Mehmet Akif Ersoy Üniversitesi

Sağlık Bilimleri Enstitüsü Dergisi

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Mehmet Akif Ersoy Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi
YAZARLARA BİLGİ

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).

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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).

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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.

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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).
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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..
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IV- Submission of Articles (Blind Peer-Review)

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Araştırma Makaleleri / Research Articles

MAKU J. Health Sci. Inst. 2021, 9(1): 1-6.
doi: 10.24998/maeusabed.869812

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

Research Article / Araştırma Makalesi

Assessing the Susceptibilty of Some Gut Bacteria to the Extract from Needles of Turkish Pine

Bazı Bağırsak Bakterilerinin Türk Çamı İğnelerinden Elde Edilen Ekstrakta Duyarlılıklarının Değerlendirilmesi

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Abstract: Plant extracts have the potential to be safe alternatives to antibiotics that disrupt the gut flora. The aim of the present study was to assess the susceptibility of some gut bacteria to the extract from needles of Turkish pine (*Pinus brutia* Ten.) using microdilution method in an anaerobic chamber. Turkish pine needle extract promoted the growth of *Bifidobacterium bifidum*, *Bifidobacterium infantis*, and *Lactobacillus acidophilus* from gut commensals at 0.2-6.25 mg/mL, 0.4-6.25 mg/mL, and 0.4-1.6 mg/mL dose ranges, respectively ($P<0.05$). However, the extract had a potential inhibitory activity on *Bifidobacterium* species starting from 12.5 mg/mL, on *L. acidophilus* starting from 6.25 mg/mL, and on *L. casei* starting from 3.13 mg/mL concentrations ($P<0.05$). Minimal inhibitory concentration (MIC) was 25 mg/mL for all commensal species ($P<0.05$). Turkish pine needle extract also showed a potential inhibitory activity against gut pathogens *Escherichia coli* and *Clostridium perfringens* from 0.4 mg/mL dose and against *Staphylococcus aureus* and *Fusobacterium nucleatum* from 0.8 mg/mL dose ($P<0.05$). The MICs were 6.25, 12.5, 25, and 50 mg/mL for *S. aureus*, *F. nucleatum*, *E. coli*, and *C. perfringens*, respectively ($P<0.05$). It was concluded that using the Turkish pine needle extract in a dose range of 0.2-6.25 mg/mL, where it protected most of the commensal bacteria and was toxic against some of the pathogens, might produce desirable impacts in the gut.

Keywords: Antibacterial, Gut bacteria, MIC, Plant extracts, Turkish pine needle.

Öz: Bitki ekstraktları, bağırsak florasını bozan antibiyotiklere güvenli alternatifler olma potansiyeline sahiptir. Bu çalışmanın amacı, anaerobik bir kabinde mikrodilüsyon yöntemi kullanılarak bazı bağırsak bakterilerinin Türk çamı (*Pinus brutia* Ten.) iğnelerinden elde edilen ekstrakta duyarlılığını değerlendirmektir. Türk çamı iğnesi ekstraktı, bağırsak yerleşik bakterilerinden *Bifidobacterium bifidum*, *Bifidobacterium infantis* ve *Lactobacillus acidophilus*'un büyümesini sırasıyla 0,2-6,25 mg/mL, 0,4-6,25 mg/mL ve 0,4-1,6 mg/mL doz aralıklarında uyarmıştır ($P<0,05$). Bununla birlikte, ekstrakt, *Bifidobacterium* türleri üzerine 12,5 mg/mL, *L. acidophilus* üzerine 6,25 mg/mL ve *L. casei* üzerine ise 3,13 mg/mL konsantrasyonlardan başlayarak potansiyel bir inhibitör aktivite göstermiştir ($P<0,05$). Minimal inhibitör konsantrasyonun (MİK), tüm yerleşik türler için 25 mg/mL olduğu gözlenmiştir ($P<0,05$). Türk çamı iğnesi ekstraktı ayrıca bağırsak patojenleri olan *Escherichia coli* ile *Clostridium perfringens*'e karşı 0,4 mg/mL dozdan ve *Staphylococcus aureus* ile *Fusobacterium nucleatum*'a karşı ise 0,8 mg/mL dozdan başlayarak potansiyel bir inhibitör aktivite göstermiştir ($P<0,05$). *Staphylococcus aureus*, *F. nucleatum*, *E. coli* ve *C. perfringens* için MİK değerlerinin sırasıyla 6,25, 12,5, 25 ve 50 mg/mL olduğu gözlenmiştir ($P<0,05$). Türk çam iğnesi ekstraktının, yerleşik bakterilerin çoğunu koruduğu ve bazı patojenlere karşı toksik olduğu 0,2-6,25 mg/mL doz aralığında kullanılmasının bağırsaklarda arzu edilen etkiler oluşturabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Antibakteriyel, Bağırsak bakterileri, Bitki ekstraktları, MİK, Türk çamı iğnesi.

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Introduction

The gut flora is a large and dynamic bacterial community that participates in normal physiological functions, but also protects against pathogens by forming a defensive barrier and competing for available substrates (Ahn et al., 1998; Canny and McCormick, 2008). Balance between commensal and pathogenic species has great importance in terms of maintaining the gut health. Conventional antibiotics can prevent the growth of both commensal and pathogenic species and decrease diversity of the gut flora (Bäumler and Sperandio, 2016). In recent years, many studies have been focused on plant extracts as natural alternatives for antibiotics.

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Turkish pine or Turkish red pine (*Pinus brutia* Ten.) is the most common pine species in Turkey which has ability to grow on a wide range of Mediterranean- and Black Sea regions (Balaban Ucar et al., 2013). The use of Turkish pine in the forest products industry has been widely accepted because of its suitability for the manufacture of desirable products (Üner et al., 2011). In a previous study, we observed that the extract from barks of Turkish pine, which containing phenolic compounds, had a potential to inhibit pathogenic bacteria in the gut while protect commensal ones (Demirtaş, 2020). Furthermore, *Pinus densiflora* (Japanese pine) leaf derived components, (1R)-(+)-α-pinene and limonene, strongly inhibited the growth of *Staphylococcus aureus*, *Escherichia coli,* and *Clostridium perfringens* without adverse effects on the growth of five commensal bacteria (*Bifidobacterium bifidum, B. longum*, *B. adolescentis*, *Lactobacillus acidophilus*, and *L. casei*) (Hwang and Lee, 2002). The needle of Turkish pine also contains several flavonoids (Kaundun et al., 1997) and essential oil components (Yener et al., 2014) with antioxidant and antibacterial capacity. However, the effects of extract from Turkish pine needle on gut bacteria have not been evaluated previously. Therefore, the aim of the present study was to assess the susceptibility of some gut bacteria to the extract from needles of Turkish pine.

Materials and Methods

Turkish pine needle extract

Turkish pine needle extract was provided by Kale Naturel Herbal Products Company, Ltd., Balikesir, Turkey.

Preparation of bacteria

Commensal bacterial species used in antibacterial tests were *Bifidobacterium bifidum* ATCC 29521, *Bifidobacterium longum* subsp. *infantis* ATCC 15697, *Lactobacillus acidophilus* ATCC 4356, and *Lactobacillus casei* ATCC 393. Pathogenic bacterial species were *Staphylococcus aureus* subsp. *aureus* ATCC 12600, *Escherichia coli* ATCC 11775, *Clostridium perfringens* ATCC 13124, and *Fusobacterium nucleatum* subsp. *nucleatum* ATCC 25586. The growth medium was Mann Rogosa Sharpe (MRS) broth for *B. infantis*, *L. acidophilus*, and *L. casei*; MRS broth with 0.05% cysteine (MRS-C) for *B. bifidum*; tryptic soy broth (TSB) for *S. aureus*; Luria–Bertani (LB) medium for *E. coli* and; liquid form of medium 2 (Hobson, 1969) for *C. perfringens* and *F. nucleatum*. Medium 2 was prepared under CO_2 as described by Hobson (1969) with only slight modification. Trypticase peptone was used instead of casitone in medium 2 (Table 1). All strains were grown for 24 h at 37°C under an atmosphere of 80% N_2, 10% CO_2, and 10% H_2 in an anaerobic chamber (Don Whitley, Whitley DG250, West Yorkshire, UK).

Table 1. Composition of medium 2 (for 100 mL)

Component	
Trypticase peptone (BD 211921 Bacto™)	1.0 g
Yeast extract (Sigma Y1625)	0.25 g
Mineral solution 1	15 mL
Mineral solution 2	15 mL
Clarified rumen fluid	20 mL
Resazurin (Sigma R7017)	0.0001 g
Sodium lactate (70% w/v)	1.0 g
Glucose	0.2 g
Maltose	0.2 g
Cellobiose (Sigma 22150)	0.2 g
Cysteine HCl (Sigma C7880)	0.05 g
$NaHCO_3$ (Sigma S5761)	0.4 g
Deionized water	to 100 mL

Mineral solution 1 – 3 g/L K_2HPO_4 (Sigma P3786); Mineral solution 2 – 3 g/L KH_2PO_4 (Sigma P9791), 6 g/L $(NH_4)_2SO_4$ (Sigma A4915), 6 g/L NaCl (Sigma S7653), 0.6 g/L $MgSO_4 \bullet 7H_2O$ (Sigma 230391), and 0.6 g/L $CaCl_2$ (Sigma C1016). Clarified rumen fluid – ruminal fluid brought from the slaughterhouse was mixed and filtered through three layers of cheesecloth to partition into liquid and solid (digesta) fractions. The liquid fraction was centrifuged at 15000 rpm, and the clear supernatant was used as a component of the anaerobic medium.

Antibacterial screening

The effect of Turkish pine needle extract on the growth of gut bacteria was tested by a broth dilution method in the anaerobic chamber (CLSI, 2016). A stock solution was prepared by dissolving pine needle extract in 50% ethanol. Ten serial dilutions of the extract starting at a concentration of 50 mg/mL were prepared from the stock solution in the bacterial strain specific

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growth media. Two hundred microliters of each dilution were added to wells of a 96-well plate. Next, 20 µL of the test bacteria suspension was inoculated into each well. Each bacterium was tested in triplicate wells. Plates were incubated for 24 h at 37°C in the anaerobic chamber. Bacterial growth was detected with a microplate reader at 600 nm (Epoch, BioTek, USA). The minimal inhibitory concentration (MIC) is defined as the lowest concentration of added extract at which no significant bacterial cell growth was observed. A significantly lower OD_{600} value compared to control dose (0 mg/mL) was accepted as potential inhibitory activity (Ko et al., 2018) while significantly higher value was accepted as stimulatory effect (Das et al., 2015).

Statistical analyses

Statistical analysis was carried out by the use of one-way ANOVA followed by Dunnett's test. Each well of a 96-well plate was an experimental unit. A probability value at $P<0.05$ was considered statistically significant.

