Chronicles of Precision Medical Researchers

Editor in Chief
Resul YILMAZ, Prof. Dr.

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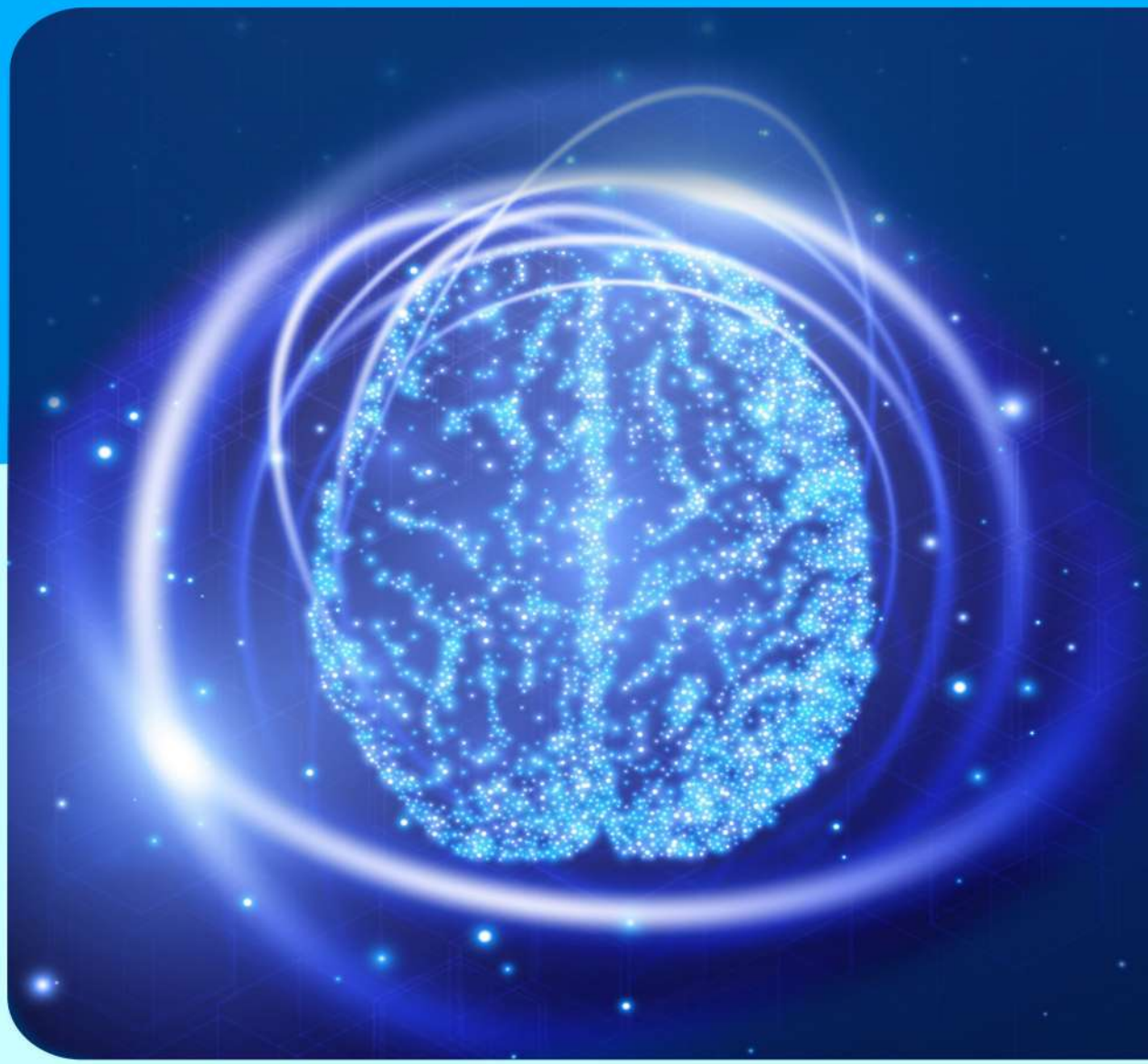

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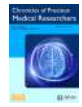

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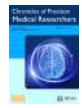

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INSTRUCTIONS FOR AUTHORS

AIM AND SCOPE

The Journal will not consider manuscripts any that have been published elsewhere, or manuscripts that are being considered for another publication, or are in press. Studies previously announced in the congresses are accepted if this condition is stated. If any part of a manuscript by the same author(s) contains any information that was previously published, a reprint or a copy of the previous article should be submitted to the Editorial Office with an explanation by the authors

A technical review is performed to confirm that all of the required documentation has been submitted and to conduct a preliminary evaluation of the manuscript and supplementary files to assess suitability for the Journal. The manuscript will be returned to the Author in the event of any deficiency.

Chronicles of Precision Medical Researchers operates a blind review process. Contributions deemed suitable are then typically sent to a minimum of two independent expert reviewers in the field of study to assess the scientific quality of the paper.

The Editor/Editors are responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final. If necessary, author(s) may be invited to submit a revised version of the manuscript. This invitation does not imply that the manuscript will be accepted for publication. Revised manuscripts must be sent to the Editorial Office within 4 (four) weeks, otherwise they will be considered as a new application. The corresponding author will be notified of the decision to accept or reject the manuscript for publication.

Statements and suggestions published in manuscripts are the authors' responsibility and do not reflect the opinions of the Editor, Associate Editors and the Editorial Board members.

The manuscript will not be returned to the authors whether the article is accepted or not. Copyright fee is not paid for the articles published in the journal. A copy of the journal will be sent to the corresponding author.

Language of the Journal

The official languages of the Journal are Turkish and English. The manuscripts that are written in Turkish have abstracts in English, which makes the abstracts available to a broader audience.

Authorship Criteria

After accepted for publication, all the authors will be asked to sign "Coyright Transfer Form" which states the following: " This work is not under active consideration for publication, has not been accepted for publication, nor has it been published, in full or in part (except in abstract form). I confirm that the study has been approved by the ethics committee. " All authors should agree to the conditions outlined in the form.

Chronicles of Precision Medical Researchers has agreed to use the standards of the International Committee of Medical Journal Editors. The author(s) should meet the criteria for authorship according to the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. It is available at www.icmje.org.

Ethical Responsibility

The protocol of clinical research articles must be approved by the Ethics Committee.

In all studies conducted on humans, the "Material and Method" section was approved by the relevant committee or the Helsinki Declaration of Principles (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/).

It should be stated in the text that all persons included in the study signed the am Informed Consent Form ".

The articles submitted to the Chronicles of Precision Medical Researchers will be deemed to have been conducted in accordance with the Helsinki Declaration of Principles, and have received ethical and legal permissions and will not be held responsible.

If the "Animal" item was used in the study, the authors stated that in the Material and Method section of the article, they protect the animal rights in their studies in accordance with the principles of Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) and that they have received approval from the ethics committees of their institutions. must specify.

In case reports, Informed Consent a should be obtained from patients regardless of the identity of the patient.

If the article includes the institution (directly or indirectly) providing financial support for the commercial connection or work, the authors; the commercial product used, the drug, the company has no commercial relationship with, or if there is any relationship (consultant, other agreements, etc.), the editor must inform the presentation page.

