Mehmet Akif Ersoy Üniversitesi
Sağlık Bilimleri Enstitüsü Dergisi

MAKÜ
BURDUR MEHMET AKİF ERSOY ÜNİVERSİTESİ

SBE
SAĞLIK BİLİMLERİ ENSTİTÜSÜ

ARALIK/DECEMBER 2023
CİLT/VOLUME 11
SAYI/ISSUE 3

Mehmet Akif Ersoy University
Journal of Health Sciences Institute

E-ISSN: 2148-2837

MEHMET AKİF ERSOY ÜNİVERSİTESİ
SAĞLIK BİLİMLERİ ENSTİTÜSÜ DERGİSİ

Mehmet Akif Ersoy University Journal of Health Sciences Institute

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Yayın Türü / Publication Type

Yerel Süreli Yayın / Local Periodical Publication

Kapak-Dizgi / Cover –Design

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Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi yılda 3 sayı olarak yayımlanır (Aralık-2019 itibariyle). Dergi, *DOAJ, Google Scholar, SciLib, Researchbib, SOBIAD, Türkiye Atıf Dizini* gibi ulusal ve uluslararası indeksler tarafından taranmaktadır.

Yıl/Year: 2023 – Cilt/Volume:11 – Sayı/Issue: 3

ISSN: 2148-2837

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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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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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MAKU J. Health Sci. Inst. 2023, 11(3): 279-285.
doi: 10.24998/maeusabed.1375286

Mehmet Akif Ersoy University
Journal of Health Sciences Institute
http://dergipark.gov.tr/maeusabed

Research Article / Araştırma Makalesi

Lower Limb Muscle Strength is Associated with Disability in Non-Specific Chronic Low Back Pain

Non-Spesifik Kronik Bel Ağrısında Alt Ekstremite Kas Kuvveti Dizabilite ile İlişkilidir

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Abstract: Low back pain is one of the most common health problems that affects daily living activities of most people at some time in their lifetime. Non-specific chronic low back pain (NS-CLBP) can be seen in 85-95% of the population. Although it is known that disability and lower limb muscle strength are affected in patients with NS-CLBP, no study investigated the relationship between these variables. The aim of this study was to identify association between disability and lower limb muscle strength in these patients. 79 patients with NS-CLBP were enrolled. The strength of knee extensor and ankle dorsiflexor muscles were measured using a hand-held dynamometer. The disability was assessed using Oswestry Disability Index (ODI). Spearman correlation analysis revealed that there were negative significant correlations between ODI score and right knee extensor muscle strength, left knee extensor muscle strength and left ankle dorsiflexor muscle strength ($r=-0.290$, $p=0.009$; $r=-0.408$, $p<0.001$; $r=-0.285$, $p=0.011$, respectively). This study showed that lower limb muscle strength was associated with disability in patients with NS-CLBP. Physiotherapy interventions such as resistance training to increase the strength of knee extensor and ankle dorsiflexor muscles may be beneficial in improving disability in patients with NS-CLBP.

Keywords: Low back pain, Disability, Muscle strength, Lower limb.

Öz: Bel ağrısı çoğu insanın hayatının bir döneminde karşılaştığı, günlük yaşam aktivitelerini etkileyen en yaygın sağlık sorunlarından biridir. Spesifik olmayan kronik bel ağrısı (SO-KBA) toplumun %85-95'inde görülebilmektedir. SO-KBA'lı hastalarda özürlülük ve alt ekstremite kas kuvvetinin etkilendiği bilinmesine rağmen bu değişkenler arasındaki ilişkiyi araştıran bir çalışma bulunmamaktadır. Bu çalışmanın amacı bu hastalarda dizabilite ile alt ekstremite kas kuvveti arasındaki ilişkiyi belirlemekti. SO-KBA'lı 79 hasta çalışmaya alındı. Diz ekstansör ve ayak bileği dorsifleksör kas kuvvetleri elle tutulur dinamometre ile ölçüldü. Dizabilite, Oswestry Dizabilite İndeksi (ODI) kullanılarak değerlendirildi. Spearman korelasyon analizi sonuçlarına göre ODI skoru ile sağ diz ekstansör kas kuvveti, sol diz ekstansör kas kuvveti ve sol ayak bileği dorsifleksör kas kuvveti arasında negatif anlamlı korelasyon vardı (sırasıyla; $r=-0.290$, $p=0.009$; $r=-0.408$, $p<0.001$; $r=-0.285$, $p=0.011$). Bu çalışma, SO-KBA'lı hastalarda alt ekstremite kas kuvvetinin dizabilite ile ilişkili olduğunu gösterdi. Diz ekstansör ve ayak bileği dorsifleksör kaslarının kuvvetini arttırmaya yönelik, dirençli egzersiz eğitimi gibi fizyoterapi uygulamaları, SO-KBA'lı hastalarda dizabilitenin azaltılmasında faydalı olabilir.

Anahtar Kelimeler: Bel ağrısı, Dizabilite, Kas kuvveti, Alt ekstremite.

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Geliş tarihi / Received : 12.10.2023
Kabul tarihi / Accepted: 30.10.2023

Introduction

Low back pain (LBP) is one of the most common health problems that affects daily living activities of most people at some time in their lifetime. LBP with no identifiable cause or pathology and lasting more than 12 weeks is diagnosed as "non-specific chronic low back pain" (NS-CLBP) and can be seen in 85-95% of individuals (Andersson, 1999; Popescu & Lee, 2020). LBP may cause disability, decreased quality of life and functional limitation (Fujii & Matsudaira, 2013).

To cite this article: TOMRUK M, SOYSAL TOMRUK M, KALEMCİ O.(2023). Lower Limb Muscle Strength is Associated with Disability in Non-Specific Chronic Low Back Pain.. MAKU J. Health Sci. Inst., 11(3), 279-285.

ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

LBP is now the leading cause of disability and productivity loss worldwide ("Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015," 2016; Popescu & Lee, 2020). The level of disability in LBP has long been regarded as a core outcome and associated with pain intensity. It also affects the ability of patients with NS-CLBP to perform maximum muscle function of lumbar region (Verbrugghe et al., 2020). In order to understand the complexity of disability in LBP, the biopsychosocial model has been used as a main framework. It is known that social, psychological, genetic and biophysical factors such as muscle strength can play a role in disabling LBP (Öncü, Ilişer, & Kuran, 2016).

Lower limb muscle strength is an essential component of mobility and performing daily functional activities. Improving muscle strength is a key linking mobility function (Kato et al., 2021). Knee extensor and ankle dorsiflexor muscles are also crucial for functional activities such as walking, standing and for maintaining balance during these activities (de Sousa et al., 2019). Dorsiflexor and knee extensor muscle strength have shown to be impaired in patients with NS-CLBP, however, underlying mechanism is unknown. Pain, kinesiophobia and/or increased disability may cause impaired lower limb muscle strength and physical activity level. Furthermore, improvement in lower limb muscle strength is useful for the effectiveness of treatment in patients with NS-CLBP.

Previous studies mostly revealed the correlation of pain and disability with the muscle strength of abdominal trunk muscle groups in patients with LBP (Hu et al., 2017; Kato et al., 2021). On the other hand, a significant difference in isokinetic muscle strength of the knee extensors and hip abductor/extensors was found between participants in the healthy control group and the LBP group in different studies (de Sousa et al., 2019). Although it is known that disability and lower limb muscle strength are affected in individuals with NS-CLBP when compared to healthy individuals, no study, to our knowledge, reported the relationship between pain, disability and knee extensor and ankle dorsiflexor muscle strength in patients with NS-CLBP. Therefore, the aim of the present study was to identify association between disability and knee extensor and ankle dorsiflexor muscle strength. The hypothesis was that there would be correlations between these variables. The results of this study may assist clinicians to have theoretical and clinical basis on better evaluation or treatment to combat increased disability of individuals with NS-CLBP.