Results

Effects of Turkish pine needle extract on gut bacteria are showed in Figure 1 and Figure 2. Turkish pine needle extract promoted the growth of *B. bifidum*, *B. infantis*, and *L. acidophilus* from gut commensals at 0.2-6.25 mg/mL, 0.4-6.25 mg/mL, and 0.4-1.6 mg/mL dose ranges, respectively ($P<0.05$). That effect was more obvious for *B. infantis*. However, the extract had a potential inhibitory activity on *Bifidobacterium* species starting from 12.5 mg/mL, on *L. acidophilus* starting from 6.25 mg/mL, and on *L. casei* starting from 3.13 mg/mL concentrations ($P<0.05$). The MIC was 25 mg/mL for all commensal species ($P<0.05$) (Table 2). Turkish pine needle extract also showed a potential inhibitory activity against gut pathogens *E. coli* and *C. perfringens* from 0.4 mg/mL dose and against *S. aureus* and *F. nucleatum* from 0.8 mg/mL dose ($P<0.05$). The MICs were 6.25, 12.5, 25, and 50 mg/mL for *S. aureus*, *F. nucleatum*, *E. coli*, and *C. perfringens*, respectively ($P<0.05$) (Table 2).

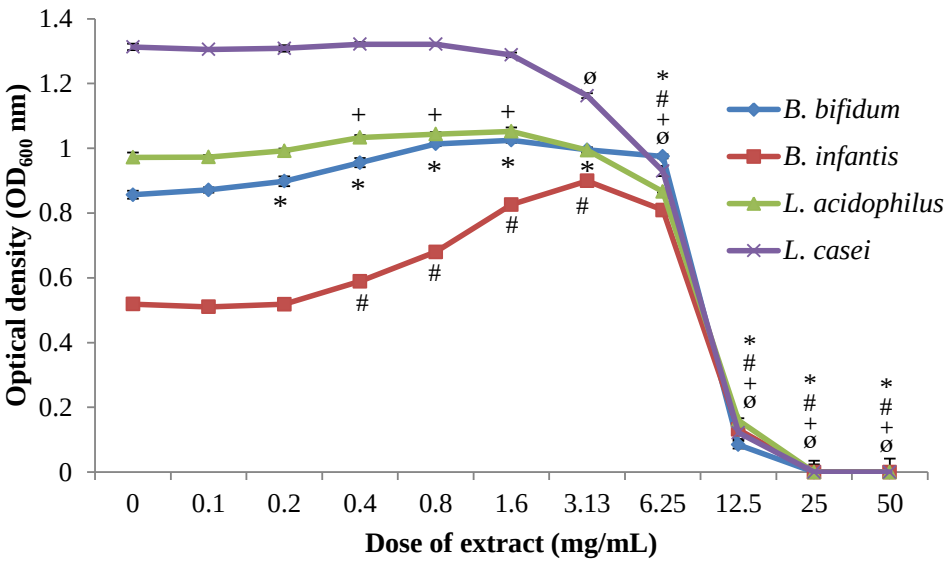

Figure 1. Effects of Turkish pine needle extract against commensal bacteria from the gut. The results represent the mean ± standard error. $^{*}P<0.05$, extract treated culture vs *B. bifidum* control; $^{\#}P<0.05$, extract treated culture vs *B. infantis* control; $^{+}P<0.05$, extract treated culture vs *L. acidophilus* control; and $^{ø}P<0.05$, extract treated culture vs *L. casei* control. Control level was 0 mg/mL of the extract.

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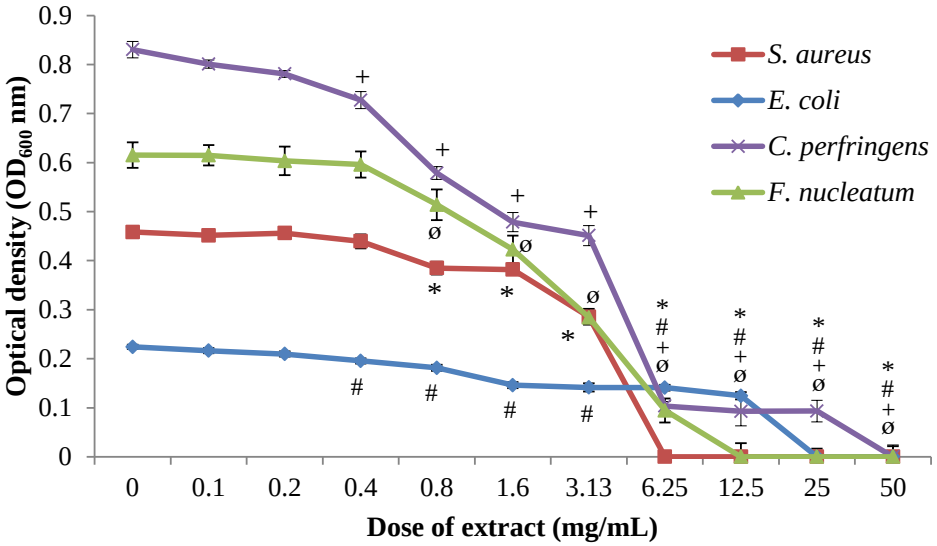

Figure 2. Effects of Turkish pine needle extract against pathogenic bacteria from the gut. The results represent the mean ± standard error. $^{*}P<0.05$, extract treated culture vs *S. aureus* control; $^{\#}P<0.05$, extract treated culture vs *E. coli* control; $^{+}P<0.05$, extract treated culture vs *C. perfringens* control; and $^{\circ}P<0.05$, extract treated culture vs *F. nucleatum* control. Control level was 0 mg/mL of the extract.

Table 2. Minimum inhibitory concentration (MIC) values of Turkish pine needle extract on gut bacteria.

Bacteria	**MIC values (mg/mL)**
Commensals	
B. bifidum	25
B. infantis	25
L. acidophilus	25
L. casei	25
Pathogens	
S. aureus	6.25
E. coli	25
C. perfringens	50
F. nucleatum	12.5

Discussion

The presence of a diverse and balanced bacterial community in the gut is of great importance for host physiology. Disruption of commensal flora in the gut is one of the major complications encountered in the treatment of infections with antibiotics (Bäumler and Sperandio, 2016). Accordingly, to determine the safe dose range of therapeutic agents that protects commensal bacteria while suppressing pathogens has great importance in terms of gut health. Turkish pine needle extract at low concentrations stimulated the growth of *B. bifidum*, *B. infantis*, and *L. acidophilus* from commensals, more prominently for *B. bifidum*. However, this stimulatory effect turned into a potential inhibitory effect on *Bifidobacterium* species starting from 12.5 mg/mL and on *L. acidophilus* starting from 6.25 mg/mL concentrations. The extract completely inhibited all commensal species at 25 mg/mL. Although there is no literature on the effects of Turkish pine needle extract on commensal gut bacteria, it was reported that low doses of several plant metabolites could stimulate bacterial growth in the gastrointestinal tract while high doses induced inhibition (Patra et al., 2012; Demirtas et al., 2019; Goker and Demirtas, 2020). Aldehydes, one of the plant secondary metabolites from the green leaf volatiles family, moderately promote the growth of *L. acidophilus* and *B. bifidum* at lower concentrations while had inhibitory effects at higher concentrations in a previous study (Goker and Demirtas, 2020). *Trans*-2-decenal, also an aldehyde from green leaf volatiles, stimulated the growth of *Fibrobacter succinogenes*, which is a fibrolytic bacterium from the rumen, at low doses

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(Demirtas et al., 2019). Similarly, saponins, another group of phytochemicals, encouraged *in vitro* bacterial growth and feed utilization in the rumen at low doses while they exhibited inhibition at high doses (Patra et al., 2012).

Escherichia coli and *S. aureus* are common foodborne pathogens that can cause severe gastro-intestinal illness (Ørskov and Ørskov, 1992; Rajkovic, 2014). The MIC value of Turkish pine needle extract for *E. coli* was 25 mg/mL in the present study. There is no literature on the effects of Turkish pine needle extract on pathogenic gut bacteria. However, Hmamouch et al. (2001) reported that the MIC value of the essential oil extracted from the needles of *P. brutia* grown in Morocco was higher than 10 mg/mL for *E. coli* (ATCC 25922). This result is consistent with the result of this study. On the other hand, it was observed that *S. aureus* was the most sensitive bacterium to Turkish pine needle extract in the present study. The extract exhibited inhibitory activity against *S. aureus* at 6.25 mg/mL dose. Extract from pine needles of *Cedrus deodara* (Himalayan cedar), with the main antibacterial component of shikimic acid, inhibited the growth of *S. aureus* (ATCC 25923) at 0.78 mg/mL (Zeng et al., 2012). The difference in MIC values is probably due to the difference in bacterial strains and also due to active ingredients in needles of the pine trees from the different origins. The dominant flavonoids found in the needles of *P. brutia* were reported as quercetin (41%), kaempferol (29%), and isorhamnetin (%23) (Kaundun et al., 1997) while the main essential oil component was reported as β-pinene (Yener et al., 2014). In this study, one or more of these active ingredients, that were likely to be contained in the extract, might be responsible for the antibacterial effects.

Fusobacterium nucleatum, which is obviously associated with colorectal cancer (Shang and Liu, 2018), was more sensitive to Turkish pine needle extract than *C. perfringens* in the present study. Extract from the barks of *P. brutia* also had an inhibitory potential on this bacterium from 150 µg/mL concentration in a previous study (Demirtas, 2020). On the other hand, *C. perfringens*, which is generally linked to gastrointestinal symptoms such as vomiting and diarrhea (Keeratirathawat et al., 2013), was the most resistant species to the used extract in this study. Turkish pine needle extract inhibited the growth of this bacterium at 50 mg/mL. Keeratirathawat et al. (2013) also reported that oils from the needles of four different *Pinus* species (*Pinus radiata*, *P. pinaster*, *P. sylvestris,* and *P. nigra*) did not exhibit any antibacterial activity against *C. perfringens*.

It was concluded that using the Turkish pine needle extract in a dose range of 0.2-6.25 mg/mL, where it protected most of the commensal bacteria and was toxic against some of the pathogens, might produce desirable impacts in the gut. Further *in vitro* and *in vivo* studies required to clarify its beneficial effects on the gut health.

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Research Article / Araştırma Makalesi

Evaluation of Antibacterial Activities of Stryax Liquidus on Staphylococcus aureus on Stainless Steel Surface

Sığla Yağının Paslanmaz Çelik Yüzeyde Staphylococcus aureus Üzerine Antibakteriyel Aktivitesinin Değerlendirilmesi

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Abstract: Sığla tree (*Liquidambar orientalis* Miller) is an endemic species in Turkey. Styrax liquidus obtained from Sığla tree and it has antiparasitic and antibacterial properties. *Staphylococcus aureus* is an important agent of mastitis. This pathogen can be found in milk and on the milk collection tank surfaces and it can produce some types of toxins. Staphylococcal enterotoxins may cause food poisoning. In this study; it was aimed to investigate the effects of the styrax liquidus solution on the bacterial culture applied to the stainless-steel surface, on different periods, experimentally. As a result of the study, it was determined that styrax liquidus was effective on *S. aureus* on the surface of the bulk tank milk at 5%, 10%, 15% and 20% concentrations. It was determined that styrax liquidus was reduced population of *S. aureus* level of 7.94 log cfu/ml. Styrax liquidus could be used as a natural antimicrobial agent in industrial surface cleaning. This is the first study to determine the disinfection properties of styrax liquidus.

Keywords: Styrax liquidus, Sığla tree, *Staphylococcus aureus*, Milk.

