased 2 weeks before and 2 weeks after calving in goats but decreased at birth and one week after birth. Bhoite et al. (2019) measured the lowest value of phosphorus on the 14th prepartum day and the highest value on the postpartum 21st day in Berari goats. In this study, unlike other studies, there was no significant difference in serum Phosphorus concentrations during the transition period.

The magnesium concentration in colostrum is about three times higher than in normal milk, and milk production in lactating cows causes rapid depletion of extracellular magnesium, resulting in hypomagnesemia if not replaced. During the transition period, inadequate serum magnesium levels are adverse metabolic conditions resulting in reduced reproductive performance. Many studies have shown that insufficient blood calcium (clinical or subclinical hypocalcemia) contributes to the incidence of peri and postpartum health problems and impaired fertility (Jeong et al., 2008). Elshahawy and Abdullaziz (2017) found that magnesium levels increased significantly in the third week compared to the first and second weeks after birth in dairy cattle. A study in Berari goats, the magnesium concentration was found to be the lowest on the postpartum 7th day and the highest on the postpartum 21st day (Bhoite et al., 2019). Boudebza et al. (2016) observed an increase in magnesium levels in the last period of pregnancy in Ouled Djellal sheep. In the study, a significant decrease occurred in serum Magnesium concentrations on the 21st postpartum day compared to the time of birth. It was thought that the decrease in magnesium concentration in the postpartum period may be related to milk production.

TNF-α has a variety of immune system functions, including antitumor activity, antimicrobial activity, and inflammation, as well as regulating many physiological functions, including appetite, fever, energy metabolism, and endocrine activity. Factors such as viruses, parasites, other cytokines, and endotoxin lipopolysaccharide (LPS) induce TNF-α production (Kushibiki, 2011). Trevisi et al. (2012) did not record a significant change in TNF-α values in the periparturient period in their study in dairy cattle. In the present study, parallel to the report of Trevisi et al. (2012), no significant difference was found in serum TNF-α concentrations during the transition period.

Adiponectin improves insulin sensitivity and lipogenesis in adipocytes and fatty acids β-oxidation in myocytes and hepatocytes. These effects occur with the activation of their receptors (adipoR1 and adipoR2) expressed in the liver, adipose tissue, and skeletal muscle. Circulating

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adiponectin in dairy cows consists mainly of high molecular weight complexes and its distribution is not affected by the lactation stage. Circulating adiponectin reaches its lowest level soon after calving, then rises between 40 and 70 days until lactation. Circulating adiponectin is inversely related to plasma fatty acids, which are the main lipolysis biomarker in dairy cows (Contreras et al., 2017). Ohtani et al. (2012) reported that there was no significant change in adiponectin concentrations in the periparturient period in Holstein dairy cattle. Komatsu et al. (2007) reported that the level of adiponectin in cattle that were not in the lactation period was two times higher than those in the lactation period. In the study, there was a significant increase in serum Adiponectin concentrations on the 7th day before birth and a significant decrease occurred at the time of birth compared to the 7th day before birth. It was concluded that the contribution of adiponectin to fatty acid oxidation, especially in the liver, could explain this situation.

Leptin is a polypeptide hormone primarily produced by fat cells and has an effective role in modulating feed intake as well as an effective role in energy homeostasis. It also provides a critical link between appetite, energy homeostasis, and reproductive function in the body (Abdelrazek et al., 2018). Rasmussen et al. (2004) reported that leptin levels were higher in the prepartum period than in the postpartum period and decreased in the first few days of birth and lactation in goats. Block et al. (2001) reported that leptin concentration in dairy cattle did not differ significantly during pregnancy, but decreased by half during the lactation period. Nowroozi-Asl et al. (2016) reported that there is a higher leptin concentration in the lactation period compared to the pregnancy period in dairy cattle. Fleming-Waddell et al. (2007) reported in their study in Callipyge sheep that leptin levels decreased in the last period of pregnancy and this situation continued in the birth and early lactation period. In the study, similar to Rasmussen et al. (2004) in their study in goats and Block et al. (2001) in their study in dairy cattle, a significant decrease in the postpartum 14th day was detected. It is thought that the reason why leptin is at a higher level in the last period of pregnancy compared to the postpartum period is to regulate food intake and balance its expenditure due to the increased energy need (Abdelrazek et al., 2018; Enriori et al., 2006).