If Ethics Committee Approval is required in the article; the received document should be sent with the article.

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The manuscript should be submitted to the Academic Plagiarism Prevention Program by the authors.

It is the authors' responsibility to ensure that the article complies with the ethical rules.

Policy of Screening for Plagiarism

The manuscripts are scanned by the Journal using the iThenticate program for determination of plagiarism and non-ethical situations. Chronicles of Precision Medical Researchers will immediately reject manuscripts leading to plagiarism.

TYPES OF MANUSCRIPT

Manuscripts should be submitted online via www.chronpmr.com

Original Articles should not exceed 3000 words and should be arranged under the headings of Abstract (not more than 300 words), Introduction, Materials and Methods, Results, Discussion, Conclusion and References.

Case Reports should not exceed 1000 words and 10 references, and should be arranged as follows: Abstract, Introduction, Case Report, Discussion and References. It may be accompanied by only one figure or table.

Letter to the Editor should not exceed 500 words. Short relevant comments on medical and scientific issues, particularly controversies, having no more than five references and one table or figure are encouraged. Where letters refer to an earlier published paper, authors will be offered right of reply.

Reviews are not accepted unless written on the invitation of the Editorial Board.

PREPARATION OF MANUSCRIPTS

All articles submitted to the Journal must comply with the following instructions:

a) Submissions should be doubled-spaced and typed in Arial 10 points.

b) All pages should be numbered consecutively in the top right-hand corner, beginning with the title page.

c) The title page should not include the names and institutions of the authors.

d) The manuscript should be presented in the following order: Title page, Abstract (English, Turkish), Keywords (English, Turkish), Introduction, Materials and Methods, Results, Discussion, Conclusion, Acknowledgements (if present), References, Figure Legends, Tables (each table, complete with title and foot-notes, on a separate page) and Appendices (if present) presented each on a separate page.

Title

The title should be short, easy to understand and must define the contents of the article.

Abstract

Abstract should be in both English and Turkish and should consist "Aim, Materials and Methods, Results and Conclusion". The purpose of the study, the setting for the study, the subjects, the treatment or intervention, principal outcomes measured, the type of statistical analysis and the outcome of the study should be stated in this section (up to 300 words). Abstract should not include reference. No abstract is required for the letters to the Editor.

Keywords

Not more than five keywords in order of importance for indexing purposes should be supplied below the abstract and should be selected from Index Medicus Medical Subject Headings (MeSH), available at www.nlm.nih.gov/meshhome.html.

Text

Authors should use subheadings to divide sections regarding the type of the manuscript as described above. Statistical methods used should be specified in the Materials and Methods section.

References

In the text, references should be cited using Arabic numerals in parenthesis in the order in which they appear. If cited only in tables or figure legends, they should be numbered according to the first identification of the table or figure in the text. Names of the journals should be abbreviated in the style used in Index Medicus. The names of all authors should be cited when there are six or fewer; when seven or more, the first three should be followed by et al. The issue and volume numbers of the referenced journal should be added.

References should be listed in the following form:

Journal article

Teke Z, Kabay B, Aytekin FO et al. Pyrrolidine dithiocarbamate prevents 60 minutes of warm mesenteric ischemia/reperfusion injury in rats. Am J Surg 2007;194(6):255-62.

Supplement

Solca M. Acute pain management: Unmet needs and new advances in pain management. Eur J Anaesthesiol 2002; 19(Suppl 25): 3-10.

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Medical Researchers

Online article not yet published in an issue

Butterly SJ, Pillans P, Horn B, Miles R, Sturtevant J. Off-label use of rituximab in a tertiary Queensland hospital. Intern Med J doi: 10.1111/j.1445-5994.2009.01988.x

Book

Sample1: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

Sample 2: Sümbüloğlu K, Akdağ B. Regresyon Yöntemleri ve Korelasyon Analizi. Hatiboğlu Yayınevi: Ankara; 2007.

Chapter in a book

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. I n: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93113.

Journal article on the Internet

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Website

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

An organization as an author

The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

Acknowledgements

The source of financial grants and the contribution of colleagues or institutions should be acknowledged.

Tables

Tables should be complementary, but not duplicate information contained in the text. Tables should be numbered consecutively in Arabic numbers, with a descriptive, self-explanatory title above the table. All abbreviations should be explained in a footnote. Footnotes should be designated by symbols in the following order: *,†, ‡, §, ¶.

Figures

All illustrations (including line drawings and photographs) are classified as figures. Figures must be added to the system as separate .jpg or .gif files (approximately 500x400 pixels, 8 cm in width and at least 300 dpi resolution). Figures should be numbered consecutively in Arabic numbers and should be cited in parenthesis in consecutive order in the text.

Figure Legends

Legends should be self-explanatory and positioned on a separate page. The legend should incorporate definitions of any symbols used and all abbreviations and units of measurements should be explained. A letter should be provided stating copyright authorization if figures have been reproduced from another source.

Measurements and Abbreviations

All measurements must be given in metric system (Système International d'Unités, SI). Example: mg/kg, µg/kg, mL, mL/kg, mL/kg/h, mL/kg/min, L/min, mmHg, etc. Statistics and measurements should always be given in numerals, except where the number begins a sentence. When a number does not refer to a unit of measurement, it is spelt out, except where the number is greater than nine.

Abbreviations that are used should be defined in parenthesis where the full word is first mentioned. Some common abbreviations can be used, such as iv, im, po, and sc.

Drugs should be referred to by their generic names, rather than brand names.

Editorial Correspondence

Prof. Dr. Resul YILMAZ
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Checklist for Manuscripts

Review guide for authors and instructions for submitting manuscripts through the electronic submission, website at

http://www.chronpmr.com

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Medical Researchers

YAZARLARA BİLGİ

AMAÇ ve KAPSAM

Chronicles of Precision Medical Researchers Dergisi, dört ayda bir yayımlanır ve üç sayı ile bir cilt tamamlanır. Dergi; pediatri ile ilgili tüm nitelikli klinik ve deneysel araştırmaları, olgu sunumlarını ve editöre mektupları yayımlar.

Chronicles of Precision Medical Researchers Dergisi, bilimsel yayınlara açık erişim sağlar. Dergi basımından hemen sonra, makalelerin tam metinlerine ücretsiz ulaşılabilir.

Dergide yayımlanmak üzere gönderilen yazıların daha önce başka bir yerde yayımlanmamış veya yayımlanmak üzere gönderilmemiş olması gerekir. Daha önce kongrelerde sunulmuş çalışmalar, bu durum belirtilmek koşuluyla kabul edilir. Makale, yazar(lar) ın daha önce yayımlanmış bir yazısındaki konuların bir kısmını içeriyorsa bu durum belirtilmeli ve yeni yazı ile birlikte önceki makalenin bir kopyası da Yayın Bürosu'na gönderilmelidir.