Materials and Methods

Design

This research was designed as cross-sectional study. Data was acquired between January 2019 and January 2020. The study followed the principles of the Declaration of Helsinki and was approved by the local university ethics committee. All participants provided written informed consent.

Participants

Patients who applied to the neurosurgery clinic with complaints of LBP were included in the study. After verbal and written information had been given about the procedure by physiotherapists, patients eligible and willing to participate in the study were enrolled in accordance with the inclusion criteria.

Inclusion criteria were: (i) age between 18 and 65 years, (ii) LBP with no identifiable cause or pathology, (iii) LBP lasting more than 12 weeks. Exclusion criteria were: (i) presence of perceived weakness, motor deficit or paraesthesia in the lower limbs, (ii) specific spinal pathologies/diseases such as disc herniation, malignancy, inflammatory joint and bone diseases, vertebral fracture, scoliosis, (iii) previous history of back surgery, (iv) neurologic, metabolic, and cardiovascular disorders, (v) mental and cognitive disorders that could affect cooperation, and (vi) pregnancy.

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

Procedure

Sociodemographic characteristics were noted. Patients were asked to complete the Numeric Pain Rating Scale (NPRS) and the Oswestry Disability Index (ODI).

Hand-held dynamometer (MicroFET 3, Hoggan Health Industries, UT, USA) was used to assess knee extensor and ankle dorsiflexor muscle strength. Patients were seated on the edge of the treatment table bedside (height 100 cm) with hip and knee at 90° flexion for knee extensor muscle strength assessment whereas they were lying on the bed with ankle in neutral position for ankle dorsiflexor muscle strength assessment. Dynamometer was placed just above the malleolus and over the metatarsal heads on the dorsum of the foot, respectively. Patients pushed against the dynamometer for 5 s with their maximum force as much as they could do for each condition. Dynamometer was hold with both hands to resist against patient's movement force and extremity was stabilized during each test. Strength values were normalised for size differences by dividing by the 2/3 power of body mass in kilograms and expressed as body weight-normalised peak torque (N/kg) (Jaric, Radosavljevic-Jaric, & Johansson, 2002). Measurements were repeated three times and the highest score was used for analysis. Hand-held dynamometry was reported to have good to excellent reliability and validity for measures of lower extremity muscle strength (Kimura et al., 2018; Mentiplay et al., 2015).

Self-reported pain both in rest and in activity were assessed using the NPRS. Individuals were asked to choose a number between 0 (indicating no pain) and 10 (indicating the worst pain) that expresses their pain intensity (Childs, Piva, & Fritz, 2005).

The pain-related disability was assessed using the validated Turkish version of the ODI. The ODI was shown to have good psychometric properties and suit to assessment of patients with LBP. This index includes 10 questions and each of them was scored between 0 and 5. Total point of index were calculated as 100 points. Higher scores reflect higher level of disability (Yakut et al., 2004).

Statistical Analysis

All data were analyzed using the IBM SPSS software (version 23.0 for Windows; IBM Corp, Armonk, NY). Shapiro-Wilk Test, histograms and probability plots were used to examine the normality of the data. Variables were presented as median (min - max) and interquartile range (25% - 75%) since most of the variables were not normally distributed. Spearman test was used to calculate the correlation coefficients and their significance. Strength of correlation was defined as very weak for r values between 0.00–0.19, weak for r values between 0.20–0.39, moderate for r values between 0.40–0.69, strong for r values between 0.70–0.89, and very strong for r values over 0.90 (Streiner, Norman, & Cairney, 2014). To infer statistical significance, an overall 5% type-I error level was used ($p < 0.05$).

Results

121 patients with LBP assessed for eligibility. 32 patients who did not meet the inclusion criteria (low back pain less than 12 weeks, specific spinal pathologies, etc.) and 10 patients who declined to participate were excluded. A total of 79 patients (55 females, 24 males) with NS-CLBP were enrolled (Table 1).

Table 1. Distribution of patients with non-specific chronic low back pain according to gender.

	n	**%**
Gender, %		
Female	55	69.6
Male	24	30.4

Table 2 shows the demographic and clinical characteristics of patients with NS-CLBP. Values were presented as median, minimum, maximum and interquartile ranges (25% - 75%).

Spearman correlation analysis revealed that ODI score was significantly correlated with pain – activity, right knee extensor muscle strength, left knee extensor muscle strength and left ankle dorsiflexor muscle strength ($p<0.05$). There was a

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

weak and positive relationship between ODI score and pain – activity (r = 0.324, p = 0.004). A weak and negative correlation was found between ODI score and right knee extensor muscle strength (r = -0.290, p = 0.009). Left knee extensor muscle strength was moderately and negatively correlated with ODI score (r = -0.408, p < 0.001). While right ankle dorsiflexor muscle strength did not significantly correlate with ODI score (p = 0.073), there was a weak, negative, significant correlation between left ankle dorsiflexor muscle strength and ODI score (r = -0.285, p = 0.011) (Table 3).

Table 2. Demographic and clinical characteristics of patients with non-specific chronic low back pain

	Median	**min**	**max**	**IQR (25% - 75%)**
Age, years	44.0	18.0	74.0	18.0 (37.0 - 55.0)
BMI, kg/m²	26.7	18.9	39.1	4.8 (24.1 - 28.9)
Pain (NPRS)				
Pain - Rest	4.0	0.0	10.0	5.0 (2.0 - 7.0)
Pain - Activity	8.0	3.0	10.0	3.0 (7.0 -10.0)
Muscle Strength				
R-Knee Extensor, N/kg	2.22	1.02	4.39	1.16 (1.74 - 2.90)
L-Knee Extensor, N/kg	2.17	0.95	4.49	1.22 (1.65 - 2.87)
R-Ankle Dorsiflexor, N/kg	2.27	0.5 1	4.39	1.23 (1.70 - 2.93)
L-Ankle Dorsiflexor, N/kg	2.32	0.48	3.99	1.10 (1.77 - 2.87)
Disability				
ODI score	28.0	5.0	80.0	17.0 (20.0 - 37.0)

BMI Body mass index, *L* Left, *NPRS* Numeric pain rating scale, *ODI* Oswestry disability index, *R* Right.

Table 3. Correlation matrix between disability and assessed variables

	Age	**BMI**	**Pain - rest**	**Pain - activity**	**R-Knee Extensor MS**	**L-Knee Extensor MS**	**R-Ankle Dorsiflexor MS**	**L-Ankle Dorsiflexor MS**
ODI score	r = 0.136	r = 0.141	r = 0.177	**r = 0.324**	**r = -0.290**	**r = -0.408**	r = -0.204	**r = -0.285**
	p = 0.231	p = 0.216	p = 0.118	**p = 0.004***	**p = 0.009***	**p < 0.001***	p = 0.071	**p = 0.011***

**Spearman Correlation Analysis: p<0.05*
BMI Body mass index, *L* Left, *MS* Muscle strength, *ODI* Oswestry disability index, *R*

Discussion

In this study, we tried to find out whether disability is related to lower limb muscle strength or not in patients with NS-CLBP. Our findings revealed that disability was related to both left and right knee extensor muscle strength and left ankle dorsiflexor strength in a negative way in patients with NS-CLBP. While there was a moderate relationship between disability and only left knee extensor muscle strength, all the other correlations were weak. On the other hand, right ankle dorsiflexor strength was not significantly correlated with disability. Besides, pain in activity was significantly and positively correlated with disability in patients with NS-CLBP.