In response to starvation in ruminants, ghrelin concentrations increase before scheduled meals and feeding suppresses ghrelin secretion. These observations suggest a role for ghrelin in stimulating feed intake, and responses to ghrelin administration supported this hypothesis. In addition to effects on feed intake, ghrelin has been shown to reduce fat oxidation, increase insulin secretion, and affect a wide variety of processes related to energy balance. Finally, as the endogenous ligand for the growth hormone secretagogue receptor, ghrelin provided a new avenue to investigate the regulation of GH (Growth hormone) secretion (Bradford and Allen, 2008). Vargová and Kováč (2016) reported in their study in cattle that ghrelin concentration decreased before birth, increased in the early postpartum period, and reached the highest level 6 weeks after birth. Temizel et al. (2018) reported that ghrelin levels decreased 1 week before birth and tended to increase 1 week after birth. Küçükşen (2017) reported that the ghrelin concentration was lower in the 4th week compared to the 6th week after birth in sheep. In the study, it was found that there was a significant increase in ghrelin concentrations on the 7th day before birth compared to the 14th day before birth. This increase can be explained by the knowledge that Ghrelin levels in ruminants increase to stimulate appetite against hunger (Bradford and Allen, 2008).

Conclusion

In this study, metabolic profile and changes in adipose tissue were evaluated in Romanov sheep. It is thought that Adiponectin, Leptin, and Ghrelin concentrations differ in the periparturient period in Romanov sheep, and this is due to the changes in the adipose tissue during the periparturient period. In the evaluation of metabolic profile,

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changes in NEFA, Cholesterol, AST, GGT, Total protein, BUN, Creatinine, and Magnesium concentrations are thought to be occurred to meet the energy needs in the periparturient period and to tolerate the disorders that may occur before and after birth.

As a result, it was concluded that the evaluation of metabolic profile and changes in adipose tissue in the periparturient period in Romanov sheep may be important in the diagnosis of diseases with a subclinical course.

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Case Report / Olgu Sunumu

Diagnosis of Mycoplasma agalactiae from Various Specimens of Goats

Keçilerin Çeşitli Örneklerinden Mycoplasma agalactia'nın Teşhisi

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Abstract: The aim of this study was to determine the presence of Mycoplasma infection by bacteriological methods and to reveal the prevalence of the disease in a goat farm with pneumonia, mastitis and arthritis symptoms and deaths. This study was carried out in a Saanen goat farm in Isparta province between January 2015 and January 2017. Samples (milk, intra-articular fluid, internal organs of deceased animals) were brought to XXXX University, Faculty of Veterinary Medicine Microbiology Laboratory and examined by bacteriological methods. Blood samples were collected from 813 goats in aged 1-6 years in the goat farm. Blood sera were tested for *Mycoplasma agalactiae* with a commercial ELISA kit (*Mycoplasma agalactiae* Antibody test kit, IDEXX, France) according to the kit instructions. *Mycoplasma* colonies were isolated from all samples. As a result of serological examination, 83 (10.2%) animals were positive, 9 (1.1%) animals were suspicious, and the rest were negative by ELISA. The seropositivity of *M. agalactiae* was ranged from 5.1 % to 28.7% according to age, and it was found quite high in three-year-old animals. With this study, it was concluded that the seroprevalence of M. agalactiae in goats is quite high in goats aged three years and older, ELISA positive animals can be detected in asymptomatic animals, and ELISA test can be used to determine the seroprevalence of the disease in herds.

Keywords: ELİSA, Goat, *Mycoplasma agalactiae.*

Öz: Bu çalışmanın amacı, pnömoni, mastitis ve artritis sempomları ile birlikte ölümler görülen bir keçi çiftliğinde Mycoplasma enfeksiyonunun varlığını bakteriyolojik yöntemlerle belirlemek ve hastalığın prevalansını ortaya koymaktır. Bu çalışma 2015 Ocak- 2017 Ocak ayları arasında Isparta ilinde bir Saanen keçi çiftliğinde yapıldı. XXXX Veteriner Fakültesi Mikrobiyoloji Laboratuvarı'na getirilen örnekler (hangi örnekler) bakteriyolojik metotlarla incelendi. Ayrıca keçi çiftliğinde yaşları 1-6 arasında değişen 813 keçiden kan örnekleri toplandı. Kan serumları *M. agalactiae* varlığı yönünden ticari bir ELISA kiti (*Mycoplasma agalactiae* Antikor test kiti, Idexx, France) ile kit prospektüsüne uygun olarak test edildi. Örneklerden Pleura Pneumonia Like Organism (PPLO) besiyerine ekimler yapıldı ve *Mycoplasma* spp. kolonileri tüm örneklerden saf olarak izole edildi. Serolojik muayene sonucunda ELISA ile 83 (%10.2) hayvan pozitif, 9 (%1.1) hayvan şüpheli ve geri kalanı negatif olarak saptandı. *M. agalactiae* enfeksiyonunun seropozitifliği, yaşlara göre değerlendirildiğinde, %5.1 ile %28.7 arasında değiştiği, üç yaşındaki hayvanlarda oldukça yüksek olduğu belirlendi. Bu çalışma ile keçilerde *M. agalactiae*'nın seroprevalansının üç yaş ve üzerindeki keçilerde oldukça yüksek olduğu, semptom göstermeyen hayvanlarda ELISA pozitif hayvanların tespit edilebileceği, sürülerden hastalığın seroprevalansını belirlemede ELISA testinin kullanılabileceği kanaatine varıldı.