Gerekli tüm belgelerin sunulduğunu teyit etmek ve dergiye uygunluğunu değerlendirmek için makale ve ek dosyaların ön değerlendirmesini yapmak üzere teknik bir inceleme yapılır. Herhangi bir eksiklik olması halinde makale yazara iade edilecektir. Chronicles of Precision Medical Researchers Dergisi kör bir inceleme süreci yürütmektedir. Uygun görülen yazılar daha sonra makalenin bilimsel kalitesini değerlendirmek için çalışma alanında en az iki bağımsız uzmana gönderilir. Editör / Editörler makalelerin kabulü veya reddi ile ilgili nihai karardan sorumludur.

Editörün kararı kesindir. Gerekli olduğu durumlarda, yazar(lar) dan düzeltme istenebilir. Yazardan düzeltme istenmesi, yazının yayımlanacağı anlamına gelmez. Bu düzeltmelerin en geç 21 gün içinde tamamlanıp dergiye gönderilmesi gereklidir. Aksi halde yeni başvuru olarak değerlendirilir. Sorumlu yazara yazının kabul veya reddedildiğine dair bilgi verilir.

Dergide yayımlanan yazıların etik, bilimsel ve hukuki sorumluluğu yazar(lar)a ait olup Editör, Editör Yardımcısı ve Yayın Kurulu'nun görüşlerini yansıtmaz.

Dergide yayımlanması kabul edilse de edilmese de, yazı materyali yazarlara geri verilmez. Dergide yayımlanan yazılar için telif hakkı ödenmez. Bir adet dergi, sorumlu yazara gönderilir.

Derginin Yazı Dili

Derginin yazı dili Türkçe ve İngilizcedir. Dili Türkçe olan yazılar, İngilizce özetleri ile yer alır. Yazının hazırlanması sırasında, Türkçe kelimeler için Türk Dil Kurumundan (www.tdk.gov.tr), teknik terimler için Türk Tıp Terminolojisinden (www.tipterimleri.com) yararlanılabilir.

Yazarlık Kriterleri

Dergide yayınlanması uygun bulunan tüm yazıların araştırma ve yayın etiğine uygun hazırlandığı, varsa sağlanan fonun kaynağının tanımlandığı, başka yerde yayımlanmadığı veya yayımlanmak üzere gönderilmediği, çalışmaya katılan tüm yazarlar tarafından yazının son halinin onaylandığı, yayımlanacak yazı ile ilgili telif haklarının dergiye devredildiği, tüm yazarların imzaları ile "Yayın Hakkı Devir Formu"nda belirtilmesi gerekir.

Chronicles of Precision Medical Researchers Dergisi, Uluslararası Tıp Dergileri Editörleri Kurulu'nun (International Committee of Medical Journal Editors) "Biyomedikal Dergilere Gönderilen Makalelerin Uyması Gereken Standartlar: Biyomedikal Yayınların Yazımı ve Baskıya Hazırlanması (Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication)" standartlarını kullanmayı kabul etmektedir. Bu konudaki bilgiye www.icmje.org adresinden ulaşılabilir.

Etik Sorumluluk

Etik Sorumluluk / Kurallar: Klinik araştırma makalelerinin protokolü Etik Komitesi tarafından onaylanmış olmalıdır.

İnsanlar üzerinde yapılan tüm çalışmalarda "Gereç ve Yöntem" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklarasyonu'na (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır.

Çalışmaya dahil edilen tüm kişilerin Bilgilendirilmiş Onam Formu'nu imzaladığı metin içinde belirtilmelidir.

Chronicles of Precision Medical Researchers Dergisi'ne gönderilen makalelerdeki çalışmaların Helsinki İlkeler Deklarasyonu'na uygun olarak yapıldığı, kurumsal etik ve yasal izinlerin alındığı varsayılacak ve bu konuda sorumluluk kabul edilmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntem bölümünde hayvan haklarını Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda koruduklarını, çalışmalarında ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Olgu sunumlarında hastanın kimliğinin ortaya çıkmasına bakılmaksızın hastalardan "Bilgilendirilmiş rıza" alınmalıdır.

Makalede ticari bağlantı veya çalışma için maddi destek veren kurum (doğrudan veya dolaylı) mevcut ise yazarlar; kullanılan ticari ürün, ilaç, firma ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar vs.), editöre sunum sayfasında bildirmek zorundadır.

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Makalede Etik Kurul Onayı alınması gerekli ise; alınan belge makale ile birlikte gönderilmelidir.

Makale yazarlar tarafından akademik intihal önleme programından geçirilmelidir.

Makalenin etik kurallara uygunluğu yazarların sorumluluğundadır.

İntihal Taraması Politikası

Makaleler, intihal ve etik olmayan durumların belirlenmesi için iThenticate programı kullanılarak Journal tarafından taranır. Chronicles of Precision Medical Researchers Dergisi intihallere yol açan makaleleri derhal reddedecektir.

YAZI TÜRLERİ

Yazılar, elektronik ortamda www.chronpmr.com adresine gönderilir.

Orijinal makaleler, 3000 sözcük sayısını aşmamalı, "Öz (en fazla 300 kelime), Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç, Kaynaklar" bölümlerinden oluşmalıdır.

Olgu Sunumu, "Öz, Giriş, Olgu Sunumu, Tartışma, Kaynaklar" şeklinde düzenlenmelidir. En fazla 1000 sözcük ile sınırlıdır. Sadece bir tablo veya şekil ile desteklenebilir.

Editöre Mektup, yayımlanan metinlerle veya mesleki konularla ilgili olarak 500 sözcüğü aşmayan ve beş kaynak ile bir tablo veya şekil içerecek şekilde yazılabilir. Ayrıca daha önce dergide yayınlanmış metinlerle ilişkili mektuplara cevap hakkı verilir.

Yayın Kurulu'nun daveti üzerine yazılanlar dışında derleme kabul edilmez.

MAKALENİN HAZIRLANMASI

Dergide yayınlanması istenilen yazı için aşağıdaki kurallara uyulmalıdır.

a) Yazı; iki satır aralıklı olarak, Arial 10 punto ile yazılmalıdır.

b) Sayfalar başlık sayfasından başlamak üzere, sağ üst köşesinde numaralandırılmalıdır.

c) Online makale sistemine yüklenen word dosyasının başlık sayfasında (makalenin adını içeren başlık sayfası), yazarlara ait isim ve kurum bilgileri yer almamalıdır.

d) Makale, şu bölümleri içermelidir: Her biri ayrı sayfada yazılmak üzere; Türkçe ve İngilizce Başlık Sayfası, Öz, Abstract, Anahtar Sözcükler, Keywords, Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç, Açıklamalar (varsa), Kaynaklar, Şekil Alt Yazıları, Tablolar (başlıkları ve açıklamalarıyla beraber), Ekler (varsa).

Yazının Başlığı

Kısa, kolay anlaşılır ve yazının içeriğini tanımlar özellikte olmalıdır.

Özetler

Türkçe (Öz) ve İngilizce (Abstract) olarak yazılmalı, Amaç, Gereç ve Yöntem, Bulgular ve Sonuç (Aim, Materials and Methods, Results, Conclusion) olmak üzere dört bölümden oluşmalı, en fazla 300 sözcük içermelidir. Araştırmanın amacı, yapılan işlemler, gözlemsel ve analitik yöntemler, temel bulgular ve ana sonuçlar belirtilmelidir. Özette kaynak kullanılmamalıdır. Editöre mektup için özet gerekmemektedir.