Until now, to our knowledge, there is only one study investigated the relationship between disability and any indicators of lower limb muscle strength in individuals with NS-CLBP (Shin, 2020). Shin examined the association between

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

maximum voluntary isometric contraction asymmetry of hip extensor muscles and the disability of sixty-one office workers with NS-CLBP. Results showed that there were no significant correlations between left/right hip extensor strength asymmetry and disability in NS-CLBP (Shin, 2020).

Cai&Kong investigated low back and lower limb muscle performance in male and female recreational runners with CLBP (Cai & Kong, 2015). They compared knee extensor, hip extensor and hip abductor strength between male and female runners with CLBP and healthy runners. Results showed that runners with CLBP exhibited diminished knee extensor strength compared to healthy runners, whereas no differences were found in terms of hip extensor and abductor strength. Although the interrelation between disability and knee extensor strength was not evaluated in their study, these results indicate that CLBP negatively affects knee extensor strength (Cai & Kong, 2015). Taken into consideration with the results of our study, the diminished knee extensor strength in CLBP could be one of the reasons of the occurred disability in these patients.

In most studies examined the association between disability and muscle strength in patients with CLBP, strength of lumbar region muscles has been evaluated rather than that of lower limb muscles (Hu et al., 2017; Iwai, Nakazato, Irie, Fujimoto, & Nakajima, 2004; Pranata et al., 2017; Shin, 2020; Steele et al., 2019; Verbrugghe et al., 2020). One study reported that disability was negatively correlated with the ratio of the lumbar extensor and flexor strength in office workers with CLBP and suggested that improving the ratio of the lumbar extensor and flexor strength might be important in order to improve disability (Shin, 2020). Supporting this, Hu et al investigated correlations between lumbar neuromuscular function and pain, lumbar disability in patients with NS-CLBP. Both lumbar flexor and extensor muscles strength had a correlation with pain and function in different flexion and extension angles. Results suggested that the decrease of lumbar muscle strength leads to an increase in pain intensity and lumbar disability (Hu et al., 2017). Another study also examined the relationship between isokinetic trunk muscle strength and the functional disability level of NS-CLBP in collegiate wrestlers. Significant correlations between lumbar extensor parameters in different angles and disability were found. However, none of the trunk flexor parameters were significantly correlated with the disability. These results suggested that the relatively low strength of trunk extensors might be one of the factors related to disability level of NS-CLBP in collegiate wrestlers (Iwai et al., 2004). On the other hand, a more recent study reported that neither abdominal nor back muscle strength was associated with disability in NS-CLBP (Verbrugghe et al., 2020).

Pranata et al reported that lumbar extensor muscle force control was associated with disability in people with CLBP. They recruited 33 CLBP and 20 healthy people and compared force control of the lumbar extensors of the two groups. They found out that lumbar extensor muscle force control was compromised in CLBP group as compared to healthy individuals. In addition, the inability to accurately control muscle force production alone explained 19% of the variance of self-reported disability in CLBP group. Therefore, they concluded that the ability to control lumbar extensor muscle force is a significant predictor of self-reported disability in people with CLBP (Pranata et al., 2017). Another study published in 2019 showed that isolated lumbar extension strength was weakly correlated with disability in participants with CLBP, suggesting that improvements in isolated lumbar extension strength might be related to positive and meaningful clinical outcomes such as disability (Steele et al., 2019).

Some studies examined whether lumbar muscle strength training was able to increase the strength of lumbar muscles, thereby decreasing the disability level. Steele et al applied isolated lumbar extension resistance training at a frequency of once a week for 12 weeks in order to improve the strength of the lumbar extensors in participants with CLBP. Results of the study showed that

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

isolated lumbar extension resistance training increased the strength of the lumbar extensors, thereby improving disability and pain in CLBP (Steele, Bruce-Low, Smith, Jessop, & Osborne, 2020). Similar to this study, Helmhout et al applied a progressive 11-week lumbar extensor strength training program, once a week to patients with CLBP and measured disability, pain intensity and sagittal lumbar mobility before and after the treatment. At the end of 11th week, statistically significant 23% to 36% decrease in disability and 28% decrease in pain was found. They concluded that specific lumbar strengthening showed clinically relevant improvements in disability and pain, whereas those improvements did not necessarily relate to improvements in lumbar mobility (Helmhout et al., 2017).

The major strength of this study is that, to the best of our knowledge, this is the first study to investigate the relationship between disability and the strength of knee and ankle joint muscles in patients with NS-CLBP.

There were some limitations to this study. We found that only right ankle dorsiflexor strength was significantly correlated with disability, not left ankle dorsiflexor strength. Lower limb dominance may be a contributing factor for the relationships between disability and lower limb muscle strength. Unfortunately, this variable was not examined in this study. Another limitation could be the use of hand-held dynamometry test instead of isokinetic muscle strength test, the "gold standard" method for evaluating muscle strength, because our department did not have an isokinetic dynamometer. A self-reported questionnaire, ODI, was used to assess disability in the present study. Although using self-reported questionnaires is an easy, quick, and apprehensible method, it should be remembered that results can be subjective.

In conclusion, the results of this study showed that lower limb muscle strength was associated with disability in patients with NS-CLBP. Physiotherapy interventions such as resistance training to increase the strength of knee extensor and ankle dorsiflexor muscles may be beneficial in improving disability in patients with NS-CLBP.

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To cite this article: TOMRUK M, SOYSAL TOMRUK M, KALEMCİ O.(2023). Lower Limb Muscle Strength is Associated with Disability in Non-Specific Chronic Low Back Pain.. MAKU J. Health Sci. Inst., 11(3), 279-285.

ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

MAKU J. Health Sci. Inst. 2023, 11(3): 286-292.
doi: 10.24998/maeusabed.1375286

Mehmet Akif Ersoy University
Journal of Health Sciences Institute
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Research Article / Araştırma Makalesi

Investigation of Ghrelin and Leptin Value in Obese and Non-obese Cats

Obez ve Obez Olmayan Kedilerde Ghrelin ve Leptin Hormonlarının Araştırılması

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Abstract: Obesity is the deterioration of metabolic and physiological functions due to excessive accumulation of fat in the body. Leptin and ghrelin are two hormones involved in energy balance. There is still not enough information about these two hormones and there is very little research investigating their connection with obesity. The aim of this study was to investigate of leptin and ghrelin hormones in obese and non-obese cats. In this study, 20 cats were evaluated with the body fat measurement system in cats. Those with body fat ratio above 30% were considered obese (Group 1, n=10), those below 30% were considered as the control group (Group 2, n=10). Serum leptin (p=0.05) and ghrelin (p=0.001) values were determined in cats in both groups, and statistically significant differences were observed. A statistical difference was determined in ALT and calcium values (p< 0.001). No statistical difference was found in BUN, creatinine, total bilirubin and hematological values between obese cats and the control group. As a result, it was determined that leptin and ghrelin hormones play an important role in obesity.

Keywords: Leptin, Ghrelin, Obesity, Cat.