Öz: Sığla ağacı (*Liquidambar orientalis* Miller) Türkiye'de endemik bir ağaç türüdür. Bu ağacın özünden elde edilen sığla yağının antiparaziter ve antibakteriyel özellikleri bulunmaktadır. *Staphylococcus aureus* önemli bir mastitis etkenidir. Süt ve süt toplama tank yüzeylerinde bulunması ve salgıladığı toksinler gıda zehirlenmeleri oluşturabilir. Bu çalışmada; deneysel olarak paslanmaz çelik yüzeye uygulanan bakteri kültürü üzerine farklı sürelerde uygulanan sığla yağı içerikli solüsyonun etkilerinin araştırılması amaçlanmıştır. Çalışma sonucunda sığla yağının %5, %10, %15 ve %20 konsantrasyonlarda süt toplama tankı yüzeyinde tüm konsantrasyonlarda *S. aureus* üzerinde etkili olduğu tespit edilmiştir. Sığla yağının *S. aureus* varlığı üzerinde 7,94 log cfu/ml inaktivasyon gerçekleştirdiği belirlenmiştir. Sığla yağı endüstriyel anlamda yüzey temizliğinde doğal bir antimikrobiyal ajan olarak kullanılabilir. Bu çalışma sığla yağının dezenfeksiyon özelliklerinin belirlenmesi bakımından ilk çalışma özelliğindedir.

Anahtar Kelimeler: Sığla Ağacı, Sığla Yağı, *Staphylococcus aureus*, Süt.

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Introduction

Milk is one of the most important food in human nutrition (Haug et al., 2007). Especially for children in their growing age, it is necessary to have sufficient milk in their diets for adequate and balanced nutrition (Kandpal et al., 2012). Microbial contamination of milk is a concern for the food industry (Keyvan et al., 2018; Turkoglu and Keyvan, 2019; Keyvan et al., 2020). Especially some microorganisms that are capable of forming biofilms can maintain their vitality on these surfaces and cause contamination (Engel et al., 2017). Surface properties also play an important role in the occurrence of microbial contamination. Stainless steel is a preferred material for the food industry due to its physicochemical properties, low cost, resistance to corrosion, processing advantage and mechanical durability. In addition to these good properties, stainless steel surfaces also have a high free surface energy that causes free bacterial binding and hydrophilic properties in favor of biofilm formation (Chmielewski and Frank, 2003; Van Houdt et al., 2010).

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Staphylococcus aureus is a gram-positive bacterium and it can produce some types of toxin. Foodborne intoxications may occure due to consumption of contaminated food with these toxins (Le Loir et al., 2003). Meat products, poultry and egg products, milk and dairy products are food sources responsible for staphylococcal food poisoning (Normanno et al., 2005). In addition, *S. aureus* has the ability to adhere to equipment surfaces such as stainless steel in food processing units and to generate biofilms (Hamadi et al., 2005; Marques et al., 2007; Oulahal et al., 2008). Equipment-related contamination may occure in milk and dairy products through the biofilm created in milk processing equipment. Food poisoning may occur as a result of these contaminations (Hamadi et al., 2014). Anatolia Sığla Tree (*Liquidambar orientalis* Miller) is an endemic species in Turkey. Styrax liquidus contains alcohol, ether, acid, phenolic and volatile compounds. Antimicrobial and antioxidant properties of extracts obtained from Anatolian Sığla tree leaves were determined (Arslan and Şahin, 2016). This study is aimed to determine the antibacterial activities of styrax liquidus on *S. aureus* at different application time.

Materials and Methods

Material

Styrax liquidus was purchased from local producers. Styrax liquidus dissolved in absolute ethanol (Sigma, 1.02428) to prepare stock solution concentration of at 5%, 10%, 15% and 20%.

Bacterial Strain

American Type Culture Collection (ATCC) standard *S. aureus* (ATCC 25923) was used for the assessment of antibacterial activities of styrax liquidus.

Table 1: Experimental groups used in this study.

Experimental groups	Solution (%)	Application time (min)	Application time (min)	Application time (min)	Application time (min)
Control	-	5	10	20	60
Group I	5	5	10	20	60
Group II	10	5	10	20	60
Group III	15	5	10	20	60
Group IV	20	5	10	20	60

Decontamination of Bulk Milk Tank Surface

The surface to be used to determine the effect of styrax liquidus on *S. aureus* on the surface of the milk collection tank was produced from the milk collection tank material. For this purpose, the stainless steel surface (AISI type 304 standard stainless steel) was divided into 20x20 cm^2 pieces and five different regions were marked with a template. Before experimental bacterial contamination, the sterile steel plate surfaces were sterilized at 121 degrees for 15 minutes and covered with aluminum foil. The suspension level of *S. aureus* was adjusted 0.5 McFarland, it was applied as 1 ml a spray to the previously sterilized surface. It was waited for 30 minutes to ensure the bacterial attachment. Experimental groups were designed as group I, II, III and IV (concentration of at 5%, 10%, 15% and 20%) and control at 5 min, 10 min, 20 min and 60 min. In order to determine the effect of styrax liquidus applied to surfaces contaminated with *S. aureus* at different concentrations and durations (Table 1), samples were taken from the surfaces with sterile swabs and then placed in tubes containing peptone water (Oxoid, CM0009). Samples prepared in 6 different dilutions were inoculated on Baird Parker agar (Oxoid, CM1127) and incubated at 37 °C for 24-48 hours to determine the growth rates (ISO, 2003). Colonies that grew after incubation were counted and the effect of the styrax liquidus-

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containing solution on *S. aureus* was determined. Experimental study applied in duplicate.

Results

In the current study, 0.5 McFarland *S. aureus* was detected as an average level of 7.94 log cfu/ml. In addition, the antimicrobial effect of ethanol used to dissolve styrax liquidus was investigated. It was determined in all experimental groups that ethanol used in dissolving styrax liquidus did not have any antimicrobial effect by ethanol effect group test. In this study, the styrax liquidus has inactivated at a concentration of 5%, 10%, 15% and 20% on *S. aureus* on stainless steel surfaces. Antibacterial activities of styrax liquidus on *S. aureus* were determined as 5% concentration in at least 5 min.

Discussion

Foodborne pathogens cause significant illness and death in humans (Painter et al., 2013). Milk is a suitable environment for the growth of most pathogens (Ding et al., 2016) Factors such as the health of dairy animals, udder diseases, udder hygiene, post-pasteurization contamination, milking conditions and cleaning and disinfection of tools and equipment are effective in the occurrence of milk-borne pathogens (Oliver et al., 2005; Dhanashekar et al., 2012). Various type of microorganisms can survive on stainless steel surfaces. It may pose significant public health hazards. It has been reported that *S. aureus* survived for 4 days after contamination of stainless steel surfaces (Kusumaningrum et al., 2003). This pathogen may contaminate milk as a result of its adherence to stainless steel surfaces and by its presence on the surfaces.

In recent years, the resistance created by bacteria against antibiotics is a worldwide concern (Gootz, 2010; Nathan and Cars, 2014). There are studies reporting that natural antimicrobial agents can be used as an antibiotic alternative (Keyvan and Tutun, 2019). It has been reported that many natural antimicrobial agents are effective on pathogens (Cabarkapa et al., 2019; Porter et al., 2020). In this study, it was aimed to determine the antimicrobial effect of styrax liquidus obtained by using Sığla tree (*Liquidambar orientalis*) which is an endemic tree species on stainless steel surfaces. It is reported that Anatolian styrax liquidus can also be used as an antimicrobial in the leather industry (Bayramoğlu, 2010). Similarly, Okmen et al. (2014) determined the antioxidant and antimicrobial effects of extracts obtained from leaves of Anatolian Sığla tree. It can also be used as ointment for skin diseases and for healing wounds with its antibacterial and scatrizant effect (Aydıngöz and Bulut,2014).

In this study, the effect of styrax liquidus in different time parameters was investigated in the experimental group. In a study on the antimicrobial effects of styrax liquidus; it is emphasized that the activity occurring at 10% concentration is more effective than other concentrations (0.1%, 0.2% and 0.4%) (Sağdıç et al., 2005). In the current study, similar results were found in all time parameters. As a result of examining the effect of styrax liquidus concentrations; antimicrobial effect has been detected at all concentrations. In conclusion, it was determined that the solution prepared within the scope of this study was an effective antimicrobial agent due to the adsorption property of *S. aureus* on the surface. Studies on the effect of styrax liquidus at lower concentrations should be planned. However, due to the risk of leaving residues on surfaces, studies should be planned for solutions prepared with different solvents.

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Research Article / Araştırma Makalesi

Nurses' Knowledge Level about High-Alert Medications

Hemşirelerin Yüksek Riskli İlaçlar Hakkındaki Bigi Düzeyleri

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Abstract: This study was conducted to investigate nurses' knowledge of high-alert medications. Nurses' Knowledge of High-Alert Medications Questionnaire was used to evaluate nurses' knowledge level in a university hospital's clinics where high-alert medications were frequently administered. The questionnaire items, which have two subscales, "drug administration" and "drug regulation", were rated on a 3-point Likert type scale. The study population comprised 187 nurses, and the study sample included 77 nurses as the response rate was 57%. The correct response rate was 61% for the "Drug administration" subscale and 62.1% for the "Drug regulation" subscale. The item with the lowest correct response rate (7.8%) in the "Drug administration" subscale was "Chemotherapeutic drugs' doses should be calculated according to body surface area in adults and according to body weight in children". The item with the lowest correct response rate (10.4%) in the "Drug regulation" subscale was "For pediatric dosage calculations, teaspoon units should be used". The present study results supported the assumption that nurses' knowledge of high-alert medications is inadequate.

Keywords: High-Alert Medications, Medication Error, Nursing

Öz: Bu çalışma, hemşirelerin yüksek riskli ilaçlar hakkındaki bilgilerini araştırmak için yapılmıştır. Değerlendirmede Hemşirelerin Yüksek Riskli İlaç Bilgisi anketi bir üniversite hastanesinin yüksek riskli ilaçların sıklıkla uygulandığı kliniklerinde kullanılmıştır. Ölçeğin "ilaç yönetimi" ve "ilaç düzenleme" olmak üzere iki alt ölçeğinin maddeleri 3'lü Likert tipi bir ölçekle derecelendirilmiştir. Çalışma popülasyonu 187 hemşireden oluşmaktadır ve yanıt oranı % 57 olduğu için 77 hemşire araştırma örneklemini oluşturmuştur. Doğru yanıt oranı "ilaç yönetimi" alt ölçeği için % 61 ve "ilaç düzenlemesi" alt ölçeği için % 62.1'dir. İlaç uygulama alt ölçeğinde "Kemoterapötik ilaçların dozları yetişkinlerde vücut yüzey alanına ve çocuklarda vücut ağırlığına göre hesaplanmalıdır" ifadesi en düşük doğru yanıt oranına (%7,8) sahip maddedir. İlaç düzenlemesi alt ölçeğinde "Pediatrik doz hesaplamaları için çay kaşığı birimleri kullanılmalıdır" ifadesi en düşük doğru yanıt oranına (%10,4) sahip madde olmuştur. Bu çalışmanın sonuçları, hemşirelerin yüksek riskli ilaçlar hakkındaki bilgilerinin yetersiz olduğu varsayımını desteklemektedir.

Anahtar Kelimeler: Yüksek Riskli İlaçlar, İlaç Hatası, Hemşirelik.