Anahtar Kelimeler: ELİSA, Keçi, *Mycoplasma agalactiae.*

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Introduction

Mycoplasma agalactiae (*M. agalactiae*), belonging to the genus *Mycoplasma* in the class Mollicutes, is a Gram-negative, non-spored, non-capsulated, usually immobile, polymorphic bacterium with a very small genome and no cell wall that causes infectious agalactiae disease in sheep and goats (Kumar et al., 2014; Reji et al., 2018). Instead of a cell wall, they have a three-layered unit membrane composed of lipids, carbohydrates and proteins (Jay and Tardy, 2019; Kumar et al., 2014).

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Contagious agalactia is an acute, subacute or chronic disease characterized by mastitis, kerataconjunctivitis and arthritis. The causative agent is isolated from milk, joint fluid, eye and nasal discharges, feces, urine samples of infected animals and internal organs of dead animals. The disease is transmitted to susceptible animals by direct and indirect routes, usually through the digestive tract and less commonly through the respiratory and ocular mucosa (Göçmen et al., 2015; Kumar et al., 2014; Reji et al., 2018). Infectious agalactia has been known for more than 200 years. The presence of this disease was first reported in Italy in 1816 (Jay and Tardy, 2019). Infectious agalactia, which is included in the list of notifiable diseases of the World Organization for Animal Health (OIE), is seen in many parts of the world, especially in Mediterranean countries (Assunçao et al., 2007; Göçmen et al., 2015; Kumar et al., 2014; OIE, 2008). Infectious agalactia is known to vary from asymptomatic to chronic forms (Göçmen et al., 2015; Keskin, 2018). In acute form, widespread fever and in some cases, neurological symptoms are observed, while in chronic form, anorexia, weakness, lagging behind the flock, loss of appetite, and decreased milk production are observed (Reji et al., 2018). The incubation period of the disease, which can vary between 1 and 8 weeks, has a morbidity rate of 30-60% and a mortality rate of 20%. However, during the suckling period, the mortality rate can increase up to 40-70% due to the occurrence of septicemia in animals. Sheep in the nursing period are more susceptible to the disease (Bohach et al., 2021).

The aim of this study was to determine the presence of Mycoplasma infection by bacteriological methods and to reveal the prevalence of the disease in a goat farm with pneumonia, mastitis and arthritis symptoms and deaths.

Material and Method

This study was conducted in a Saanen goat farm located in Isparta province between 2015 and 2017. The goats on the farm had not been vaccinated for mycoplasma. Samples were collected from milk, joint contents of sick goats and internal organs of deceased animals. These samples were transported under cold chain conditions to the Department of Microbiology, Faculty of Veterinary Medicine, XXXX University. Additionally, blood samples were obtained from 813 goats with ages ranging from 1 to 6 years, and they were transported to the laboratory under cold chain conditions for serological examinations.

Bacteriological Culture

The milk, joint contents, and internal organ samples brought to the laboratory were inoculated onto Blood agar (Oxoid, UK) with 7% defibrinated sheep blood, MacConkey agar (Merck, Germany), and PPLO agar supplemented with *Mycoplasma* supplement (Oxoid, UK). Petri dishes were incubated at 37°C with 5% CO2 in an incubator for 5-7 days. To separate the isolated *Mycoplasma spp.* colonies from other bacterial colonies, subcultures were performed on PPLO agar without *Mycoplasma* supplement.