Anahtar Sözcükler

Türkçe Öz ve İngilizce Abstract bölümünün sonunda, Anahtar Sözcükler ve Keywords başlığı altında, bilimsel yazının ana başlıklarını yakalayan, Index Medicus Medical Subject Headings (MeSH)'e uygun olarak yazılmış en fazla beş anahtar sözcük olmalıdır. Anahtar sözcüklerin, Türkiye Bilim Terimleri'nden (www.bilimterimleri.com) seçilmesine özen gösterilmelidir.

Metin

Yazı metni, yazının türüne göre yukarıda tanımlanan bölümlerden oluşmalıdır. Uygulanan istatistiksel yöntem, Gereç ve Yöntem bölümünde belirtilmelidir.

Kaynaklar

Chronicles of Precision Medical Researchers Dergisi, Türkçe kaynaklardan yararlanmaya özel önem verdiğini belirtir ve yazarların bu konuda duyarlı olmasını bekler.

Kaynaklar metinde yer aldıkları sırayla, cümle içinde atıfta bulunulan ad veya özelliği belirten kelimenin hemen bittiği yerde ya da cümle bitiminde noktadan önce parantez içinde Arabik rakamlarla numaralandırılmalıdır. Metinde, tablolarda ve şekil alt yazılarında kaynaklar, parantez içinde Arabik numaralarla nitelendirilir. Sadece tablo veya şekil alt yazılarında kullanılan kaynaklar, tablo ya da şeklin metindeki ilk yer aldığı sıraya uygun olarak numaralandırılmalıdır. Dergi başlıkları, Index Medicus'ta kullanılan tarza uygun olarak kısaltılmalıdır. Kısaltılmış yazar ve dergi adlarından sonra nokta olmamalıdır. Yazar sayısı altı veya daha az olan kaynaklarda tüm yazarların adı yazılmalı, yedi veya daha fazla olan kaynaklarda ise üç yazar adından sonra et al. veya ve ark. yazılmalıdır. Kaynak gösterilen derginin sayı ve cilt numarası mutlaka yazılmalıdır.

Kaynaklar, yazının alındığı dilde ve aşağıdaki örneklerde görüldüğü şekilde düzenlenmelidir.

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Dergilerdeki yazılar

Teke Z, Kabay B, Aytekin FO et al. Pyrrolidine dithiocarbamate prevents 60 minutes of warm mesenteric ischemia/reperfusion injury in rats. Am J Surg 2007;194(6):255-62.

Ek sayı (Supplement)

Solca M. Acute pain management: Unmet needs and new advances in pain management. Eur J Anaesthesiol 2002;19(Suppl 25):3-10.

Henüz yayınlanmamış online makale

Butterly SJ, Pillans P, Horn B, Miles R, Sturtevant J. Off-label use of rituximab in a tertiary Queensland hospital. Intern Med J doi: 10.1111/j.1445-5994.2009.01988.x

Kitap

Örnek 1: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.
Örnek 2: Sümbüloğlu K, Akdağ B. Regresyon Yöntemleri ve Korelasyon Analizi. Hatiboğlu Yayınevi: Ankara; 2007.

Kitap bölümü

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. I n: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93113.

İnternet makalesi

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Web Sitesi

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 July 2002]. Available from: www.cancer-pain.org

Yazar olarak bir kuruluş

The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

Açıklamalar

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Tablolar

Tablolar metni tamamlayıcı olmalı, metin içerisinde tekrarlanan bilgiler içermemelidir. Metinde yer alma sıralarına göre Arabik sayılarla numaralandırılıp tablonun üstüne kısa ve açıklayıcı bir başlık yazılmalıdır. Tabloda yer alan kısaltmalar, tablonun hemen altında açıklanmalıdır. Dipnotlarda sırasıyla şu semboller kullanılabilir: *, †, ‡, §, ¶.

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Şekil alt yazıları, her biri ayrı bir sayfadan başlayarak, şekillere karşılık gelen Arabik rakamlarla çift aralıklı olarak yazılmalıdır. Şeklin belirli bölümlerini işaret eden sembol, ok veya harfler kullanıldığında bunlar alt yazıda açıklanmalıdır. Başka yerde yayınlanmış olan şekiller kullanıldığında, yazarın bu konuda izin almış olması ve bunu belgelemesi gerekir.

Ölçümler ve Kısaltmalar

Tüm ölçümler metrik sisteme (Uluslararası Birimler Sistemi, SI) göre yazılmalıdır. Örnek: mg/kg, µg/kg, mL, mL/kg, mL/kg/h, mL/kg/min, L/min, mmHg, vb. Ölçümler ve istatistiksel veriler, cümle başında olmadıkları sürece rakamla belirtilmelidir. Herhangi bir birimi ifade etmeyen ve dokuzdan küçük sayılar yazı ile yazılmalıdır.

Metin içindeki kısaltmalar, ilk kullanıldıkları yerde parantez içinde açıklanmalıdır. Bazı sık kullanılan kısaltmalar; iv, im, po ve sc şeklinde yazılabilir.

İlaçların yazımında jenerik isimleri kullanılmalıdır.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

The investigation of appendiceal size and volume in pediatric appendectomy specimens in terms of histopathological diagnosis, seasonal variability, age, and gender

Pediatrik apendektomi örneklerinde histopatolojik tanı, mevsimsel değişkenlik, yaş ve cinsiyet açısından apendiks boyutu ve hacminin incelenmesi

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ABSTRACT

Aim: Acute appendicitis is a common condition mostly in children with unclear etiology that is treated with an emergency appendectomy. However, some unexpected diagnoses called as "negative appendectomy" that do not require treatment may be detected histopathologically. In this study, it was aimed to investigate the histopathologic diagnoses of pediatric appendectomy specimens, considering the macroscopic dimensions and volume of the specimens for the first time in the literature and comparing them with age and gender groups, and seasons of the operations to achieve additional data in preventing negative appendectomy.

Material and Method: A total of 122 cases were included in this study. The length, longest diameter, and shortest diameter, as well as the volume of each specimen, were measured during the macroscopic examination. The specimens were evaluated for histopathologic diagnosis according to age, gender, and the season in which the operation was performed.

Results: The male-to-female ratio was 1.2. Histopathologically, there were 81 (74.6%) inflammatory diseases [mainly acute appendicitis (65.5%)], and 31 (25.4%) non-inflammatory diseases [mainly lymphoid hyperplasia (21.3%)] that were considered negative appendectomy. Inflammatory diseases were operated mostly in winter (p=0.0099), while non-inflammatory diseases were operated mainly in autumn (p=0.0099). The length, longest diameter, and appendiceal volume were significantly greater in inflammatory than in non-inflammatory ones (p=0.0006, p=0.0126, and p=0.0016, respectively). Length and volume were more significant in acute appendicitis than in lymphoid hyperplasia (p=0.0124 and p=0.0358, respectively). In patients ≤12 years, lymphoid hyperplasia was more common in females than in males (p<0.001). In patients >12 years, acute appendicitis was more common in females than males (p<0.034).