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Introduction

Although one of the National Patient Safety Goals is improving high-alert medications' safety, ensuring drug safety remains a severe problem among health professionals (Tang et al., 2007; Lu et al., 2013). One of the main reasons for nurses' medication errors is a lack of relevant knowledge (Lu et al., 2013). Medication errors, mostly, may not lead to severe harm, but misadministration of high-alert medications can lead to the patient's death (Hsaio et al., 2010; Institute for Safe Medication Practices (ISMP), 2015).

Institute for Safe Medication Practices (ISMP) identified that the first five high alert medications are "insulin, opiates and narcotics, injectable concentrated potassium chloride, intravenous (IV) anticoagulants, and chloride solutions above 0.9%" (Belknap, 2001, pp. 339; ISMP, 2017). Based on this medication classification, studies (Franke et al., 2009; Otero et al., 2014) have been conducted to make these high-alert medication

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groups specific for patient groups. These drugs are potentially harmful, even when they are administered appropriately. Therefore, high-alert medications should be administered under supervision, and there are essential points to be taken into consideration during implementation (Lu et al., 2013).

One of the most critical issues that can cause harm to the patient during the intravenous administration of high-alert medications is the method of drug administration (Hicks et al., 2004). Studies have shown that the factor leading to errors during high-alert medications administration is administering the drug at the wrong rate. Hicks et al. (2004) showed that 6.2% of the medication errors were due to misadministration techniques. The cause of 97% of the 265 IV medication errors was administering drugs faster than the recommended rate. Hsaio et al. (2010) pointed out that the administration of concentrated electrolytes or epinephrine at a high rate could cause harm to the patient. They reported that nurses' knowledge levels in this regard should be assessed.

Besides the administration rate, the drug administration technique includes other factors, such as route, timing, and administration dose. In their medication error analysis, Hicks et al. (2004) reported that 1.9% of the errors were due to incorrect dosing and 2.6% were due to the administration's incorrect route. Nurses' inadequate skills to calculate drug doses increase the incidence of errors occurring during the preparation of infusions by 15-49% (Parshuram et al., 2008).

In addition, the storage of high-alert medications in easily accessible areas, keeping look-alike and sound-alike medications together, lack of warning labels on medicines, and the use of illegible handwriting and inappropriate abbreviations cause many avoidable errors (Hsaio et al., 2010; Lu et al., 2013). The precautions to be taken differ depending on the group the high-alert medication belongs to (Lo, et al., 2013). These precautions include the regulation and storage of high-alert medications (Lu et al., 2013). For example, the storage of insulin and heparin vials in the same place may lead to confusion. Neuromuscular blocking agents and concentrated electrolytes should not be stored together with other routine stocks in easily accessible areas (Paparella, 2004; Loria, 2012). Narcotics should be stored in double-locked cabinets by two separate staff (Cohen et al., 2007). Not to confuse look-alike and sound-alike medications, verbal orders should not be accepted; they should be stored at different cabinets, different product labels should be used for different products, reminders or alarms should be used. Independent double-check and bar-code systems should be used, and possible errors should be reported (Tuohy and Paparella, 2005; Cohen et al., 2007).

Although many nurses frequently use high-alert drugs in the care, studies show that nurses do not have sufficient knowledge about high-alert drug administrations (Tang et al., 2007; Hsaio et al., 2010; Sahmsuddin and Safie, 2012; Lu et al., 2013). Only one study (Kucukakca and Ozer, 2016) has been conducted to assess nurses' knowledge of high-alert medications in our country. Therefore, this study aims to determine the knowledge level on high-alert medications of the nurses who work in a university hospital's intensive care units and emergency services.

Materials and Methods

This descriptive study was conducted between February 2016 and January 2017 in a university hospital. The nurses were recruited from a university hospital's intensive care units of neurology, internal medicine, neurosurgery, general surgery, anaesthesia and reanimation clinics and emergency services (N=187). The study comprised nurses working only in these units as high-alert medications are mostly used in the hospital's internal medicine clinic, surgical clinic, and emergency departments. Nurses with less than six months of experience were excluded from the study. One hundred thirty-six eligible nurses were enrolled in the study. Thirty of them refused to participate in the study, and 29 nurses were on leave. When those were excluded, the study was completed with 77 nurses. The response rate of the study was 57% of the sample.

Data were collected using the sociodemographic characteristic form, including age, gender, years of experience in nursing and clinic and Nurses' Knowledge of High-Alert Medications Questionnaire by closed envelope method. Hsaio et al. (2010) developed this questionnaire consisted of 20 questions divided into two parts: In part A, there are ten questions examining drug administration such as drug delivery routes and dosage. In part B, there are questions on how high-alert medications should be stored, regulated and prescribed. The items in both sections are rated as "true", "false", and "I do not know".

The questionnaire was translated into Turkish after author permission was received from Hsaio et al. (2010) by four nursing instructors and one English language specialist. The researchers reviewed all translated versions to develop the tool in Turkish. Then, the English language specialist translated the initial version of the questionnaire back into English. The questionnaire statements were drawn between the original English text statements and translated text from Turkish into English, and revisions that considered necessary were made. The questionnaire's clarity and relevance to the topic were evaluated by five academics and five nurses who were experts in their fields. Each expert rated the form's content using a 3-point Likert scale (3: appropriate, 2: I have no idea, 1: inappropriate).

At the end of the assessment, three items whose content validity index value was lower than 0.62 were removed from the scale, and the questionnaire included 17 items. The items removed from the questionnaire were items 5, 9, and 10 in Part B. Reliability analysis was conducted to determine the questionnaire's internal consistency. Cronbach's alpha was 0.63 for part A and 0.74 for part B.

The data were analyzed with SPSS 22.0 (Statistical Package for the Social Sciences Version 22.0). Statistical advice was obtained from a statistician to analyze the data. The sample was analyzed using the descriptive statistics used to describe the sample characteristics. Frequencies and percentages were used to describe the correct answer rates.

Study approvals were obtained from the Scientific Research and Publication Ethics Committee of the University (27344949-605.01-25785) and the hospital (69631334-044-23454), where the study was to be conducted. The participating nurses were informed about the aim of the study, and their verbal consents were obtained. The participants were assured that they could refuse to participate in or withdraw from the study at any time, and the data were rendered anonymous.

Results

As shown in Table 1, of the 77 participants, 64 were women, 13 were men, and their mean age was 29.51 ± 5.60 years. Of the nurses, % 49.3 had 1-5 years of experience in nursing. A total of 17 questions were answered by 77 nurses (response rate 57%), with an average overall correct answer rate of 65.5%.

While of the participants, 61% chose the correct options in Part A (Drug administration), 24.9% chose the wrong options and 14% chose the option "I do not know". Of the nurses, 89.6% chose the correct option for the item that "cc or mL is the dosage expression for insulin injection", 85.7% for the item that "10% Ca gluconate, and 10% $CaCl_2$ are the same drug and can be used interchangeably, and 84.4% for the item that "when an emergency such as ventricular fibrillation happens, push fast 15% KCl 10 mL into IV".

Table 1. Distribution of correct responses by the sociodemographic characteristics of the nurses.

Variable			Correct Answers		
	n	(%)	$\overline{X}$	SD	P value
Gender					
Female	64	83.1	11	2.21	0.22
Male	13	16.9	11.84	2.64	
Age (years)					
20-25	18	23.4	9,88	3,23	
25-30	31	40.3	11.35	1.76	**0.024**
31-35	19	24.6	11.31	1.76	
>36	9	11.7	12.55	1.74	
Education					
License	73	94.8	11.07	2.23	0.14
MSc	4	5.2	12.25	2.36	
Nursing experience					
6 months-1 year	10	13	11,60	2.71	
1-5 years	38	49.3	10.65	1.66	0.17
6-10 years	17	22.1	11.17	1.91	
>10 years	12	15.6	12.25	2.45	
Length of service in the clinic					
6 months-1 year	28	36.4	10.46	3.04	
1-5 years	30	39	11.50	1.40	0.18
6-10 years	13	16.8	11.23	1.87	
>10 years	6	7.8	12.33	2.16	
Clinic					
Emergency	34	44.1	11.26	2.81	
Anesthesia & Reanimation IC	10	13.0	11.50	0.97	
Neurosurgery IC	10	13.0	10.70	1.70	0.90
Neurology IC	6	7.8	11.50	1.22	
Internal Medicine IC	7	9.1	11.28	2.36	
General Surgery IC	10	13.0	10.50	2.46	

In this part, the item with the lowest correct response rate (7.8%) was "chemotherapeutic drugs' doses should be calculated according to body surface area in adults and according to body weight in children". Many participating nurses (64.8%) did not know that the port A route should not be used for blood drawing or drug administration (Table 2).

While of the participants, 62.1% chose the correct options in Part B (Drug regulation), 33% chose the wrong options, and 4.8% chose the option "I do not know". In this part, the item with the lowest correct response rate (10.4%) was "For pediatric dosage calculations, teaspoon units should be used". While 22.1% of the nurses correctly knew that the term "unit" should not be abbreviated as "U" in the dose expression, 96.1% of the nurses accurately knew that distinctive labels should be used for look-alike drugs (Table 2).

A statistically significant relationship was found between the number of correct responses given by the participating nurses and their ages ($F= 3.34$, $p<0.05$). There was no significant relationship between the number of correct answers provided by the participating nurses and the variables such as gender, education level, length of service in the clinic ($p>0.05$).

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Table 2. Ranking of knowledge of drug administration (Part A) and drug regulation (Part B) by correct answer rate (n =77).

Item	Question	Correct Option (T/F)	Correct Responses (%)	Wrong Responses / do not know (%)	Rank
Part A					
4	"cc" or "mL" is the dosage expression for insulin injection	F	89.6	9.1/1.3	1
3	10% Ca gluconate and 10% $CaCl_2$ are the same drug and "can be used interchangeably"	F	85.7	0/14.3	2
6	When an emergency such as ventricular fibrillation happens, push fast 15% KCl 10 mL into IV	F	84.4	6.5/9.1	3
2	When an emergency happens, fast IV push 10% $CaCl_2$ 10 mL in 1–2 minutes	F	71.4	16.9/11.7	4
8	Insulin syringe can be replaced by 1 mL syringe	F	71.4	23.4/5.2	5
9	Fast IV infusion of 3% NaCl 500 mL for patient who has low sodium level	F	63.6	32.5/3.9	6
1	Fast IV push 1:1000 epi 1 amp for patient who has mild allergic reaction	F	61	15.6/23,4	7
7	15% KCl better added to Ringer's solution for rapid infusion	F	45.5	19.5/35.1	8
10	Port-A route can be used for blood withdrawal and drug injection generally	F	29.9	64.9 /5.2	9
5	Chemotherapeutic drugs' doses should be calculated according to body surface area in adults and according to body weight in children	F	7.8	61.0/31.2	10
Part B					
2	Use distinctive labeling on look-alike drugs	T	96.1	2.6/1.3	1
1	Use "Amp" or "Vial" for dose expression instead of "mg" or "gm"	F	94.8	3.9/1.3	2
4	For convenience, heparin and insulin should be stored together in the refrigerator	F	87.0	10.4/2.6	3
7	15% KCl is frequently used, so it should be easily and freely accessed by nurses	F	64.9	29.9/5.2	4
6	If patient can tolerate, potassium can be administered orally instead of IV route	T	59.7	31.2/9.1	5
3	"U" is used instead of "unit" to express the amount of doses	F	22.1	74/3.9	6
8	For pediatric dosage calculations, teaspoon units should be used	F	10.4	79.2/10.4	7

T/F, true /false; KCL, potassium chloride; Ca, calcium; NaCl, sodium chloride; Epi, epinephrine; $CaCl_2$, calcium chloride; IV, intravenous; BW, body weight; BSA, body surface area.