Öz: Obezite, vücutta fazla miktarda yağ birikmesine bağlı olarak metabolik ve fizyolojik fonksiyonlarının bozulmasıdır. Leptin ve ghrelin enerji dengesini ile ilgili iki hormondur. Bu iki hormon hakkında hala yeterince bilgi yoktur ve obezite ile bağlantısını araştıran araştırmalar çok azdır. Bu çalışmanın amacı obez ve obez olmayan kedilerde leptin ve ghrelin hormonlarını araştırmaktır. Çalışmada kedilerde vücut yağ ölçüm sistemiyle 20 kedi değerlendirildi. Vücut yağ oranı, %30'un üzerinde olanlar obez (Grup 1, n=10) olarak değerlendirildi, %30'un altında olanlar ise kontrol grubu (Grup 2, n=10) olarak değerlendirildi. Her iki grupta olan kedilerde serum leptin (p=0,05) ve ghrelin p=0,001) değerleri belirlendi ve istatiksel olarak anlamlı farklılıklar gözlendi. ALT ve kalsiyum değerlerinde (p< 0,001) istatistiksel farklılık belirlendi. Obez kediler ile kontrol grubu arasında BUN, kreatinin, total bilirubin ve hematolojik değerler açısından istatistiksel bir fark bulunamadı. Sonuç olarak obezitede leptin ve ghrelin hormonları önemli rol oynadıkları saptandı.

Anahtar Kelimeler: Leptin, Ghrelin, Obezite, Kedi.

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Geliş tarihi / Received : 21.08.2023 Kabul tarihi / Accepted: 17.10.2023

Introduction

Obesity is often the result of excessive dietary intake or inadequate energy use, resulting in a state of positive energy balance (German, 2006). Many factors can predispose a cat to obesity, including genetics, the amount of physical activity and the energy content of the diet (German, 2006). Obesity is generally defined as a body fat percentage above 30%, and normal cats are expected to have between 10% and 30% body fat percentage (Hoelmkjaer and Bjornvad, 2014).

In 1999, Japanese scientists discovered the gastrointestinal peptide hormone ghrelin as the endogenous ligand for growth hormone receptor (GHR)1a, which can stimulate the release of growth hormone (GH) from the anterior pituitary gland. Ghrelin was found to modulate systemic metabolism through activation of orexigenic neural circuits. It is a 28 amino acid lipopeptide

To cite this article: AKGÜN Ş, ŞAHİNDURAN Ş.(2023). Investigation of Ghrelin and Leptin Value in Obese and Non-obese Cats.. MAKU J. Health Sci. Inst., 11(3), 286-292.

ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

hormone secreted from tissues and organs such as the hypothalamus, pituitary, thyroid gland, salivary gland, small intestine, kidney, heart, pancreas, lung, placenta, gonads, immune system, breast, mainly from the fundus of the stomach. Ghrelin is also known as the apetite hormone (Müller et al., 2015). In adult mammals, ghrelin is most densely released from gastric tissue (Bang et al., 2007). It is suggested that ghrelin acts as a meal initiation or hunger hormone, signaling gastrointestinal (GI) fuel status to the central nervous system (CNS) to regulate food intake and energy (Kojima and Kangawa, 2005).

Ghrelin in metabolism, food intake and body weight plays an important role in regulation. Therefore, ghrelin may be a potential drug target for body weight regulation. Ghrelin levels are inversely proportional to energy stores and increase with weight loss in response to body weight changes and decrease with weight gain. Circulating ghrelin levels decrease with obesity, but when obese individuals lose weight, ghrelin levels increase to tolerate this weight loss (İlhan and Erdost, 2009).

The peptide hormone leptin plays a role in regulating food intake, body mass, reproductive function, fetal growth, proinflammatory immune responses, angigonesis, and lipolysis. Leptin is a product of the obese gene. Following the synthesis and secretion of fat cells in white adipose tissue, it binds to and activates the leptin receptor (LEP-R) (Obradovic et al., 2021). Feline leptin is partially protein bound in the circulation. As with other species, circulating leptin primarily reflects body fat mass in cats, and weight loss is associated with decreased peripheral blood leptin levels. Leptin levels are slightly increased during feeding compared to the fasting state (Backus et al., 2000).

The aim of this study is to determine the changes in the values of leptin and ghrelin hormones in obese and non-obese cats.

Materials and Methods

Animal Material

The research material consisted of 20 cats of both sexes and different breeds, aged between 1 and 11 years. The groups were divided into two as control (10) and obese (10). Ten of the blood samples were collected from obese cats with a body fat percentage above 30% (obese) and 10 from non-obese cats with a body fat percentage below 30% (control) according to the body fat measurement system. There are cats of different breeds, 4 of which are infertile females and 6 of which are male sterile, with ages ranging from 5 to 10 years in the obese group. The control group consisted of 10 cats with ideal weight over 1 year old. According to the body fat measurement system, the groups were divided into two as obese cats with a body fat percentage above 30% (Group 1, n=10) and as control non-obese cats with a body fat percentage below 30% (Group 2, n=10).

Methods

During the study, the weight, chest circumference and leg lengths of all cats were measured and their body mass indexes were calculated. Those with a body mass index greater than 7 were considered obese. A total of 5 cc blood was collected from all cats for haematological and biochemical examination. The collected blood was centrifuged at 4000 rpm for 10 minutes. The obtained sera were separated and stored in a -20°C freezer until used as aliquots.

Body Fat Measurement System

.Rib cage value: 9. Rib cage circumference passing over rib

.Leg index value: Distance between patella and calcaneal rump

.The body fat ratio of cats with ideal weight is between 15%-30%,

.Those who are considered extremely thin and have less than 20% fat,

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Those who are overweight or obese are considered as cats with a body fat ratio of 30% or more.

Ghrelin and Leptin Test Protocol

Ghrelin enzyme was measured by ELISA (Enzyme-Linked Immunosorbent Assay) method. Cat Ghrelin ELISA kit (Bioassay Technology Laboratory Cat Ghrelin BT-LAB Kit Cat. NO. E0117CAT LOT 202202009) and cat Leptin ELISA kit (Bioassay Technology LaboratoryCat Leptin BT-LAB Kit Cat. No. E0079Cat LOT 202202009) were used in the study. Procedures were performed according to the kits procedure. In this study, all samples were taken in the morning after a 2-hour fast to minimize the effects of daily ghrelin dynamics.

Statistical analysis: IBM SPSS 26.0 for Windows package program was used to evaluate the study data. The normal distribution of the groups in the analyzes was evaluated using the Shapiro-Wilk test. Due to the normal distribution of the data, between measurements Paired t-test was used for comparisons. Pearson Correlation analysis was used to determine the relationship between variables. p value <0.05 was considered statistically significant.

Results

In obese cats (Group1), compared to the control group (Group2), decreased leptin value (p< 0,05), increased ghrelin, glucose, ALT, calcium values (p< 0.001) and statistical difference was determined. No statistical difference was found between the obese cats and the control group in terms of BUN, creatinine, and total bilirubin values (Table 1).

No statistically significant difference was found between obese cats and control group in terms of WBC, RBC, PLT, NEU, HGB, HCT values in hematological findings (Table 2).

Table 1. Leptin, ghrelin and some other biochemical findings in obese and control groups.

	Group 1 ***(n=10)*** $\bar{x} \pm ss$	**Group 2** ***(n=10)*** $\bar{x} \pm ss$	***p***
Leptin (ng/ml)	2,03±,45	4,54±2,46	0,05
Ghrelin (ng/L)	440,49±305,12	35,07±20,05	0,001
Glucose (mg/dl)	215,00±34,18	165,70±21,17	<0,001
ALT (U/L)	168,00±53,53	52,20±7,29	<0,001
ALP (U/L)	41,20± 5,11	37,20±2,29	0,43
BUN (mg/dl)	20,50±3,53	19,50±3,56	0,470
Creatinine (mg/dl)	1,02±15	1,02±,0.96	1,00
Ca (mg/ml)	15,47±3,51	9,71±0,85	<0,001
T.Bil (mg/dl)	20±,02	20±,01	0.108

Table 2. Hematological findings in cats in the obese and control groups.