Conclusion: In this study, histopathological diagnoses observed in appendectomy specimens were evaluated for the first time in the literature according to macroscopic appendix size and volume, as well as age, gender, and seasonal variations. The obtained data have the potential to provide additional information to the literature regarding epidemiological, appropriate preoperative, and pathological approaches.

Keywords: Appendectomy, appendicitis, carcinoid, fibrous obliteration, Enterobius vermicularis, pediatric specimens

ÖZ

Amaç: Akut apandisit, çoğunlukla çocuklarda görülen, etiyolojisi belirsiz yaygın bir durumdur ve acil apendektomi ile tedavi edilmektedir. Bununla birlikte, tedavi gerektirmeyen bazı beklenmedik tanılar, histopatolojik olarak tespit edilebilmektedir ve bunlar "negatif apendektomi" olarak adlandırılmaktadır. Bu çalışmada negatif apendektomi vakalarının önlenmesinde literatüre katkı sağlayabilecek ek verilere ulaşmak amacı ile pediatrik apendektomi örneklerinde saptanan histopatolojik tanılar literatürde ilk kez makroskopik apendektomi boyutları ve hacimleri göz önünde bulundurularak, yaş ve cinsiyet grupları ve operasyonların yapıldığı mevsimlerle karşılaştırılarak incelenmiştir.

Gereç ve Yöntem: Bu çalışmaya toplam 122 olgu dahil edilmiştir. Her bir örneğin uzunluğu, en uzun çapı, en kısa çapı ve hacmi makroskobik inceleme sırasında ölçülmüştür. Örnekler, yaş, cinsiyet ve operasyonun gerçekleştirildiği mevsime göre histopatolojik teşhis açısından değerlendirilmiştir.

Bulgular: Erkek-kadın oranı 1.2 olarak saptanmıştır. Histopatolojik olarak, 81 (%74.6) inflamatuar hastalık [çoğunlukla akut apandisit (%65.5)] ve negatif apendektomi olarak değerlendirilen 31 (%25.4) non-inflamatuar hastalık [çoğunlukla lenfoid hiperplazi (%21.3)] tespit edilmiştir. İnflamatuar hastalıkların genellikle kış mevsiminde (p=0.0099), non-inflamatuar hastalıkların ise genellikle sonbaharda (p=0.0099) opere edildiği saptanmıştır. Uzunluk, en uzun çap ve apendiks hacminin, inflamatuar hastalıklarda non-inflamatuar hastalıklara göre önemli ölçüde daha fazla olduğu gözlenmiştir (sırasıyla p=0.0006, p=0.0126 ve p=0.0016). Uzunluk ve hacmin, akut apandisitte lenfoid hiperplaziden daha fazla olduğu saptanmıştır (sırasıyla p=0.0124 ve p=0.0358). 12 yaşından küçük hastalarda, lenfoid hiperplazinin erkeklerde kızlara göre daha yaygın olduğu izlenmiştir (p<0.001). 12 yaşından büyük hastalarda ise akut apandisitin, kızlarda erkeklere göre daha yaygın görüldüğü tespit edilmiştir (p<0.034).

Sonuç: Bu çalışmada, apendektomi materyallerinde izlenen histopatolojik tanılar literatürde ilk kez makroskopik appendiks boyutunun ve hacminin yanı sıra yaş, cinsiyet, ve mevsimsel değişkenliklere göre değerlendirilmiştir. Elde edilen veriler, epidemiyolojik, uygun preoperatif ve patolojik yaklaşım konusunda literatüre ek veriler sağlayabilecek niteliktedir.

Anahtar Kelimeler: Apendektomi, apandisit, karsinoid, fibröz obliterasyon, Enterobius vermicularis, pediatrik spesmenler

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INTRODUCTION

Appendectomy is one of the most common urgent operations in the surgical routine, mainly performed for acute appendicitis (1). Acute appendicitis is seen in all age groups. However, it occurs more frequently in children and adolescents (2,3). Overall lifetime risk is 8.6% for males and 6.7% for females (4).

The etiology of acute appendicitis has not been fully clarified and considered multifactorial (3,5,6). Nutrition, hygiene, and genetic predisposition are claimed to be the primary factors in the development of acute appendicitis (3,7). In addition, some environmental factors, such as regional and seasonal variation have been noted to be responsible for the development of acute appendicitis, in some studies in the literature, from different geographic locations, and only a few from Turkey (3,5).

Lumen obstruction is the most common cause of acute appendicitis (1). Obstruction often develops due to fecaliths and lymphoid hyperplasia (1). However, there are some rare causes of obstruction detected incidentally in the appendectomy specimens such as neoplasms and parasites that require additional treatment (1). Obstruction causes lumen dilation, thickening of the appendix wall, and even perforation due to luminal bacterial overgrowth, inflammation, and ischemia (8,9). Therefore, imaging methods such as ultrasonography (USG) and abdominopelvic computer tomography (CT) are often used to determine the changes in the appendiceal dimensions to confirm acute appendicitis and rule out negative cases along with the clinical scoring methods and laboratory findings (10). Similarly, an increase in the appendix diameter and dilatation in the lumen can be easily detected during the macroscopic examination of appendectomy specimens with acute appendicitis that are submitted to the pathology laboratory. On the contrary, approximately 8.9% (range 1-40%) of the pediatric appendectomy specimens with a preoperative diagnosis of appendicitis show neither macroscopical nor microscopical features of appendicitis, called negative appendectomy (11). Therefore, it is of great importance to know both the macroscopical and histopathological findings of acute appendicitis and normal appendix in children, to exclude false positive cases and prevent negative appendectomies.

In the current study, we aimed to examine the pediatric appendectomy specimens performed for preliminary diagnosis of acute appendicitis to explore the spectrum of the histopathological diagnoses, particularly the unexpected ones, correlate with the age and gender of the patients, the seasons when the operation performed, and the dimensions and volume of the appendix measured during a macroscopical examination to serve additional data to the literature about epidemiology and a proper preoperative and pathological approach.

MATERIAL AND METHOD

After obtaining ethical approval from the Ethics Committee of Akdeniz University for this retrospective study (26.04.2023/number 354), electronic archive records, pathology reports, and histological sections of 122 patients who underwent appendectomy diagnosed with acute appendicitis between January 2012 and December 2018 at the Department of Pathology of Bozok University Faculty of Medicine were reviewed. The age, gender, macroscopical findings, histopathological diagnosis of the cases, and the seasons of the operation were obtained from the pathology reports.

Three dimensions [length (x), longest diameter (y), and shortest diameter (z)] (**Figure 1**) of each appendectomy specimen were recorded according to the macroscopic examination data, and the appendix volume was calculated by multiplying these dimensions with each other. Cases with neutrophil leukocyte infiltration in the appendix wall were considered inflammatory diseases. Those without neutrophil leukocyte infiltration in the appendix wall were considered non-inflammatory diseases that indicated negative appendectomy.