Discussion

In the present study, 90% of the nurses answered correctly that "cc" or "mL" should not be used as a unit of dose measurement in insulin injections, and 74% of them were aware that 1 mL injectors should not be used as an insulin injector. Similar results were reported by Hsaio et al. (2010) and Lu et al. (2013). Although nurses have this knowledge, they are still forced to apply insulin injections using 1 mL injectors or tuberculin injectors in our experiences. Although most insulin products come from companies in 100 units / mL, due to the recent increase in obesity, insulin resistance, and the use of insulin pumps, the use of 500 units / mL insulin has also begun to increase. However, clinics do not have an insulin injector designed to measure 500 units of insulin dose. Therefore, the nurses have to administer 500 units of insulin using 100 units / mL insulin injectors, tubercle injectors or 1 mL injectors. This leads to the administration of insulin in high doses (Prescrire International, 2014).

It is reported that 26% of patient safety incidents related to insulin were caused by administering the wrong insulin dose and resulted in severe harm and deaths (Sharpe, 2012). Therefore, companies must produce injectors suitable for high-dose insulin products for patients to receive the appropriate dose of medicine. Insulin should be administered only with insulin injectors, and all healthcare professionals should be informed and trained about such errors.

Concentrated electrolytes come at the top of high-alert medications and errors made during these medications' administration lead to fatal outcomes in patients treated with medications. When these solutions are administered as an IV bolus injection, they bring severe consequences. For instance, 15% KCl may cause cardiac arrest (Grissinger, 2011; Gyeongae, 2014). In the present study, one-third of the nurses did not choose the correct option for the item that "3% NaCl and 10% $CaCl_2$ solutions should not be administered fast", and more than half of them (55%) did not choose the correct option about how 15% KCl should be administered. Similar results have been reported in other studies (Hsaio et al., 2010; Chen et al., 2014). Hsaoi et al. (2010) also showed that more than 30% of the nurses did not understand that "15% KCl should not be administered by IV bolus under any circumstances". These results show that more time should be allocated to pharmacology lessons in nursing education and that this information should be updated with in-service training when necessary.

In this part, the item with the lowest correct response rate (7.8%) was "Chemotherapeutic drug doses should be calculated according to body surface area in adults and according to body weight in children". The low correct answer rates related to the same issue were reported in Hsaio et al.'s (2010) and Lu et al.'s (2013) studies too (24.6%, 33.3%, respectively). Chemotherapy drugs are included in the high-alert medications classification, and doses of these drugs are of great importance in terms of the treatment's efficacy (Yu et al., 2013). Body surface area is a variable with a difficult constitutional body and physiological assessment (Geriņa-Bērziņa et al., 2013). Despite some limitations, it remains the most commonly used parameter regarding chemotherapy of cancer patients. The dosage of chemotherapeutic drugs has been based on the patients' physiologic variables related to drug metabolism and elimination, such as basal metabolic rate, renal function and hepatic function. It varies by individuals' body surface area (Sacco et al., 2010). It is reported that medication errors occur with high incidence (44%) in chemotherapy due to the lack of specific knowledge and training of health professionals in chemotherapy, prescription, preparation and administration. It leads to fatal patient safety incidences, such as chemotherapy overdose or dose calculation errors (Khan et al., 2012; Yu et al., 2013). Nurses, therefore, should have adequate knowledge and training about chemotherapy in nursing school and throughout the in-hospital continuing education.

Of the nurses, 64.9% chose the correct option for the item 15% KCl is frequently used, so nurses should easily and freely access it. However, about one-third of the nurses (35.1%) in the present

study do not know the correct answer was shocking. In 2002, in line with the national patient safety goals, concentrated electrolytes were removed from the patient care units unless clinically necessary, and nurses' easy access to this medication was prevented. This measure mentioned above was taken due to tragic errors such as fast intravenous administration of concentrated potassium made by nurses because they lacked the necessary knowledge. Although potassium chloride is removed from clinics, nurses in hospitals where 24-hour pharmacy service is not available are able to get this medication from the drug cabinets at nights and on weekends. Therefore, this drug still poses a threat to patient safety in clinics (Grissinger, 2011). Although limited access to potassium chloride has reduced fatal errors, nurses should be aware of the risks associated with the use of this drug. The results of the present study support the view that nurses should be educated about the subject.

Of the participating nurses, 74% chose the incorrect option for the item "U is used instead of the unit to express the amount of doses". Similarly, the incorrect response rate in Hsaio et al.'s (2010) study was 62.3%. Administration of insulin, a vital drug for patients with diabetes, in high doses results in hypoglycemia, coma and death, and in low doses results in hyperglycemia and ketoacidosis. Insulin administration errors usually occur due to the use of abbreviations when medication orders are given. The use of 'U' instead of 'unit' often results in a 10-fold overdose because 'U' is mistaken for '0'. In addition, using 1 mL injectors as an insulin injector leads to the administration of insulin in overdoses (ISMP, 2015). These results indicate that more attention should be given to nursing education and that nurses' knowledge should be strengthened through in-service training.

Many nurses (79.2%) in the current study did not know that teaspoon should not be used as a unit in pediatric dosing calculations. The present study results are consistent with those of Hsaio et al.'s study (2010). The most common medication error in paediatrics and neonatal units is the dose calculation errors. In the US, each year, more than 70,000 children are admitted to emergency departments due to "medication overdoses" (Franke et al., 2009). Medication overdose is associated with the use of inappropriate dose-measuring devices (Neville et al., 2015). Yin and colleagues (2014) reported that 39.4% of parents made an error in measuring the intended dose. When medicine is given with teaspoons or dessertspoons of different sizes, children can receive a medication overdose or underdose. The medication overdose can bring about consequences as severe as liver failure. If the child gets a medication underdose, then he/she has to take the medication in shorter periods because the desired effect is not achieved in the child. Therefore, when children are administered medicines, injectors or measuring spoons must be used. Although these errors are mostly known as errors made by parents, it is noteworthy that nurses who are health professionals did not know that teaspoons/dessertspoons should not be used as a dose-measuring device (Yin et al., 2014). These errors may be due to the widespread use of spoons because the measuring spoons provided with liquid medicine cannot always be kept in the medicine carton package. Our study results support that this issue should be emphasized more in nursing education.

While such sociodemographic characteristics of the participating nurses as sex, education level, length of employment and the clinics they worked in did not affect the number of correct responses they gave (all $p > 0.05$). There was only a significant correlation between the nurses' age and correct responses ($F = 3.34$, $p < 0.05$). Similarly, in the literature, a significant relationship has been determined between the nurses' age and their knowledge levels (Lu et al., 2013, Hsaio et al., 2010). Although no statistically significant correlation was determined between the participants' length of service and their knowledge levels, the nurses with more than ten years of length of service had a higher number of correct responses. Similar studies have also shown that as the length of service increases, so does the number of correct responses. Besides, nurses' education level might have affected the knowledge level in the present study; of the participants, 93.5% had

an undergraduate degree, which is thought to yield this result.

Conclusions

The study had some limitations, as the sample included nurses working in only one university hospital, so the results cannot be generalized. Our results should be interpreted with great caution due to biased sampling. Also, while filling out the questionnaires, the participants may have been influenced by each other; therefore, their answers may not reflect their actual responses.

Despite these limitations, the current study results support the view that nurses' knowledge of high-alert medications is inadequate. The majority of the nurses lack information, especially about chemotherapeutic drugs' doses, pediatric dosage calculations and unite. Nurses' knowledge of high-alert medications should be updated via in-service training, and that the time allocated to pharmacology courses in the nursing curriculum should be increased.

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Research Article / Araştırma Makalesi

Effects of Synthetic Cannabinoids (JWH-018) on Antibody Response to HBV Vaccination

Sentetik Kannabinoidlerin (JWH-018) Hepatit B Aşılamasına Antikor Yanıtı Üzerindeki Etkisi

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Abstract: Synthetic cannabinoids can affect the immune system and can cause some changes in immune response. The immune response to the Hepatit B vaccine is complex. Studies on hepatitis B vaccine antibody response and JWH-018 are extremely limited. The main aim of this study was to investigate the effect of JWH-018 on anti-HBs Ag changes before or after Hepatitis B vaccination. The study was performed on C57BL6 mice (n=25). The mice were divided into 3 groups. The control group was given the Hepatitis B vaccine 3 times with intervals of 3 weeks. Group 1 was administered JWH-018 (before) + Hepatitis B vaccine (after). Group 2 was treated Hepatitis B vaccine (before) + JWH-018 (after). Blood samples were collected at the end of the drug and vaccine administration. The control group's Anti-Hbs Ag titer mean was found to be lower than the mean of other groups. When the within-group data was evaluated, it was observed that there was a statistical difference between the data of Group 2 (p=0,017). When Anti-Hbs AG titer was evaluated between group, it was observed that there was a statistical difference in the first (p = 0,018) and third measurements (p=0,005). A total of 5 mice from the experimental groups died at different stages of the study. In this study, the use of JWH-018 has been shown to be effective on the anti-HBs parameter. In addition, we believe that the scientific value of our study will be possible by understanding the relationship between cannabinoid system and immune system.

Keywords: Hepatitis B, Immunity, JWH-018, Mice, Vaccination.

Öz: Sentetik kannabinoidler bağışıklık sistemini etkileyebilir ve bağışıklık tepkisinde bazı değişikliklere neden olabilir. Hepatit B aşısının oluşturduğu antikor yanıt üzerine sentetik kannabinoidlerin etkilerini inceleyen çalışma sayısı oldukça kısıtlıdır. Bu çalışmanın temel amacı, JWH-018'in Hepatit B aşılamasından önce veya sonra anti-HBs Ag değişiklikleri üzerindeki etkisini araştırmaktır. Çalışma, C57BL6 fareleri (n = 25) üzerinde yapıldı. Fareler 3 gruba ayrıldı. Kontrol grubuna 3 hafta aralıklar ile 3 kez sadece Hepatit B aşısı uygulandı. Grup 1'e önce JWH-018 uygulandı sonrasında Hepatit B aşısı uygulandı. Grup 2'ye önce Hepatit B aşısı uygulandı sonrasında JWH-018 uygulandı. İlaç ve aşı uygulamasının sonunda kan örnekleri toplandı. Kontrol grubunun Anti-Hbs Ag titresi ortalamasının diğer grupların ortalamasından daha düşük olduğu bulundu. Grup içi veriler değerlendirildiğinde, Grup 2 verileri arasında istatistiksel bir fark olduğu gözlenmiştir (p = 0,017). Gruplararsı Anti-Hbs Ag titresi değerlendirildiğinde, birinci (p = 0,018) ve üçüncü ölçümde (p = 0,005) istatistiksel fark bulundu. Ayrıca, deney gruplarından toplam 5 fare, çalışmanın farklı aşamalarında öldü. Bu çalışmada, JWH-018 kullanımının anti-HBs parametresi üzerinde etkili olduğu gösterilmiştir. Çalışmamızın bilimsel değerinin kannabinoid sistem ile bağışıklık sistemi arasındaki ilişkiyi anlayamaya yardımcı olacağına inanıyoruz.