	Group 1 ***(n=10)*** $\bar{x} \pm ss$	**Group 2** ***(n=10)*** $\bar{x} \pm ss$	***p***
WBC (0^9/L)	12,06±2,41	11,70±3,82	0,805
RBC (0^12/L)	9,08±2,07	9,02±3,10	0,963
PLT (0^9/L)	154,80±63,42	153,10±70,70	0,955
NEU (10^9/L)	7,34±1,34	7,55±2,46	0,813
HGB (g/dl)	11,51±,2,87	10,59±,1,36	0,375
HCT (%)	0,399±0,41	0,399±0,47	0,680

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Discussion

Obesity is multifactorial nutritional disorder in pets. Many factors can predispose a cat to obesity, including genetics, the amount of physical activity and the energy content of the diet (German, 2006). The causes of obesity are not clear as there are many different variables that play a role in its development (Speakman, 2004).

Leptin and ghrelin are two hormones that maintain energy homeostasis. As an anorexigenic hormone, leptin is a means of long-term regulation of energy balance (Yalçın et al., 2017). Ghrelin and cholecystokinin in the short-term hormonal regulation of eating; Insulin, leptin and peptide YY are effective in long-term hormonal regulation. Leptin, a prototypical adipoquinolan, is the best-characterized of the adipokines for cats and dogs (Zoran, 2019). Leptin is an important regulator of fat mass, and its concentration in serum is positively correlated with fat mass (Hoenig et al., 2007).

In this study, in the serum analyzes collected after a 2-hour fasting in the morning in obese and normal body condition cats of different ages and genders, were decrease in leptin levels in obese cats, while in levels of ghrelin, glucose, alt and calcium an increase was observed. Leptin is positively correlated with body fat mass. It is a strong marker in obese cats. In parallel with the increase and decrease in leptin in the development and recovery phases of obesity, physiological increases and decreases in the vascularity of adipose tissue have been determined. This suggested that leptin acts as a local regulator of angiogenesis. (Crandall et al., 1997). Obesity occurs in the absence of leptin and high leptin levels(Auwerx and Staels, 1998). Decreased leptin production in adipocytes leads to the development of obesity (Friedman and Halaas, 1998). It has been known since 1997 that congenital leptin deficiency causes obesity in humans (Montague et al., 1997). The decrease in leptin in our study suggests that obese cats' congenital leptin deficiency and preference for diet food may be associated with weight loss processes and exercise before coming to the clinic. Appleton et al (2000) reported in their study that weight loss was associated with a decrease in leptin levels (Fried et al., 2000). In addition, it should be kept in mind that leptin secretion peaks between 00:00 and 4:00 hours due to its diurnal rhythm and is lowest between 8:00 and 12:00 hours, decreases in prolonged fasting and increases in overfeeding (Wallace, 2000). Ghrelin, an orexigenic hormone plays a role in the initiation of food intake (Yalçın et al., 2017). Orexigenic activation of ghrelin is regulated by neurons in the hypothalamus that harbor specific receptors. Ghrelin is a versatile metabolism regulator (Öztürk and Arpacı, 2008).

Leptin is known to have an effect on circulating ghrelin levels. Tschop et al. (2001) showed that fasting plasma ghrelin levels were negatively correlated with fasting plasma leptin levels in obese humans. However, in another study, fasting plasma leptin and ghrelin concentrations were not negatively correlated in obese children and adolescents (Ikezaki et al., 2002). Diabetes can be predicted to develop when the liver finally becomes insulin resistant and/or insulin secretion is too low to handle the increased glucose production (Hoenig, 2012). It can be difficult to discern possible causes of hyperglycemia in the cat.

Opitz (1990) found transient hyperglycemia in 320 cats in his study. The frequency and degree of stress hyperglycemia has been proven to be associated with different types of primary disease. Including animals with diabetes mellitus or pancreatic disease in this study; A glucose concentration equal to or greater than 140mg/dl (7.77mmol/l) in fasted animals was defined as hyperglycemia. Martin et al. (2010) showed that obese cats have higher glucose concentrations than lean cats in a study they conducted. In our study, the serum glucose levels of obese cats were found to be significantly higher than those of non-obese cats.

Hepatic circulatory disorders have been associated with obesity and fatty liver in humans. However, there is limited information in the veterinary literature regarding the effects of different body

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condition scores (BCS) on liver hemodynamic indices in dogs. Belotta et al. (2018), in the liver sonographic examination of 3 groups of dogs, which they separated according to body condition score; obese dogs found a higher percentage of abnormal hepatic vein spectral waves than ideal weight dogs. Accordingly, obesity was associated with changes in portal vein indices and hepatic vein spectral wave. These changes were accompanied by significant differences in some liver enzyme activities and may be a sign of early liver disease. In another study conducted on obese people, 29% of the patients had an elevated ALT enzyme (Engelmann et al., 2014). In another study, it was stated that adolescent obese people showed an increase in ALT levels compared to normal people (Man et al., 2017). In contrast, AST and GGT levels of the healthy group were higher in goats with liver metabolic dysfunction compared to the sick goats on day 15 of lactation (Kaya and Bozkurt, 2022). In our study, while an increase in ALT level was detected, there was no significant difference in ALP level between the two groups.

Obesity is largely caused by an imbalance in energy intake and expenditure. On the other hand, several studies have revealed that obese or diabetic patients are more likely to have micronutrient deficiencies such as vitamins and minerals. In addition to their effects on bone metabolism, vitamin D and calcium may contribute to the metabolic disorder associated with obesity (Karima et al. 2016). Obesity is associated with vitamin D deficiency, hyperparathyroidism, and secondary hypercalcemia (Shah and Chauhan, 2016). Morbidly obese patients are known to have abnormal calcium metabolism compared to non-obese patients, but the clinical significance of this is unknown (Hamoui et al., 2004). In our study, significant differences were found in calcium levels in obese cats compared to non-obese cats (<0.001). No significant hematological difference was detected between the obese and non-obese two cat groups, and it is in line with previous studies (Moura de Lima et al., 2021).

Conclusion

Obesity is an increasingly common health problem in cats and can predispose cats to many diseases. The obesity development process is affected by many factors. Leptin and Ghrelin seem to play a key role in the appetite center. In this study, Leptin and Ghrelin levels were examined in obese cats without a pathological disease. In the study, it was observed that these two hormones were negatively correlated with each other. While negative correlation was found with leptin in obese individuals, positive correlation was found with ghrelin. For drug studies targeting obesity and indirectly diabetes mellitus, further investigation of the effects of these two hormones would be meaningful.

Ethics Approval

This research was carried out on the basis of the permission of Mehmet Akif Ersoy University Local Animal Ethics Committee dated 17.03.2021 and numbered 744.

Conflict of Interest

The authors declare that there have no conflict of interests.

Author Contributions

The design of the study and evaluation of the results were executed by the contribution of Ş. AKGÜN and Ş. ŞAHİNDURAN. All authors also contributed to the preparation of the manuscript.

Acknowledgments

This study was supported by Burdur Mehmet Akif Ersoy University Scientific Research Projects Commission (Project No: 0762-YL-21).