ELISA

The serum samples were obtained from the 813 blood samples brought to the laboratory by centrifuging at 3000 rpm for 5 minutes. The serum samples were tested using an indirect ELISA (*Mycoplasma agalactiae* Antibody test kit, Idexx, France) according to the kit procedure. The OD (optical density) values of the samples were determined using an ELISA reader with a 450 nm filter.

Results

Mycoplasma spp. colonies were isolated in pure form from the milk, joint contents, and internal organ samples sent to the laboratory (Figure 1). When these colonies were subcultured on PPLO agar without supplement, PPLO colonies were observed. These colonies were considered as *Mycoplasma spp.*

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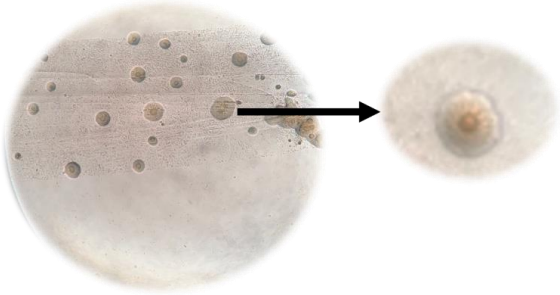

Figure 1. Microscopic image of *Mycoplasma spp.* colonies.

In this study, 83 (10.2%) animals were found to be positive, 9 (1.1%) animals were considered suspicious, and the rest of the animals were negative by ELISA (Table 1). When evaluating the *M. agalactiae* seropositivity according to age, it was found to range from 5.1% to 28.7%, with a significant increase in three-year-old animals. The seropositive animals identified animals were sent to slaughter, while the suspicious goats were placed in a separate area and tested again with ELISA after one month. The positive animals were sent for slaughter. The entire herd was screened with ELISA every 6 months until all animals tested negative, and the positively identified animals were removed from the herd.

Table 1. Distribution of *M. agalactiae* infection by age.

	Age of animals					
ELISA	**1 year**	**2 year**	**3 year**	**4 year**	**5+ year**	**Total**
Positive	12 (%5.1)	5 (%2.3)	42 (%28.7)	13 (%12.2)	11 (%10.09)	83 (%10.2)
Negative	220 (%93.6)	208 (%95.8)	104 (%71.2)	92 (%86.7)	97 (%88.9)	721 (%88.6)
Suspect	3 (%1.2)	4 (%1.8)	0	1 (%0.94)	1 (%0.91)	9 (%1.1)
Total	235	217	146	106	109	813

Discussion

Contagious agalactia, characterized by deaths in young animals, abortions in pregnant animals, and most importantly, decreased milk production, causes significant economic losses in goat farming. Rapid and accurate diagnosis of *M. agalactiae* is crucial for the control and prevention of this disease (Keskin, 2018). Various samples such as milk, blood, serum, nasal swabs, joint fluid, and vaginal swabs are used for the diagnosis of *M. agalactiae*. Studies on *Mycoplasma* have been reported in many countries worldwide (Azevedo et al., 2006; Bandeira et al., 2008; Lin et al., 2022; Mohan and Uzoukwu, 1985). In the study conducted by Kinde et al. (1994) in California, the introduction of new goats without showing any clinical symptoms into a farm with 600 goats resulted in the occurrence of arthritis, polyarthritis, and mastitis in the animals within a short period of 4 weeks, followed by sudden deaths. Milk samples and postmortem examinations of the dead animals were analyzed using bacteriological methods, and a diagnosis of *M. agalactiae* was made.

Azevedo et al (2006) investigated the causes of death of animals in a goat farm in Brazil between 2001 and 2002 in which mastitis and polyarthritis in goats, polyarthritis and conjunctivitis symptoms in kids and lambs were observed, first by bacteriological methods and then by molecular methods. 89 *Mycoplasma* spp. isolates were obtained

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from 107 samples (11 milk, 8 joint fluid, 22 nasal fluid, 66 ear fluid).