Anahtar Kelimeler: Hepatit B. Bağışıklık, JWH-018, Fare, Aşılama

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Introduction

Hepatitis B viruses can be prevented by vaccination (Hou et al., 2005; Thanavala et al., 2005). The vaccination has certain periods (20 mcg of HBs antigen at months 0–1–6) (Hwang et al., 2010). After 3 times vaccination, the antibody titer for seroconversion is considered >10 mIU/ml. (Florani et al., 2004). Many factors can affect seroconversion (drug addiction, aging, diseases etc) (Marsland et al., 2001). The immune response to the Hepatit B vaccine is complex and regulated by some genes (Milich et al., 2003). In addition, dendritic cells can initiate the immune response by

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presenting the antigen to T_h and T_C. T_h cells can stimulate B lymphocytes with various cytokines and secrete anti-viral cytokines such as IFN-γ, TNF-α (Chen et al., 2019, Koziel, 1998). Drugs used by substance addicts can affect the immune system (Δ9-THC etc.). One of these drugs is JWH-018 (structurally similar to Δ9-THC) (Showalter et al., 1996). JWH-018 can stimulate the immune system through the endogenous cannabinoid system (ECS). ECS has two dominant receptors. These receptors help regulate functions in the central and peripheral nervous system (Matsuda et al., 1990; Munro et al., 1993). JWH-018 can stimulate both dominant receptors (Aung et al., 2000). The CB_2 receptor can stimulate immune system cells and conduct immune modulation (Every-Palmer, 2011). Studies on hepatitis B vaccine antibody response and JWH-018 are extremely limited. The main purpose of this study was to investigate the effect of JWH-018 on antibody titration before and after the Hepatitis B vaccine.

Materials and Methods

Animal Model

All experiments were conducted in 25–30 g adult male C57BL/6 mice at the age of 8–10 weeks old. The mice were placed in standard plastic, steel cover and watery cages in the laboratory. Photoperiod, constant heat and humidity were applied by automatic mechanism. Food and water were provided *ad libitum*. Ethics Committee permission was obtained from Mehmet Akif Ersoy University Animal Experiments Local Ethics Committee (2017/268).

Drug and Dose Selection

There are studies reporting death associated with JWH-018 (1-naphthalenyl(1-pentyl-1H-indol-3-yl)-methanone) (Cayman Chemical, CAS: 209414-07-03) in the literature (Mir et al., 2011; Hermans-Clausen et al., 2013). Considering the literature, the number of studies investigating the relationship between JWH-018 and Anti HBs Ag parameters is quite limited

Therefore, we prefered to use the first detected synthetic cannabinoid (JWH-018) in our study (EMCDDA, 2010). In this study, JWH-018 dose was selected based on previous studies in mice (Ossato et al., 2015). The dose of JWH-018 was considered 1 mg/kg intraperitoneal (i.p). Also, Engerix B (20 μg 1 ml) (GlaxoSmithKline) was determined as the Hepatitis B vaccine. In a previous study using Engerix B the dose of this vaccine was determined as 2 μg per capita for C57BL/6 mice. The dose for seroconversion was determined 3 times at intervals of three weeks (Sleijffers et al., 2002).

Drug preparation and Treatment

JWH-018 (1 mg / kg) was prepared in absolute ethanol (1%) and salin (99%). It was administered by i.p. injection (1 ml, 30G, 8 mm). Engerix B (20 μg 1 ml) was administered intramuscular (i.m.) injection at a volume of 0.1 ml/per capita by vehicle (30G, 8 mm).

Setting up Animal Groups

Weight analysis was performed after dividing the mice into groups. The weights of control, group 1 and group 2 were measured (Respectively: 32.2±1.11; 32.16±1,17; 32.03±1.03 gr and p=0.91). Mice were divided into 3 groups [(control group (n=7), group 1 (n=9) and group 2 (n=9)]. The control group in this study will be used as a control for both group 1 and group 2.

Drug Administration

Control group; it was immunized with Engerix B (2 μg) at 3 times for 3-week intervals. Group 1; JWH-018 was administered once a week for 4 weeks. At the end of this period, 2 μg Engerix B was immunized 3 times at 3-week intervals. Group 2; it was immunized 3 times at 3-weeks intervals with Engerix B (2 μg). At the end of this period JWH-018 was administrated once a week for 4 weeks.

Collection of blood samples

Blood samples were collected from tail veins of animals by using heparinized syringe. 20 μl of blood was collected from each mouse and it was

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collected 3 times with an interval of 2 weeks. Blood samples were added to 20 µl of citrate buffer, which was previously placed in eppendorf tubes. Blood samples were centrifuged for 3 minutes at 3000 rpm to separate the plasma. Plasma samples were stored at 20°C until assayed.

ELISA

11 ml of PBS (Merck) and 3.22 µl of HBsAg protein (Fitzgerald 10 - 1324) were added to a falcon tube (Isolab). Out of which 100 µl of prepared PBS and HBS ag liquid was added to the tube, and covered with aluminum foil and stored in refrigator (+ 4 °C). Next day, the plate was washed 3 times with PBS + Tween (Merck). 22 ml of PBS and 110 mg of BSA (Sigma-Aldrich) were added to other falcon tube and it was added to each well 200 µl and incubated (1 h at 37 °C). The plate was washed 3 times with PBS + Tween. 1/100 plasma was added to wells and was incubated 1 h at 37°C. After that it was washed 3 times with wash buffer. Alkaline phosphatase-labeled of polyvalent antibody diluted in a ratio of 1:1000 was added to 100 µl each well and incubated (1 h at 37°C). Plate was washed 4-5 times with a washing buffer. 100 µl pNPP (Merck) prepared in substrate buffer was added to each well and incubated for 30 minutes. The absorbance was measured with an ELISA reader at 405 nm after 30 minutes of incubation

Statistical Analysis

The analysis of the data was done with the SPSS program (Version 22, IL, USA). Descriptive parameters were represented n, mean±standard deviation (Mean±Sd). ANOVA test was performed to compare the groups. Post-hoc Tukey test was performed to determine in which group the statistical difference originated from. The Tukey test was represented in the table with a "letter" (Different letters represent significant difference between sub-groups). A p-value less than 0.05 ($p \leq 0.05$) was considered as statistically significant.

Results

Anti-HBS Ag measurements of the control groups were on mean lower than group 1 and group 2. Also, totaly 5 mice died in experimental (Group 1-2) groups.

Within-Group Comparison: Statistical difference was not detected in both control group and group 1 ($p>0.05$). The final measurement (3^{th}) of the Group 2 was higher than other measures (1^{th} and 2^{nd}) and was statistically significant ($p<0.05$).

Between Groups Comparison: Statistical difference was measured in the first and third measurements of the groups ($p<0.05$).

Table 1: Anti HBs Ag parameters comparison within groups

Group	Measure	n	Mean±Sd*	p
Control	1^{th}	7	0.61±0.10a	0.896
	2^{nd}	7	0.61±0.11a	
	3^{th}	7	0.64±0.10a	
Group 1	1^{th}	6	1.23±0.38a	0.752
	2^{nd}	6	1.03±0.57a	
	3^{th}	6	1.18±0.40a	
Group 2	1^{th}	7	0.78±0.24a	0.017
	2^{nd}	7	0.78±0.24a	
	3^{th}	7	1.20±0.35b	

*OD: 405 nm

Table 2: Anti HBs Ag parameters comparison between groups

Group	Measure	n	Mean±Sd*	p
Control	1^{th}	7	0.61±0.10ab	0.018
Group 1		6	1.23±0.38a	
Group 2		7	0.78±0.24b	
Control	2^{nd}	7	0.61±0.11a	0.123
Group 1		6	1.03±0.57a	
Group 2		7	0.78±0.24a	
Control	3^{th}	7	0.64±0.10a	0.005
Group 1		6	1.18±0.40b	
Group 2		7	1.20±0.35b	

*OD: 405 nm

Discussion

Hepatitis B is a major public health problem. Many people have been infected with this disease. It is estimated that around 350 million people carry HBV (Kuo et al., 2004). It is possible to prevent the disease with the vaccine. When the antibody titer is higher than 10 mIU/ml, it is considered as

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seroconversion (Floreani et al., 2004). There are factors that affect seroconversion. These factors include immunosuppressive diseases, aging, etc (Marsland et al., 2001). JWH-018 is an addictive material that acts on the endogenous cannabinoid system (ECS). ECS has two dominant receptors. These receptors help regulate functions in the central and peripheral nervous system (Matsuda et al., 1990; Munro et al., 1993). JWH-018 stimulate both CB_1 and the CB_2 receptor (Aung et al. 2000). Compared to THC, this effect remains lower (Showalter et al., 1996). ECS can play immunmodulatory role on the immune system (Kleain and Cabral, 2006). This role is dose-dependent and can lead to immunosuppression or immunproliferation in immune cells (Croxford and Yamamura, 2005). Very few studies focused or investigated on the relationship between anti-HBs Ag and JWH-018. Because of that we thought that it was an important topic to investigate. The main purpose of this study was to investigate the effect of JWH-018 on the anti-HBs Ag parameter.

During the study, 5 mice from the experimental groups (Group 1 and Group 2) were died. No death occurred in mice from control group. In the literature, it has been reported that JWH-018 is toxic and deadly for humans (Labay et al., 2016). Also, there are studies reporting death associated with JWH-018 (Mir et al., 2011; Hermanns-Clausen et al., 2013). But similar studies did not report death in various doses (Marshell et al., 2014, Mutluay et al., 2019). In our study, the mice died just in the experimental groups, but it did not die in the control group.

Therefore, we think that the deaths may be related to the dose of JWH-018. We were evaluated anti-HBs Ag parameter within-groups and between groups. In all measurements, mean of control group was lower than both group 1 and group 2. In our study, mean anti Hbs Ag titer of the control group was measured in the range of 0.61-0.64 OD. Anti-HbsAg mean of various study were measured in the range of 0.4 - 0.6 OD (Li et al., 2014, Wu et al., 2016). The data obtained from the control group of our study is supported by other studies in the literature. We could not find any study supporting that the mean of the experimental groups was higher than the control group. We are suggesting that this situation may be related to immune response mechanisms (against both vaccines and viruses).

The first immune response to Hepatitis B Virus is known to be given by Natural Killer (NK) cells. NK cells stimulate various T lymphocyte cells by secreting IFN-γ (Kakimi et al., 2000). DC present antigen to Th and Tc. Th cells secrete cytokines (IL-4, IL-10, TNFα etc.) that activate B lymphocytes to create an immune response (Chen et al., 2019). In vaccine-specific response, antigen-specific B and T lymphocytes and various cytokines are known to play roles (Filippelli et al., 2014).

JWH-018 is structurally similar to THC. Studies on THC have shown that THC has a suppressor effect on immune system cells (Eisenstein snd Meissler, 2015; Roth et al., 2015). THC and other cannabinoids have immunosuppressive effect in both in vivo and in vitro studies (NK, DC, macrophage, mast cells B and T lymphocytes etc.) (Samson et al., 2003; Do et al., 2004). Another study has shown that B lymphocytes induce transition from IgM to IgE (Agudelo et al., 2008). But in another study, synthetic cannabinoids have proliferative effect on B cells, NK and neutrophils (Lee et al., 2001). In a study about the use of THC (marijuana smokers) and Hepatitis B vaccine, anti-HBs Ag parametres of marijuana smokers and non-smokers were compared. However, it was observed that difference between them was not statistically significant (Kiertscher et al. 2018).