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MAKU J. Health Sci. Inst. 2023, 11(3): 293-299.
doi: 10.24998/maeusabed.1334612

Mehmet Akif Ersoy University
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Research Article / Araştırma Makalesi

Histological Demostration of Changes in Connective Tissue Components in Uterine Tissue Undergoing Decidualization on Days 4th, 5th and 8th Days of Mause Pregnancy

Fare Gebeliğinin 4., 5. ve 8. Günlerinde Desidualizasyon Geçiren Uterus Dokusunda Bağ Dokusu Elemanlarındaki Histolojik Değişimin Gösterilmesi

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Abstract: This study examined the changes in connective tissue elements of the uterine undergoing decidualization on the 4th, 5th, and 8th days of pregnancy by histochemical methods. Forty Balb/c 6-8 weeks-old female mice divided into four groups as non-pregnant estrous phase, 4th, 5th, and 8th-day pregnancy models. Five µm thick sections were taken from paraffin blocks obtained from uterine tissues. Samples were stained with Hematoxylin&Eosin, Mallory Azan, Orsein, and Periodic Acid Schiff stains. As a result of the staining, the uterine tissue in the non-pregnant estrus phase showed standard histological structure. On the 4th day of pregnancy, the amount of intensely stained collagen and elastic fiber decreased on the 5th day of gestation; On the 8th day of pregnancy, it was determined that the density of the fibers increased again. As a result, both increased collagen and elastic fibers for its placement to an elastic-solid uterine tissue and increased carbohydrates for its nutrient needs and immune privilege were demonstrated in the uterus for the 4th-day embryo. The decrease in connective tissue elements with the acceleration of decidualization on the 5th and increased collagen and elastic fibers in the myometrium and the PAS + NK cells in the endometrium on the 8th-day was noted.

Keywords: Connective tissue, Decidualization, Histochemistry, Pregnancy.

Öz: Bu çalışmada, fare gebeliğinin 4., 5. ve 8. günlerinde desidualizasyon geçiren uterus dokusunun bağ dokusu elemanlarındaki değişim histokimyasal yöntemlerle incelendi. Çalışmada, 40 adet 6-8 haftalık Balb/c ırkı fareler, gebe olmayan östrus fazı, 4., 5. ve 8. gün gebelik modelleri şeklinde dört gruba ayrıldı. Uterustan elde edilen parafin bloklardan 5 µm kalınlığında kesitler alındı. Örnekler, Hematoksilen&Eosin, Mallory Azan, Orsein ve Periyodik Asit Schiff boyaları ile boyandı. Boyamalar sonucunda gebe olmayan östrus fazındaki uterus dokusunda standart histolojik yapı izlendi. Gebeliğin 4. gününde yoğun boyanan kollajen ve elastik lif miktarının gebeliğin 5. gününde azaldığı; gebeliğin 8. gününde ise liflerin yoğunluğunun tekrar arttığı belirlendi. Sonuç olarak, 4 günlük embriyonun uterus içerisine yerleşmesi ve ihtiyaçlarına rahat ulaşması için elastikiyete sahip sağlam bir uterus dokusu oluşumu kolajen ve elastik liflerin artışı da, beslenmesi için gerekli olan karbonhidrat artışı da PAS reaksiyonu ile gösterildi. 5. günde desidualizasyonun da hız kazanmasıyla bağ dokusu elemanlarındaki azalma, 8 günde ise embriyonunda büyümeye başlamasıyla miyometriumda kollajen ve elastik lif miktarının, endometriumda ise PAS+ NK hücrelerinin artışı dikkat çekti.

Anahtar Kelimeler: Bağ doku, Desidualizasyon, Histokimya, Gebelik.

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Geliş tarihi / Received : 04.08.2023
Kabul tarihi / Accepted: 12.10.2023

Introduction

Successful pregnancy depends on a healthy uterus suitable to receive and support a fertilized embryo and the process of decidualization. The stromal cells surrounding the embryo also change during gestation, a process crucial for implantation known as decidualization. The uterus is an essential organ that undergoes morphological and physiological changes during pregnancy to support the development of the embryo and fetus. The

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

uterine wall has three layers: the endometrium, myometrium, and perimetrium (Mescher, 2018). The endometrial mucosa is a thick layer of connective tissue containing numerous glands, fibroblasts, and abundant extracellular substances. The myometrium surrounds the endometrium and undergoes growth during pregnancy through the enlargement of smooth muscles (hypertrophy) and increased muscle fibers (hyperplasia). The myometrium contains collagen and elastic fibers, especially in the loose connective tissue between the muscle bundles, to strengthen the uterus during pregnancy. Fibroblasts, histiocytes, macrophages, and mast cells are also present (Kierszenbaum and Tres, 2021).

In mice, decidualization, the process of stromal cell transformation in the uterus, occurs after the blastocyst attaches to the uterine epithelium (Wang et al., 2020). Decidualization occurs in the anti-mesometrial side of the uterus, where implantation takes place (Croy et al., 2014). The connective tissue stromal cells change, and decidual cells form the decidua uterine mucosa called (Ramathal et al., 2010). Decidua formation in mice begins around the 4.5-5th day of pregnancy following implantation (Das, 2010; Ramathal et al., 2010). It has been reported in the literature that changes in the number and distribution of many cells and fibers in the uterine tissue in the preparation of the endometrium for embryo implantation, and development has been reported in the literature (Teodoro et al, 2003; Stumm and Zorn, 2007).

The aim of this study is to investigate the changes in the connective tissue elements of the uterine tissue undergoing decidualization on the 4th, 5th, and 8th days of pregnancy by histochemical methods and to contribute to the literature on this subject.

Materials and Methods

The Akdeniz University Animal Experiments Local Ethics Committee approved the experimental protocol with protocol number 2022.01.007. In the study, 40 Balb/c female mice, of about 6-8 weeks old and weighing 20±25 g. were provided from the Akdeniz University Experimental Animals Research and Application Center. Each mouse was kept in standard laboratory conditions with a 12-hour dark/light cycle at 21±2 °C room temperature.

The mice were randomly divided into four groups were established, with 10 animals in each group representing the non-pregnant estrus phase (EP) and days 4 (P4), 5 (P5), and 8 (P8) of pregnancy. While forming the groups, vaginal smears were made to determine the estrus phase of non-pregnant female mice and stained with toluidine blue. Mice with a squamous (crustaceous) structure and a predominance of large, non-nucleated epithelial cells were included in the experiment. Two female mice were left in the same cage with a male mouse to mate, and pregnancy was detected by vaginal plate. Females with a vaginal plaque were accepted on the 1st day of pregnancy. To determine whether females on the 4th day of pregnancy are pregnant, one of the uterine horns was washed with PBS, and the tubal fluid obtained after washing was examined under the microscope, and the presence of blastocyst was determined. Tissue samples were taken from the other uterine horn not washed for the blastocyst. To determine whether the females were pregnant on the 5th day of pregnancy, females were sacrificed 3-4 minutes after the tail vein injection of Chicago Blue. Mice whose implantation sites were observed as blue bands were confirmed to be pregnant. On the 8th day of pregnancy, the implantation sites can be seen with the naked eye. Females with implantation sites were included in the experiment. The mice were anesthetized with ketamine (100 mg/kg; Alfasan) + xylazine hydrochloride (10 mg/kg; Bayer). Mice were sacrificed by cervical dislocation, and uterine tissue samples were collected and fixed in a 10% formaldehyde solution. Paraffin blocks were prepared from these tissues, and sections with a thickness of 5 μm were obtained. The sections were deparaffinized and rehydrated. The samples' histopathology was evaluated via Hematoxylin&Eosin (H&E) staining and also preferred to stain with Mallory's Azan (MA) for collagen fibers, Orcein for elastic fibers, and

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Periodic Acid Schiff (PAS) to show glycogen content in uterine decidua cells.. The slides were examined using an axioplan microscope (Zeiss, Germany) and photographed.