According to age and gender, the patients were divided into four groups: Group 1 (≤12 years old, female), Group 2 (≤12 years old, male), Group 3 (>12 years old, female), and Group 4 (>12 years old, male).

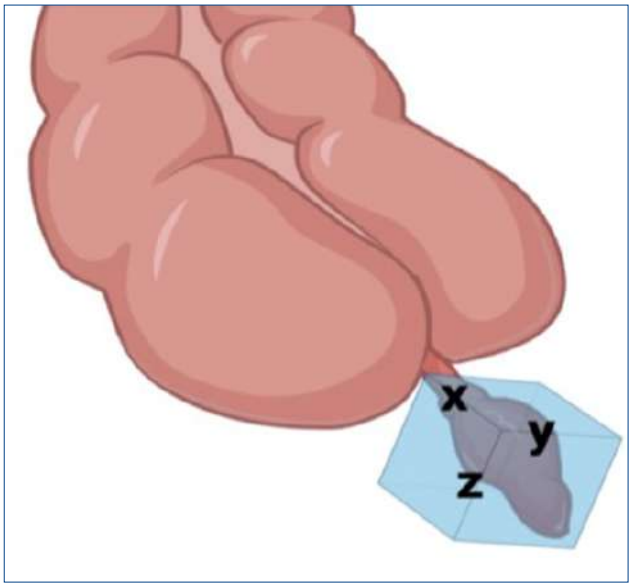

Figure 1. The illustration of the length (x), longest diameter (y), and shortest diameter (z) of appendix vermiformis.

Statistical Analysis

After evaluating the normality in the groups, One-way ANOVA and multiple comparison tests (Dunn's/Tukey's) were used. The student's t-test was preferred for pairwise percentage comparisons. A difference of $p<0.05$ between the groups was considered significant. The groups with a difference between them were indicated in the columns by writing the letter symbol given for each group over the p-value. The drawings were made with the BioRender (U.S.) program.

RESULTS

Of the 122 patients, 67 (54.9%) were male, and 55 (45.1%) were female. The male-to-female ratio was 1.2. The ages of the patients ranged from 1 to 18 years (mean: 12). Lumen dilatation (n=106, 86.8%), luminal fecalith (n=103, 84.4%), periappendiceal fibrin (n=89, 72.9%), and perforation (n=2, 1.6%) were determined in macroscopical records (**Table 1**). Histopathologically, there were six different inflammatory diseases in descending order of frequency: acute appendicitis (n=80, 65.5%), perforated appendicitis (n=8, 6.5%), phlegmonous appendicitis (n=3, 2.4%), necrotizing appendicitis (n=2, 1.6%), vasculitis (n=1, 0.8%), and granulomatous appendicitis (n=1, 0.8%). Four different microscopical diagnoses of non-inflammatory diseases were detected: lymphoid hyperplasia (n=26, 21.3%), enterobiasis (n=2, 1.6%), neuroendocrine tumor (n=1, 0.8%), and fibrous obliteration (n=1, 0.8%), in decreasing order of frequency. And, one case was reported as normal appendix vermiformis (n=1, 0.8%). The detailed macroscopical and microscopical findings are given in **Table 1** according to the groups based on age and gender.

There was no statistically significant difference between inflammatory and non-inflammatory diseases according to the age and gender groups ($p>0.05$). However, lymphoid hyperplasia was more common in Group 1 than Group 2 while acute appendicitis was more common in Group 3 than Group 4 ($p<0.001$, $p<0.034$, retrospectively) (**Table 1**).

The mean value of x, y, and z dimensions, and the total appendiceal volume in inflammatory diseases were 6.5±1.4 cm (range, 3-11.4 cm), 1.8±0.6 cm (range, 0.5-5 cm), 1.1±0.3 cm (range, 0.5-2 cm), and 13.1±0.7 cm^3 (range, 3-30 cm^3), respectively. The mean value x, y, and z dimensions, and the total appendix volume in non-inflammatory diseases were as 5.8±2.1 cm (range, 2.1-9.6 cm), 1.2±0.6 cm (range, 0.6-3.7 cm), 0.7±0.3 cm (range, 0.4-1.9 cm), and 7.6±1.8 cm^3 (range, 1.5-19.4 cm^3), respectively. X and y dimensions and the total appendix volume of the inflammatory diseases were more significant than the non-inflammatory ones ($p=0.0006$, $p=0.0126$, and $p=0.0016$, respectively). The mean value of x, y, and z dimensions and the total appendix volume in lymphoid hyperplasia, the most common non-inflammatory disease in the study, were 5.3±0.3 cm (range, 2.9-8.7 cm), 1.2±0.13 cm (range, 0.6-3.7 cm), 0.8±0.07 cm (range, 0.5-1.9 cm), and 8.7±2.2 cm^3 (range, 1.5-58.3 cm^3), respectively. When acute appendicitis and lymphoid hyperplasia were compared in terms of these measurements, only the x dimension and the total volume were statistically significantly greater in acute appendicitis than in lymphoid hyperplasia ($p=0.0124$ and $p=0.0358$, respectively). There was no statistically significant difference between the x, y, and z dimensions or the total appendix volume of the inflammatory and non-inflammatory diseases according to the age and gender groups ($p>0.05$).

Table 1: Macroscopical and microscopical findings of all cases according to the groups based on age and gender.

		Group 1[a]	%	Group 2[b]	%	Group 3[c]	%	Group 4[d]	%	P value
	Total (n)	**34**	**27,87**	**28**	**22,95**	**21**	**17,21**	**39**	**31,97**	
Macroscopical Findings										
Lumen dilatation	106 (86.8%)	31	25.41	23	18.85	17	13.93	35	28.69	<.001[c,d]
Luminal fecalith	103 (84.4%)	29	23.77	23	18.85	17	13.93	34	27.87	<.001[c,d]
Periappendiceal fibrin	89 (72.9%)	22	18.03	25	20.49	13	10.66	29	23.77	<.013[c,d]
Perforation	2 (1.6%)	0	0	0	0	1	0.82	1	0.82	>.05
Microscopical Findings										
Acute appendicitis	80 (65.5%)	18	14.75	26	21.31	10	8.20	26	21.31	<.034[c,d]
Perforated appendicitis	8 (6.5%)	2	1.64	0	0	4	3.28	2	1.64	<.049[c,b]
Phlegmenous appendicitis	3 (2.4%)	1	0.82	0	0	1	0.82	1	0.82	>.05
Necrotizing appendicitis	2 (1.6%)	2	1.64	0	0	0	0	0	0	>.05
Vasculitis	1 (0.8%)	1	0.82	0	0	0	0	0	0	>.05
Granulomatous appendicitis	1 (0.8%)	0	0	0	0	0	0	1	0.82	>.05
Lymphoid hyperplasia	26 (21.3%)	10	8.20	2	1.64	6	4.92	8	6.56	<.001[a,b]
Enterobiasis	2 (1.6%)	0	0.00	1	0.82	0	0	1	0.82	>.05
Fibrous obliteration	1 (0.8%)	1	0.82	0	0	0	0	0	0	>.05
Carcinoid tumor	1 (0.8%)	0	0	1	0.82	0	0	0	0	>.05
Normal appendix vermiformis	1 (0.8%)	0	0	0	0	0	0	1	0.82	>.05

The most common season that appendectomy operations performed was winter (n=43, 35.2%), followed by autumn (n=42, 34.5%), summer (n=23, 18.8%), and spring (n=14, 11.5%), respectively (**Table 2**). In parallel with those findings, surgery for inflammatory diseases was performed mainly in the winter and least in the spring (p=0.0099). However, surgery for non-inflammatory diseases was performed chiefly in the autumn and least in the spring (p=0.0099). There was no statistically significant difference between the seasons of the operation for inflammatory or non-inflammatory diseases according to the age and gender groups (p>0.05). Detailed information about the cases regarding the seasonal distribution is given in **Table 2** and **Table 3**.