Conclusion

This study showed that JWH-018 was effective on anti-HBs Ag parameter. Low mean of anti-HBs Ag level in control group was appropriate for our two-way hypothesis. In general, orginal articles show that synthetic cannabinoids are responsible for suppression of immune system cells. However, very few studies have reached result of immunproliferation. We think that our study is very valuable in terms of proving the relationship between JWH-018 and Anti-Hbs parameter. However, further studies need to be done to understand causation.

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Research Article / Araştırma Makalesi

Physical Activity Level During COVID-19 Global Pandemic and Its Relation to Well-Being

KOVİD-19 Global Pandemisi Sırasında Fiziksel Aktivite Düzeyi ve İyilik Hali ile İlişkisi

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Abstract: Many countries implemented lockdowns to prevent the spread of novel coronavirus disease 2019 (COVID-19). Turkey is one of these countries where people were obliged to experience altered daily routines in May 2020. We aimed to identify physical activity level and well-being of people during COVID-19 outbreak and investigate the relationship among them. An on-line questionnaire was used to obtain data regarding descriptive characteristics and exercise habits. Individuals volunteered to participate in the study filled the questionnaire published in an on-line survey platform (Google Forms) in May 2020. Physical activity level was questioned and well-being of the individuals was measured by WHO-5 Well Being Index. Spearman and Kendall analyses were used. The survey was completed by 378 adults. Approximately three quarters (75.1%) of participants self-reported that they did not do any vigorous physical activity and nearly half of them (48.1%) self-reported not to do any moderate physical activity. Well Being Score was positively correlated with vigorous physical activity (days per week) ($p=0.039$, $r=0.106$). Our results showed that increased physical activity level is associated with improved well-being in adults. Effective strategies such as doing regular physical exercise should be used to decrease negative effects of pandemic on well-being and physical activity level.

Keywords: COVİD-19, Physical Activity, Well-Being, Exercise.

Öz: Birçok ülke yeni koronavirüs hastalığı 2019'un (KOVİD-19) yayılmasını önlemek için kısıtlamalar uyguladı. Türkiye, Mayıs 2020'de insanların değişen günlük rutinlerini yaşamak zorunda kaldığı bu ülkelerden biridir. Biz KOVİD-19 salgını sırasında fiziksel aktivite düzeyi ve iyilik hali arasındaki ilişkiyi araştırmayı amaçladık. Tanımlayıcı özellikler ve egzersiz alışkanlıkları ile ilgili verileri elde etmek için çevrimiçi bir anket kullanıldı. Çalışmaya katılmaya gönüllü kişiler, Mayıs 2020'de çevrimiçi bir anket platformunda (Google Formlar) yayınlanan anketi doldurdu. Bireylerin fiziksel aktivite düzeyi sorgulandı ve bireylerin iyilik hali WHO-5 İyilik Hali İndeksi ile ölçüldü. Spearman ve Kendall analizleri kullanıldı. Anket 378 erişkin tarafından tamamlandı. Katılımcıların yaklaşık dörtte üçü (% 75,1) hiç şiddetli fiziksel aktivite yapmadıklarını ve yaklaşık yarısı (% 48,1) hiç orta şiddetli fiziksel aktivite yapmadıklarını belirtti. İyilik hali skoru, şiddetli fiziksel aktivite (haftalık gün) ile pozitif korelasyon gösterdi ($p=0.039$, $r=0.106$). Sonuçlarımız, erişkinlerde artan fiziksel aktivite düzeyinin iyilik hali ile ilişkili olduğunu göstermiştir. Bu nedenle, pandeminin iyilik hali ve fiziksel aktivite düzeyleri üzerindeki olumsuz etkilerini azaltmak için düzenli olarak fiziksel egzersiz yapılması gibi etkin stratejiler kullanılmalıdır.

Anahtar Kelimeler: KOVİD-19, Fiziksel Aktivite, İyilik Hali, Egzersiz.

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Introduction

Sars-CoV-2 virus first infected the people in China in 2019 and is still being spread worldwide during mid-2020. This outbreak was declared as COVID-19 global pandemic by World Health Organization (WHO) (Sohrabi et al., 2020). Because of the negative effects of COVID-19 throughout the world, people were obliged to experience altered daily routines (Silvestri, 2020).

In order to prevent rapid spread of the outbreak and to decrease the rate of daily new cases, governments either forced or advised their citizens to stay at home and keep social distance. Schools, offices, gyms, shopping centers and indoor areas

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including restaurants and theatres were closed, social organizations like sport events, competitions and concerts were cancelled and even in many countries, nationwide curfews were imposed. Turkey is one of these countries in which social life was highly restricted throughout Spring Season 2020.

This stressful context as mandatory behavioral changing including staying home and social isolation was thought to influence both physical and mental health during COVID-19 pandemic (Burtscher et al., 2020). It is also well-known that enhanced time spent in sitting and sedentary lifestyle negatively affects physical health of an individual (Nieman and Wentz, 2019). In addition, public movement restrictions or strict quarantine situation increased some emotions such as sadness, anxiety, anger etc. and the fear of death has raised (Schuch et al., 2020).

During COVID-19 pandemic, encouragement of physical activity (PA) at home has become more essential than ever for both physical and mental health of the people (Burtscher et al., 2020; Nieman and Wentz, 2019). Lubans et al. (2016) suggested that regular PA provides benefits on immunologic responses as well as enhanced mood and coping stress. However, it is still unknown what PA level of people is and whether there is a relationship between PA level and well-being in such an extraordinary period of time caused by the global pandemic. Therefore, we aimed to identify PA level and well-being of people living in Turkey during COVID-19 outbreak and investigate the relationship among them. We hypothesized that PA level and well-being would be correlated significantly during COVID-19 pandemic.

Materials and Methods

Design

This was a cross-sectional study that was carried out in May 2020, during partial lockdown procedures implemented by the Turkish government for COVID-19 global pandemic. The study was performed in accordance with the ethical guidelines of Declaration of Helsinki. Ethics committee of local university approved the study (Protocol number: GO-2020/121).

Participants

Individuals who were volunteered to take part in the study and filled the questionnaire published in an on-line survey platform (Google Forms) were screened for eligibility. Inclusion criteria were: (i) being age between 18 and 65 years, (ii) having no COVID-19 findings or diagnosis. The exclusion criteria were: (i) hospitalization for any reasons, (ii) mental and cognitive disorders that could prevent filling out the questionnaire, (iii) not able to mobilize independently. Written informed consent was provided to individuals prior to participating and individuals were obliged to approve "Informed Consent Form" on-line to view the questionnaire in the next step.

Outcome Measures

The on-line questionnaire was used to obtain data regarding descriptive characteristics (age, gender, height, weight, educational status), home exercise habits, PA levels and well-being of the individuals.

The part of the questionnaire related to the PA level contained questions on number of days with vigorous PA per week (0-7 days), duration of vigorous PA per day (none, <15 min, 16-30 min, 31-45 min, 46-60 min, 61-90 min, 90min<), number of days with moderate PA per week (0-7 days), duration of moderate PA per day (none, <15 min, 16-30 min, 31-45 min, 46-60 min, 61-90 min, 90min<), number of days (0-7 days) with at least 10 minutes walking in the corridor, time spent sitting or lying down per day (none, <15 minutes, 16-30 minutes, 31-45 minutes, 46-60 minutes, 61-90 minutes, 90 minutes <) (Olsson et al., 2016; Matthews et al., 1997).

We used the WHO-5 Well-Being Index to measure well-being of individuals. The WHO-5 is a short self-reported measure of current mental well-being (World Health Organization Regional Office for Europe, 1998). Bech (1999) declared that this index contains five positively phrased items. The participant is asked to rate how he or she feel well each of the 5 statements during last

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14 days. Each of the 5 items is ranked between 5 (all of the time) and 0 (none of the time). The scores are summed to obtain a total raw score ranging from 0 to 25 (0 is absence of well-being and 25 is maximal well-being). Then, the raw score is multiplied by four in order to translate it to a percentage scale from 0 (absent) to 100 (maximal). The highest scores indicate a strong sense of well-being. Eser et al. (2019) indicated WHO-5 as a valid and reliable scale for Turkish population.

Statistical Analyses

All data were analyzed using SPSS 25.0 for Windows. The variables were investigated using visual (histograms, probability plots) and Kolmogorov-Smirnov test was used to determine whether the data is normally distributed. Descriptive statistics were expressed as frequencies and percentages for categorical variables. Continuous variables were presented as median (minimum-maximum) and interquartile range since they were not normally distributed. Mann-Whitney U test was used to compare of continuous variables with abnormal distribution and ordinal variables in between group analysis. The correlation coefficients and their significance were calculated using Spearman test. Kendall test was used to investigate the associations between non-normally distributed and/or ordinal variables. Strength of correlation was interpreted as very weak, weak, moderate, strong and very strong for different r values (Akoğlu, 2018). A 5% type-I error level was used to infer statistical significance ($p<0.05$).

Results

A total of 390 individuals participated in the study in May 2020, during partial lockdown procedures implemented by the Turkish government for COVID-19 global pandemic. 7 surveys were discarded due to missing item responses. Survey of 5 individuals who did not meet inclusion criteria (3 were younger than 18 years and 2 were older than 65 years) were also excluded. As a result, data obtained from 378 individuals were used for the analyses. Characteristics and distribution of demographic characteristics, and PA behavior of surveyed participants are presented in Table 1 and Table 2, respectively.

Table 1. Characteristics of surveyed participants

	Median (min-max)	**IQR**
Age, years	32 (18-65)	17
BMI, kg/m^2	24.16 (16.02-44.06)	5.81
Vigorous Physical Activity, days per week	0 (0-7)	0
Moderate Physical Activity, days per week	1 (0-7)	2
Time Spent walking in corridor, days per week	0 (0-7)	3
WHO-5 Well-Being Index Score	60 (0-100)	25

IQR Interquartile range, *BMI* body mass index, *COVID-19* Coronavirus disease 2019, *WHO-5* The 5-item World Health Organization

When the participants were divided into two groups in terms of presence/absence of doing exercise at home, between-group comparisons showed that age and BMI of the participants who do not exercise at home were significantly higher than those of the participants who do exercise at home ($p=0.001$, $p<0.001$, respectively). The number of days with vigorous and moderate PA, time spent walking in the corridor and WHO-5 Well-Being Index scores of the participants who exercise at home were significantly higher than those of the participants who do not exercise at home ($p<0.005$) (Table 3). In addition, there was no statistically significant difference between physical activity level of participants who had to go to work and those who did not ($p>0.05$).