Results

The examinations performed on tissue sections stained with Mallory Azan, Orsein, and PAS stain in the non-pregnant estrus phase and on the 4th, 5th, and 8th days of pregnancy are shown in Figure 1. The connective tissue of the endometrial layer for EP appeared normal, and the collagen fiber arrangement in the uterus's surface and deep layers showed a regular course. However, the density of elastic fibers in the uterine tissue was low, as observed in the preparations stained with Orcein. The PAS reaction indicated a normal appearance of the basement membrane, uterus, and glandular epithelial surface in the uterine tissue (Figure 1.EP). On the 4th day of pregnancy (Figure 1.P4), notable changes were observed in the uterine tissue. Decidualization, the process of preparing the endometrium for implantation, was spreading toward the anti-mesometrial side. The endometrial stroma exhibited a looser structure in this region, and the uterine glands were predominantly located near the myometrium rather than in the decidual area. Collagen fibers were present between the endometrial stromal cells and around the glands, as well as in the connective tissue between the smooth muscles of the myometrium. Elastic fibers were observed on the surface parts of the uterine epithelium. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, and glandular epithelial cells, indicating the presence of glycogen in the uterine decidua cells.

Further changes were evident in the uterine tissue by the 5th day of pregnancy (Figure 1.P5). Blood vessels originating from secondary decidual cells were observed in the decidual area, indicating increased vascularization. The maternal blood vessels dilated, and the glands in the endometrial stroma became scattered and more minor. Decidualization occurred predominantly in the anti-mesometrial area, leading to the emergence of the primary decidual region. Collagen fibers became sparse in the endometrial stroma, and their density decreased in the connective tissue between the smooth muscles of the myometrium. Weak staining of elastic fibers was observed between the longitudinal muscle bundles of the myometrium. Elastic fibers arranged in black strands were also observed around the luminal epithelium. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, surface of glandular epithelial cells, and vessel walls, indicating the presence of glycogen.

On the 8th day of pregnancy (Figure 1.P8), as the primary decidual zone regressed and the secondary decidual zone emerged, more intense collagen fibers were observed around the decidual cells in the endometrium. Elastic fibers were observed between the longitudinal muscle bundles of the myometrium, and positive staining was detected on the surface of blood vessels. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, surface of glandular epithelial cells, and vessel walls. Additionally, a granular PAS reaction was strongly detected in decidual cells, and the cells thought to be uterine natural killer (uNK) cells were also observed.

These observations provide insights into the dynamic changes that occur in the uterine tissues during different stages of pregnancy, highlighting alterations in the histological structure, distribution of collagen and elastic fibers, and the presence of glycogen in uterine decidua cells.

Discussion

The development of the embryo to the blastocyst stage, implantation into the uterine endometrium, and forming a functional placenta are crucial for establishing a pregnancy. The success of implantation ultimately depends on ensuring proper trophoblast growth and regulating invasion into the endometrium to establish a blood supply for the conceptus (Dimitriadis et al., 2005).

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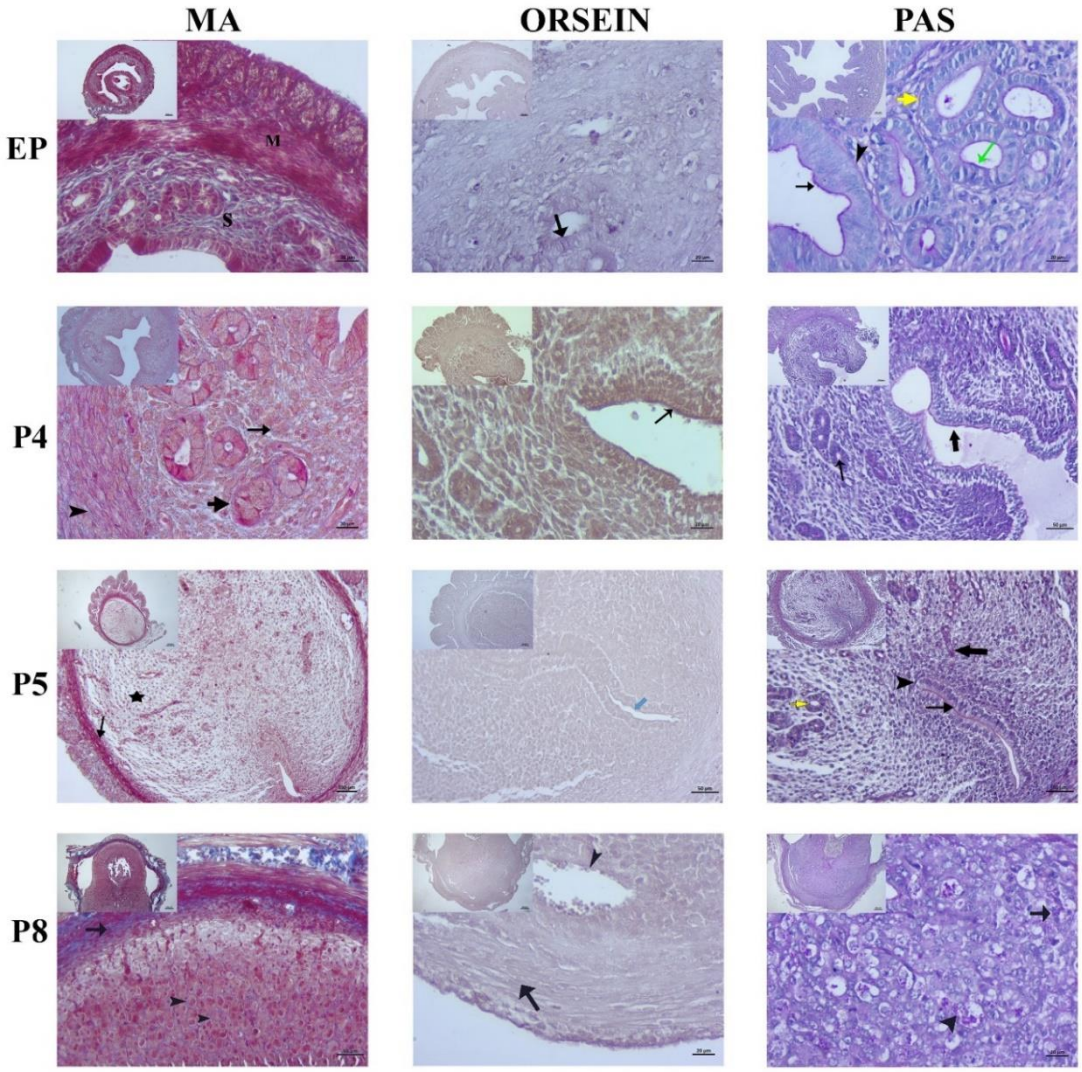

Figure 1. Light microscopic images of mouse non-pregnant estrus phase and uterine tissue from the 4th, 5th, and 8th day of pregnancy. Regular distribution of collagen fibers in the connective tissue of the endometrial stroma (S) and myometrium (M) in the non-pregnant estrus phase (EP) mouse uterus. In the P4, collagen fibers were seen between stromal cells of the uterine endometrium (thin arrow), around the uterine glands (thick arrow), and in the connective tissue between smooth muscles of the myometrium (arrowhead). In the P5, Decreased density of collagen fibers (asterisk), which are scattered and sparse in the endometrial stroma, in the connective tissue between the smooth muscles of the myometrium (arrow). In the P8, dense collagen fibers in the myometrium (arrow), collagen fibers around decidual cells in the endometrium (arrowheads). MA staining method. Bar: 20-100 μm. The density of elastic fibers in the surface parts of the uterine epithelium (arrow) in the P4 and uterine gland (arrow) in the EP. Reduced density of elastic fibers on the surface of the uterine epithelium (blue arrow) in the P5. Increased density of elastic fibers between the muscle bundles of the myometrium (arrow). Also, prominent elastic fiber structure on the surface of the blood vessels (arrowheads) in the P8. Orcein Staining method. Bar: 20-100 μm. Normal appearance of the basement membrane (yellow arrow), uterus (thin arrow and arrowhead), and glandular epithelial surface (green arrow) in the uterine tissue in the EP. PAS positivity on the surface parts of the uterine epithelium (thick arrow) and the surface of uterine gland epithelial cells (thin arrow) in the P4. PAS staining method. PAS reaction with decreased intensity on the surface of the uterine epithelium (arrow) and basement membrane (arrowhead) and PAS reaction on the surface of the uterine gland epithelial cells (yellow arrow) and vessel walls in the uterus (thick arrow) in the P5. Strong PAS reaction in granular form in uterine decidua cells (arrowhead) and uNK cells (arrow) in the P8. PAS staining method. Bar: 20-100 μm.