In a study conducted in and around Ankara, the first isolation of *M. agalactiae* from milk, joint fluid, nasal discharge and conjuctival fluid samples was realized (Beşe and Arda, 1968). Kızıl and Ozdemir (2006) in Elazığ, they collected milk samples from 47 goats showing symptoms of fever, mastitis, and arthritis, as well as from 20 asymptomatic goats. They investigated the samples using both bacteriological and molecular methods and reported that 17 of the samples were diagnosed with *M. agalactiae* using both methods. Ongor et al. (2011) in eastern Turkey, they collected 692 nasal swab samples from 44 goat herds with nasal discharge. They reported isolation of *Mycoplasma* sp. in 6 of the samples. In another study conducted in same region. Çetinkaya et al. (2009) reported that *Mycoplasma capricolum subsp. capripneumoniae* was isolated and identified from 12 of 32 lung samples collected from 10 different sheep and goat flocks. The samples were subjected to bacteriologic and molecular investigations. In studies conducted in Turkey, reports have been made of *M. agalactiae* in cases of mastitis, arthritis, keratitis, pneumonia, nasal discharge, and anorexia symptoms in cattle (Şababoğlu et al., 2018), sheep (Beşe and Arda, 1968; Göçmen et al., 2015), and goats (Çetinkaya et al., 2009; Kızıl and Ozdemir, 2006; Ongon et al., 2011). This study, similar to the reported studies, isolated *Mycoplasma spp*. colonies on PPLO agar from goats showing mastitis and arthritis symptoms, as well as from the internal organs of deceased animals. This indicates that *Mycoplasma* spp. can be easily isolated from samples taken from goats exhibiting clinical symptoms of contagious agalactia. The isolation of the pathogen from all animals suggests that *Mycoplasma* spp. may be responsible for the deaths in the goat farm. In this study, the serological diagnosis of the infection was performed using ELISA. It was found that out of the animals tested, 83 (10.2%) were positive, 9 (1.1%) were suspected, and the remaining animals were negative for the infection. It was determined that the seroprevalence of *M. agalactiae* is quite high in goats aged 3 years and above, ranging from 5.1% to 28.7% depending on the age. According to this finding, it is believed that older goats in the farm are more susceptible to the disease. In the reported studies (Verbisck-Bucker et al., 2008; Bohach et al., 2021), contagious agalactia was reported to be more common in younger goats. The reason for this is attributed to the fact that female and young animals are usually kept in groups (Verbisck-Bucker et al., 2008). Verbisck-Bucker et al. (2008) conducted a study to investigate the epidemiology of *M. agalactiae* and found that season, gender, secondary agents, age, and reproductive periods were influential factors in the susceptibility of animals to the disease. They concluded that female goats and young animals were more susceptible to the disease. According to Bohach et al. (2021), who conducted a study in Ukraine between 2016 and 2018, they examined blood samples collected from 1,964 sheep and 1,484 goats, including different age groups, using ELISA, and reported that the most susceptible age group to *Mycoplasma spp*. infection was 1-year-old animals. In this study, the higher seroprevalence of *M. agalactiae* in 3-year-old animals compared to other age groups was thought to be associated with the fact that all animals in the herd were kept in a common area on the farm.

M. agalactiae is commonly diagnosed using culture techniques, but the time required to obtain results is considered a significant disadvantage. With advancements in technology, PCR methods have been employed. Assunçao et al. (2007) conducted a study evaluating the applicability of PCR for *M. agalactiae* diagnosis and demonstrated that it is faster and more sensitive compared to culture methods. Therefore, PCR has become the preferred method for *M. agalactiae* diagnosis today (Reji et al. 2018; Göçmen et al. 2015). In Turkey, there are few studies on *M. agalactiae*, and they are generally not focused on determining herd prevalence. The use of ELISA is important in monitoring herd health and conducting epidemiological studies, as it provides both diagnostic capabilities and time-saving advantages. The aim of this study was to establish the seroprevalence of Mycoplasma agalactia,

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therefore molecular diagnostic methods were not used in this study.

In conclusion, this study has determined that *Mycoplasma* spp. can cause symptoms such as pneumonia, mastitis, and arthritis in goats, leading to fatalities. It has been confirmed that the pathogens can be isolated from internal organs, milk, and joint fluid using the culture method. It was concluded that seroprevalence is high in goats aged three years and older, and that ELISA can detect ELISA-positive animals even in asymptomatic individuals. It was also suggested that ELISA testing can be used in the eradication of the disease from herds. The high seroprevalence of *M. agalactiae* indicates that the disease is endemic in the herd. The eradication of the disease from the herd is possible through the identification and removal of infected animals from the flock. There is a need for more studies to be conducted in Turkey and for the identification of strains causing Contagious Agalactia, in order to establish targeted prevention and control programs.

Ethics Approval

I hereby declare that Ethics Committee Approval is not required for the publication given below prepared by the study team.

Conflict of Interest

The authors declare that they have no conflict of interest.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal interests.

Authorship Contributions

During the study's preparation, all authors contributed equally.

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