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Table 2. Distribution of demographic characteristics and physical activity behavior of surveyed participants

n=378	Number (n)	Percent (%)
Gender		
Female	235	62.2
Male	143	37.8
Education Status		
Primary Education	12	3.2
High School	34	9.0
Associate Degree	65	17.2
Bachelor's Degree	164	43.4
Master Degree	54	14.2
Doctorate	49	13.0
Working Status During COVID-19		
Yes	119	31.5
No	259	68.5
Doing Exercise at Home		
Yes	216	57.1
No	162	42.9
Vigorous Physical Activity, min per day		
None	286	75.7
<15	16	4.2
16-30	26	6.9
31-45	29	7.7
46-60	14	3.7
61-90	5	1.3
90<	2	0.5
Moderate Physical Activity, min per day		
None	182	48.1
<15	43	11.4
16-30	80	21.2
31-45	47	12.4
46-60	19	5.0
61-90	3	0.8
90<	4	1.1
Time Spent Sitting, min per day		
<15	8	2.1
16-30	27	7.1
31-45	28	7.4
46-60	49	13.0
61-90	45	11.9
90<	221	58.5

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Table 3. The comparison of the variables in terms of presence/absence of doing exercise at home

	Doing exercise at home - Yes (n=216) Median (min - max)	**Doing exercise at home - No (n=162) Median (min - max)**	**p value**
Age, years	30 (18-65)	34.5 (18-60)	0.001*
BMI, kg/m²	23.03 (16.02-37.01)	25.16 (16.02-44.06)	<0.001*
Vigorous Physical Activity, days per week	0 (0-7)	0 (0-4)	<0.001*
Moderate Physical Activity, days per week	2 (0-7)	0 (0-7)	<0.001*
Time Spent walking in corridor, days per week	1 (0-7)	0 (0-7)	<0.001*
WHO-5 Well-Being Index Score	64 (12-100)	60 (0-100)	0.010*

BMI Body mass index, *WHO-5* The 5-item World Health Organization
* p <0.05, Mann Whitney *U* Test

Age was very weakly and negatively correlated with vigorous PA (days per week) (p<0.001, r=-0.186) and moderate PA (days per week) (p<0.001, r=-0.171). Furthermore, a weak and positive correlation was found between age and WHO-5 Well Being Index Score (p=0.030, r=0.267). While BMI was very weakly and negatively correlated with vigorous PA (days per week) (p=0.003, r=-0.111) and moderate PA (days per week) (p<0.001, r=-0.155), it was very weakly and positively correlated with WHO-5 Well Being Index Score (p<0.001, r=0.163).

We found a statistically significant very weak and positive correlation between vigorous PA (days per week) and WHO-5 Well Being Index Score (p=0.039, r=0.106). There was a very weak and positive correlation between time spent walking in corridor (days per week) and WHO-5 Well Being Index Score (p=0.041, r=0.105). No other significant correlations were found among assessed variables (Table 4).

Discussion

In this study, we aimed to determine PA level of Turkish population during the global outbreak of COVID-19 and whether it was related to well-being. In general, we found a positive correlation between PA level and well-being of the individuals.

The results showed that time spent on vigorous PA was associated with well-being. However, approximately three quarters of participants declared that they did not do any vigorous PA and nearly half of them did not do any moderate PA during the outbreak. We also found that both age and BMI were associated with vigorous and moderate PA level and well-being.

Staying at home or having to go to work during the pandemic can change the level of physical activity. In our study, it was found that the working status of the participants did not affect the physical activity level of the participants.

To date very limited data is available on PA level of nations during the global outbreak of COVID-19. Wang et al. (2020) reported that most of the Chinese people did not do any moderate or vigorous PA in early days of the COVID-19 outbreak. Stanton et al. (2020) declared that average PA of Australian participants was 312.5 minutes/week at the onset of the COVID-19 pandemic. In another study, Maugeri et al. (2020) found that Italian participants' vigorous PA level was 766 MET-min/week while moderate one was 523 MET-min/week during COVID-19 outbreak. Unlike other studies, we assessed not only PA level but also exercise habits at home. In our study, 57.1% of surveyed participants were doing exercise at home during COVID-19 pandemic.

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Table 4. Correlation matrix among variables

	Age, years	**BMI**, kg/m²	**Vigorous Physical Activity**, days per week	**Vigorous Physical Activity**, min per day	**Moderate Physical Activity**, days per week	**Moderate Physical Activity**, min per day	**Time spent walking in corridor,** days per week	**Time spent sitting**, min per day	**WHO-5 Well-Being Index Score**
Age, years	-	r=0.449 [a]	r=-0.186 [a]	r=-0.141 [b]	r=-0.171 [a]	r=-0.135 [b]	r=-0.028 [a]	r=-0.176 [b]	r=0.267 [a]
	-	p<0.001***	p<0.001***	p=0.001***	p<0.001***	p=0.001***	p= 0.594	p<0.001***	p<0.001***
BMI, kg/m²		-	r=-0.111 [a]	r=-0.082 [b]	r=-0.155 [a]	r=-0.135 [b]	r=-0.027[a]	r=-0.031 [b]	r=0.163[a]
		-	p=0.030*	p=0.041*	p=0.003**	p=0.001***	p=0.595	p=0.428	p<0.001***
Vigorous Physical Activity, days per week			-	r=0.920 [b]	r=0.345 [a]	r=-0.303 [b]	r=0.120 [a]	r=0.081 [b]	r=0.106 [a]
			-	p<0.001***	p<0.001***	p<0.001***	p=0.019*	p=0.075	p=0.039*
Vigorous Physical Activity, min per day				-	r=0.297 [b]	r=0.328 [b]	r=0.102 [b]	r=0.041 [b]	r=0.087 [b]
				-	p<0.001***	p<0.001***	p=0.023*	p=0.093	p=0.035*
Moderate Physical Activity, days per week					-	r=0.820 [b]	r=0.241 [a]	r=-0.066 [b]	r=0.056 [a]
					-	p<0.001***	p<0.001***	p=0.123	p=0.274
Moderate Physical Activity, min per day						-	r= 0.203 [b]	r=-0.059 [b]	r=0.037 [b]
						-	p<0.001***	p=0.177	p=0.354
Time spent walking in corridor, days per week							-	r=-0.079 [b]	r=0.105 [a]
							-	p=0.069	p=0.041*
Time spent sitting, min per day								-	r=-0.093 [b]
								-	p=0.020*
WHO-5 Well-Being Index Score									-
									-

[a] Spearman Correlation Analysis

[b] Kendall Rank Correlation Analysis

*p <0.05, **p <0.01, ***p <0.001

BMI body mass index, *WHO-5* The 5-item World Health Organization, *COVID-19* Coronavirus Disease 2019

However, a large amount of (75.1%) participants were not doing any vigorous PA. Besides, only 1.1% of the participants were doing moderate PA over 90 minutes per day while approximately half of them did not do any moderate PA. Although the participants declared that they did exercise at home, time spent on PA was poor during pandemic in our study. The reason of this result could be the wrong PA perception of Turkish people such as the belief that "doing exercise for a short time is equal to sufficient PA".

Social distancing during COVID-19 lockdown negatively affected PA behaviors such as decreased time spent on vigorous PA and increased sedentary lifestyle. Altered daily routines during COVID-19 outbreak affected all PA intensity levels as well as daily sitting time (Lesser and Nienhuis, 2020; Hall et al., 2020).

Well-being was claimed to be decreased during COVID-19 pandemic due to various reasons. Lack of access to gyms, outdoor sport areas or fields to do PA could be the reason of decreased sense of well-being (Hall et al., 2020). Moreover, many people experienced stress and anxiety in the face of isolation from normal social life. In addition to these, fear of getting illness, likelihood of losing a relative or a friend because of the viral infection and the negative impact of COVID-19 on economic status might have contributed to anxiety and stress levels (Hall et al., 2020).

The benefits of exercise are specified useful in terms of decreasing anxiety, stress and fear (Lubans et al., 2016; Stanton et al., 2020). Increased PA had positive impacts on neurobiological, psychosocial and behavioral mechanisms of mental health outcomes. For example, regular and sufficient PA triggers to release endogenous opioids, helps to have good physical self-perceptions and to improve coping stress, anxiety and fear of getting illness and enhances self-regulation skills (Lubans et al., 2016). However, when staying at home and social isolation are necessary during the COVID-19 pandemic, it is still unknown whether Turkish people meets the WHO recommendations for PA. It was declared that practicing PA at least 150 min per week of moderate to vigorous-intensity or 75 min of high intensity per week, or a combination of both was recommended by WHO (World Health Organization, 2010). To date, in Turkey there is no national tracking system for PA, and no studies have determined PA levels of the public in details.

There are limited number of studies examining the relationship between PA and well-being during COVID-19 outbreak in the literature. In a Brazilian study, Schuch et al. (2020) reported that there was a linear relationship between vigorous PA and depressive-anxietic symptom severity, suggesting dose-response association during this pandemic. In another study that conducted in France and Switzerland, Cheval et al. (2020) declared that increment of sedentary behaviors of French and Swiss people during COVID-19 was associated with decreased physical and mental health, as well. They pointed out that PA and sedentary behaviors during pandemic were related to physical and mental health. Maugeri et al. (2020) examined changes in the PA level and well-being and also investigated relationship between them during self-isolation days in Italy. Their results showed that there was significant positive correlation between PA and well-being. Lesser and Nienhuis (2020) conducted a survey that was utilized to measure participants' PA behavior, well-being and anxiety levels. Their results showed that PA was strongly associated with well-being outcomes in Canadians during COVID-19 outbreak. Stanton et al. (2020) investigated associations between psychological distress and changes in selected health behaviors of Australian people and they found that PA level was not associated with all aspects of psychological distress. Similarly, our results showed that reduced PA is related to decreased well-being in Turkish population. This result could be due to the radical change in everyday schedules and habits during COVID-19 outbreak. It could also be related to the phenomenon that PA triggers good physical self-perceptions, improve coping stress and decrease fear of getting illness or losing loved ones and enhances self-regulation skills (Burtscher et al., 2020).

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Our results also showed that people who did exercise at home had higher PA and well-being level than those who did not. It is well-known that regular exercise led to increased PA level and has benefits on mental health and psychological well-being (Lubans et al., 2016; Maugeri et al., 2020).

In this study, age and BMI were negatively correlated with PA level, whereas they were positively correlated with well-being. Ramirez et al. (2018) and Tittlbach et al. (2017) showed that PA declined with increased age and BMI. Nilsson et al. (2010) also showed that well-being improved with age in healthy individuals. However, one study claimed that age was only related to life satisfaction, which is a sub-parameter of well-being, not the overall well-being (Noor, 2008). Therefore, this was unsurprising that PA level and well-being were affected by age and BMI during the pandemic as in pre-pandemic times (Bhasin et al., 2020; Hussain et al., 2020; Ilardi et al. 2020).

To the best of our knowledge, ours is the first study investigating PA level with relation to well-being status in Turkish people during the COVID-19 pandemic. Moreover, this study was carried out during lockdown restrictions in Turkey. Therefore, timing of the data collection was convenient to accurately assess PA level and well-being during the global pandemic. However, there are also some limitations to consider. First, the study utilized a cross-sectional design therefore causality cannot be inferred. Second, all data was collected using a self-reported online survey. However, self-reported data is subject to some biases and limitations, such as honesty, response bias, sampling bias, etc.

In conclusion, our results showed that increased PA level is associated with improved well-being in Turkish adults during the COVID-19 pandemic. Effective strategies to improve PA levels should be helpful to combat reduced well-being. While staying at home, social distancing and complying with the rules of hygiene are fundamental steps to halt the pandemic, regular physical exercise should be used to decrease negative effects of pandemic on well-being and PA levels.

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