DISCUSSION

Appendectomy specimens are frequently examined in the daily pathology routine, and are primarily diagnosed as acute appendicitis, as in our study (12). The annual incidence rate of 0-4 years-old children is 1-6/10.000, while it increases to 19-28/10.000 in children <14 years old (13). It is most commonly seen between the ages of 10 and 19 (14). The rate of acute appendicitis varies among countries (13,14). Males are more commonly affected than females (13), similar to our study (male/female=1.2). However, in patients >12 years considered as adolescents, acute appendicitis was found to be more common in females than males, in the current study.

The pathogenesis of acute appendicitis includes obstruction of the appendiceal orifice that increases intraluminal pressure, resulting in small vessel occlusion and lymphatic stasis (15). Subsequent bacterial overgrowth causes neutrophil leukocyte infiltration to some or all layers of the appendiceal wall (15). As a result, the appendix wall thickens, it becomes swollen, and the diameter of the appendix increases. These data are used in imaging methods to pre-diagnose acute appendicitis correctly to make proper medical and timely surgical therapy. Also, during the routine macroscopical examination, the increase in the size of the surgically removed appendix is easily encountered. Unless it is operated on time, perforation may also be encountered in the serosal surface of the appendectomy due to ischemic necrosis that may cause fatal peritonitis and abscess, clinically. The diameter of the normal appendix is ≤6 mm (16,17). The appendix diameter over 6 mm has a sensitivity of 93%, and a specificity of 92% in acute appendicitis, radiologically (18). An appendix diameter over 10 mm is accepted as acute appendicitis (17-19). Similar to the literature, the appendix diameter was longer than 7 mm (mean=17.8±0.7 mm) in each case with acute appendicitis in our study. The length of the appendix ranges from 2 to 20 cm, and its average length is 8 to 9 cm (20). There are only a few studies in the literature investigating the relationship between appendix length and appendicitis (20). Pickhardt et al. evaluated the association between appendiceal length and the development of appendicitis according to the CT

Table 2. Distribution of appendectomy operations according to the seasons.

	WINTER			SPRING			SUMMER			AUTUMN			
Month	12	1	2	3	4	5	6	7	8	9	10	11	
Cases (n)	15	24	4	5	6	3	3	6	14	13	15	14	122
Total (n) (%)	43 (35.2%)			14 (11.5%)			23 (18.8%)			42 (34.5%)			122

Table 3. Distribution of surgical operations in terms of seasons according to inflammatory and non-inflammatory diseases, and groups based on age and gender.

	Group 1	W	SP	SM	AUT	Group 2	W	SP	SM	AUT	Group 3	W	SP	SM	AUT	Group 4	W	SP	SM	AUT
INFLAMMATORY DISEASES																				
Acute appendicitis	18	7	2	2	7	26	11	2	5	8	10	5	2	1	2	26	10	1	4	11
Perforated appendicitis	2			1	1	0					4	1		1	2	2	1	1		
Necrotizing appendicitis	2		2			0					0					0				
Phlegmenous appendicitis	1	1				0					1	1				1		1		
Vasculitis	1				1	0					0					0				
Non-necrotizing granuloma	0					0					0					1				
Total (n)	**24**	**8**	**4**	**4**	**9**	**26**	**14**	**2**	**5**	**8**	**15**	**9**	**2**	**3**	**4**	**32**	**16**	**3**	**4**	**11**
NON-INFLAMMATORY DISEASES																				
Lymphoid hyperplasia	10	2	2	1	5	2		1		1	6	2	1	3		8	1	1	3	3
Enterobiasis	0					1				1	0					1			1	
Fibrous obliteration	1				1	0					0					0				
Carcinoid tumor	0					1	1				0					0				
Total (n)	**11**	**2**	**2**	**1**	**6**	**4**	**1**	**1**	**0**	**2**	**6**	**2**	**1**	**3**	**0**	**8**	**1**	**1**	**4**	**3**

Abbreviations: AUT: autumn, SM: summer, SP: spring, W: winter, Group 1 (≤12 years old, female); Group 2 (≤12 years old, male); Group 3 (>12 years old, female), and Group 4 (>12 years old, male)

findings (20). They reported that the appendiceal length of the cases with acute appendicitis varied between 4-10 cm, in 90% of the patients (20), similar to our study (mean length=6.4±0.2 cm, range=1-11.4 cm). Dibekoğlu et al. investigated the relationship between appendiceal length and the possible risk of perforated appendicitis. However, they did not find a significant relationship between these two parameters (21). The perforation rate in pediatrics has been reported between 18-72% in the literature (22). In the present study, the perforation rate was 6.5%, strikingly low compared to the literature. It might be related to the earlier and proper clinical diagnosis, the etiology of the disease, or inadequate macroscopical sampling from the perforation area.

In the present study, we also evaluated the relationship between appendix volume and acute appendicitis for the first time in the literature and all three dimensions of the appendix, to the best of our knowledge. In addition to the length, and the longest diameter, the total appendiceal volume of the inflammatory diseases (acute appendicitis, perforated appendicitis, phlegmonous appendicitis, necrotizing appendicitis, vasculitis, granulomatous appendicitis) was demonstrated to be greater than the non-inflammatory ones (lymphoid hyperplasia, enterobiasis, fibrous obliteration, and carcinoid tumor). Moreover, in the current study, the length and total appendiceal volume of acute appendicitis were greater than lymphoid hyperplasia, a common cause of negative appendectomy that mimics acute appendicitis. Accordingly, lymphoid hyperplasia was found to be the most common cause of negative appendectomy in our study, with a rate of (21.3%).

Lymphoid hyperplasia is a common disease in children. The age and gender characteristics and the incidence differ between studies in the literature (23-25). In the current study, lymphoid hyperplasia was detected more frequently in females than males, regardless of age group. The difference between them was statistically significant under the age of ≤12. Lymphoid hyperplasia defines reactive lymphatic tissue enlargement in the appendix wall, particularly for viral gastroenteritis or mesenteric adenitis (23,25). The hyperplastic mucosal lymphoid tissue increases the maximal mural thickness and the diameter of the appendix to larger than 6 mm, which may lead to false-positive USG findings for appendicitis (26). Following the literature, the appendix diameter was ≥6 mm in each case with lymphoid hyperplasia in our study. Histopathologically, lymphoid hyperplasia describes a group of more than ten lymphoid nodules, each containing lymphoid follicles >2 mm. (25). The appendix wall usually does not include neutrophil leukocyte infiltration with lymphoid hyperplasia (26). Similar to the literature, in the present study, none of the cases of lymphoid hyperplasia accompanies acute appendicitis findings under a light microscope. Therefore, it is more plausible that lymphoid hyperplasia may be a reactive physiological response to inflammation rather than an exact cause of appendicitis. And it may regress without the need for surgery (25).