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This study was planned to investigate histochemical changes in connective tissue elements in the non-pregnant estrous phase of mouse and uterine tissue undergoing decidualization on days 4, 5, and 8 of gestation at the light microscopic level.

Decidualization is the most important determinant of pregnancy success. Decidual stromal cells help vascular adaptation, suppress inflammation, provide tolerance to fetal antigens, and are genetically reprogrammed versions of endometrial stromal cells. Unlike many mammals, decidualization tissue is formed in humans every menstrual cycle. In other species, this can occur in the presence of a blastocyst (Ng et al., 2020).

Electron microscopic examination of the uterus of pregnant mice (Abrahamsohn, 1983) showed that on day 5 of gestation, decidual cells with round nuclei and free ribosomes predominated in the cytoplasm; on days 6 to 8, the cytoplasm of these cells contained numerous granular and agranular endoplasmic reticulum, microfilament bundles, and lipid droplets in addition to well-developed Golgi complexes, mitochondria, and lysosomes. Another study reported that collagen fibers of approximately 40 nm in size in non-pregnant mouse uterine endometrium were transformed by decidual cells into fibrils larger than 400 nm showing irregular profiles (Croy et al., 2014). Spiess et al.(2007?) argued that collagen types I, III, and V are the main components of non-pregnant and pregnant mouse endometrium. When they looked at the immunolocalization of Collagen types I, III, and V, they found that it differed between implantation and inter-implantation sites in the mouse uterus during early pregnancy; Collagen type I was widely distributed in the non-decidualized endometrial stroma of the inter-implantation sites; Collagen type V was weakly expressed in the non-decidualized stroma throughout all periods but was more abundant in the decidualized areas on day 7 of pregnancy. Day ? of pregnancy, but was expressed in more significant amounts in decidualized regions (Spiess et al., 2007). In addition, the same researchers also determined that Collagen type V is associated with tiny blood vessels in the endometrium. This study determined that the density of collagen and elastic fibers stained on the 4th day of pregnancy, and decreased on the 5th day of pregnancy. The density of these fibers increased on the 8th day of pregnancy.

Various components of the endometrial extracellular matrix, especially collagen fibrils, undergo morphological and biochemical changes during rodent decidualization (Alberto-Rincon et al., 1989). In a study, it was reported by light and electron microscopic studies that collagen concentration increased in the endometrium of mice on the 7th and 8th days of pregnancy, and collagen fibrils accumulated around the decidual cells (Teodoro et al, 2003). In In this study, it was found an increase in collagen density, especially in the myometrium on the 8th day of gestation, in parallel with the mentioned information. The remodeling of ESM in the early stages of pregnancy in mice was investigated by Croy et al.,(2014) argued that collagen-containing acid phosphatase-positive granules were found in endometrial fibroblasts, suggesting that intracellular degradation of collagen occurs. The same researchers showed the presence of several collagen fibers in the endometrial stroma during the preimplantation period by analysis with transmission electron microscopy. Mutluay (2015) reported that the uterine endometrial connective tissue had a typical structure on day 0, the collagen fiber structure showed a regular course in the surface and a deep endometrial layer of the uterus, and on the 1st day of pregnancy, collagen fibers spread towards the myometrium from the bottom of the decidual area where there was cellular concentration. In this study, the endometrial connective tissue of the non-pregnant mouse uterus in the estrus phase had a standard structure, and the collagen fiber structure in the surface and deep endometrial layer of the uterus showed a regular course.

In a study with fibrillin-1, a glycoprotein involved in the formation of elastic fibers, it was reported that it was found between endometrial fibroblasts and decidual cells in mice before and after implantation, respectively, and that the organization of fibrillin-1 and its distribution in

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various regions of the endometrial stroma depended on the stage of pregnancy (Stumm and Zorn, 2007). In the same study, histochemical staining of elastic fibers revealed that elastic fibers were almost absent in the endometrial stroma during pregnancy. In contrast to this study, elastic fibers arranged in black strands were found around the endometrial luminal epithelium on days 4 and 5 of mouse pregnancy. In addition, on the 8th day of gestation, it was determined that elastic fibers were weakly stained between the myometrium muscle bundles.

In a study conducted on the rat, it was reported by PAS staining that the basement membrane structure in the uterine tissue had a regular appearance on all gestational days and continued uninterruptedly under the epithelial cells (Mutluay, 2015). In another study, PAS positivity was reported in the basement membrane on the fourth day of pregnancy in mice (Koç, 2019). In parallel with these studies, PAS positivity was found in uterine tissue during the non-pregnant estrus phase and pregnancy days.

Studies have shown that the glycoconjugate content in the cytoplasmic granules of uterine Natural Killer (uNK) cells reacts with the periodic acid Shiff's reagent (Stewart and Peel, 1980; Sur et al., 2015). Sur et al. reported that uNK cells showing intense PAS positivity were found in the decidua basalis in mice in the middle and last days of pregnancy (Sur et al., 2015). The number of these cells was reported to be very high in the middle of pregnancy, and a significant decrease was observed towards the end of pregnancy. In another study investigating the 4th, 10th, and 17th days of pregnant mice, it was reported that the cells thought to be PAS-positive uNK reached the highest amount on the tenth gestation day (Koç, 2019). In this study, cells thought to be PAS + granulated uNK were found in the uterine endometrium on day 8 of mouse pregnancy.

In conclusion, it was determined that the connective tissue content of the mouse uterus in the non-pregnant estrus phase and the mouse uterus on the 4th, 5th, and 8th days of pregnancy underwent different structural changes using by histochemical methods. The endometrial connective tissue in the non-pregnant mouse uterus in the estrus phase was observed to have a standard structure. On the 4th day of pregnancy, decidualization was observed to spread toward the anti-mesometrial side of the uterine tissue, where implantation would occur. On the 5th day of gestation, vascularization increased in the decidual area, maternal blood vessels dilated, and the glands in the endometrial stroma were scattered and considerably smaller. It was observed that decidualization occurred in the anti-mesometrial area, and the primary decidual zone appeared. On the 8th day of pregnancy, when the primary decidual zone regressed and the secondary decidual zone emerged, collagen tissue, denser in the myometrium, was observed around the decidual cells in the endometrium. At the same time, more dense elastic fibers were also observed in the myometrium. These data support other studies showing ESM remodeling in mouse endometrial stroma at the onset of pregnancy.

Source(s) of Funding:

This article was supported within the scope of TUBITAK 2209-A University Students Research Projects Support Program 2021, 2 semesters by application 1919B012104121.

Conflict(s) of Interest/ Disclosure(s):

The authors declare no conflict of interest.

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