The relationship between the seasons and the incidence of appendicitis is still debated since the frequency of it varies from region to region in the world (6,13,27). In addition to the studies reporting that it is more common in summer (6,13), there are also publications reporting that it is more common in winter (7,27,28). There are scarce investigations about the seasonal distribution of acute appendicitis in Turkey (6,7,27). Summer is the most common season of appendectomy in Adıyaman and Niğde provinces, while the winter is the most common in Kars province, located in a high and cold region similar to Yozgat, the province of our study (6,7,27). It was reported that spring was the season with the least number of appendectomies in Adıyaman, similar to ours, regardless of whether the diseases were inflammatory or non-inflammatory (6). The seasonal diversity of the infectious agents and allergens, variations in diet (consumption of excessive alcohol, high-carbohydrate and low-fiber foods, etc.), smoking, and other environmental factors such as air pollution, humidity, temperature, and precipitation, may also contribute to the etiopathogenesis of acute appendicitis (6,7,27).

Rarely parasitic infections, benign tumors, or unexpected malignancies might be detected in appendectomy specimens incidentally (1,12). Thus, all appendectomies should be sent to pathology laboratories for histopathological diagnosis and macroscopic examination should be done carefully. Specimens that seem normal on macroscopic examination should also be examined microscopically. In particular, it is crucial to sample the distal part of the appendix, to dismiss the incidental carcinoid tumors, as it is often located in this area (29). The incidence of carcinoid tumors in children is reported to be 1–2/1000 appendectomies (29). Among children, it is generally seen between the ages of 10-12 and shows a preference for girls (30). The current study observed 1 (0.8%) incidental carcinoid tumor in an 11-year-old male patient.

Enterobius vermicularis is the most common parasite detected in the appendix and cecum lumen (31). It can be seen in all age groups but is more common in childhood, predominantly in females (31). Our study detected 2 (1.6%) male patients with Enterobius vermicularis. In the literature, the frequency of Enterobius vermicularis noticed in appendectomies varies between 0.2-41.8% by the current study (31). There were no acute appendicitis findings in the appendix wall accompanying Enterobius vermicularis in our study, similar to the literature (1).

Granulomatous appendicitis is a rare entity detected in appendectomy specimens with a frequency of 0.31-0.95% (12). Both infections (e.g., tuberculosis) and non-infectious processes, particularly Crohn's disease (appendiceal involvement rate of 21%), may cause granulomatous inflammation in the appendix (12,32). In our study, a non-necrotizing granulomatous reaction was observed in a 17-year-old male patient. Since no underlying disease was found after clinical investigations, it was considered "idiopathic granulomatous appendicitis" and followed up clinically.

Localized and systemic vasculitis may affect the appendix at a rate of 0.3-1.9% (33). In the present study, leukocytoclastic vasculitis was detected in an appendectomy of a six-year-old girl operated on for acute abdomen symptoms. The skin rash appeared soon after the operation, and consequently, the patient was diagnosed with Henoch-Schoenlein purpura (HSP). HSP is the most common systemic vasculitis in children (34). Intestinal involvement of HSP may cause colicky abdominal pain that mimics acute appendicitis and lead to an unnecessary appendectomy with a rate of 5-7% (19). The onset of abdominal pain before the rash is reported rarely in the literature (34), which increases the risk of misdiagnosis, similar to our case.

Fibrous obliteration is a benign entity that obstructs the appendix lumen, particularly the distal part, by spindle cells originating from neural tissue with a myxoid or collagenous background (35). It is seen in up to 30% of the cases operated with a preliminary diagnosis of acute appendicitis (36). Following the literature, fibrous obliteration was detected in 1 (0.8%) female patient of 10 years old in our study.

The current study had some limitations, such as the retrospective nature of the study, the relatively small number of cases, and the inaccessibility of radiological images and measurements of the cases due to the problems in the hospital automation system.

CONCLUSION

Detailed pathological evaluation and novel regional epidemiological data emphasizing seasonal variations in pediatric appendectomy specimens were presented in the current study. Winter was the most common season, and spring was a minor regular season in which appendectomy was performed, in both whole cases in the research and the patients with acute appendicitis. The most common cause of negative appendectomy was lymphoid hyperplasia which was operated mainly in the autumn and least in the spring. Incidental cases such as enterobiasis, carcinoid tumor, fibrous obliteration, non-necrotizing granuloma, and vasculitis were detected. To the best of our knowledge, the value of macroscopical measurements in appendectomy specimens was evaluated for the first time in our study in the literature. And statistically significant increases, particularly in length, longest diameter, and appendiceal volume, were detected in positive appendectomies compared to the negative ones. We suggest that those comparisons might aid in reducing negative appendectomies and conducting more comprehensive further studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Akdeniz University Ethics Committee (Date: 26.04.2023, Decision No: 354).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Çocukluk Çağı Osteosarkomu: Tek Merkez Deneyimi

Childhood Osteosarcoma: The Experience of A Single Center

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ÖZ

Amaç: Bu çalışmada, çocukluk çağı osteosarkomlu hastaların klinik özellikleri, tedavi yaklaşımları ve tedavi sonuçlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: 2006-2022 yılları arasında Selçuk Üniversitesi hastanelerinde 2006-2022 yılları arasında teşhis ve tedavi edilen osteosarkomlu hastaların onkoloji dosyaları geriye dönük olarak incelendi.

Bulgular: Bu dönemde osteosarkomlu 24 çocuk çalışmaya dâhil edildi. Erkek/kız oranı 1/1'di. Hastaların yaşı 7,8 ile 17,2 yıl arasında değişiyordu (ortanca, 13,9 yıl). Tümörün yerleşim yerleri, 18 hastada apendiküler kemiklerde (%75), aksiyal kemik yerleşimi beş hastada (%20,8) ve bir hastada ekstraosseöz yerleşimliydi (%4,2) idi. En çok yerleşim yeri femur idi (n: 14, %58,3). Hastaların izlem süreleri 9 ay ile 16,2 yıl arasında değişiyordu (ortanca, 3,15 yıl). Sekiz hasta (%33,4) progresif hastalıkla kaybedildi. Genel ve olaysız sağ kalım oranları sırasıyla %58,6±11,7 ve %61±10,2 idi. Genel sağ kalım oranı üzerine tanın anındaki laktat dehidrogenaz enzim yüksekliğinin olumsuz bir etkisi gözlendi (p=0,021). Tanı anında metastatik hastalığı olan hastalarda genel sağ kalım oranı her ne kadar düşük olsa da istatistiksel olarak aradaki fark anlamlı değildi (p=0,059). Yaşa göre lenfosit sayısı değerlendirildiğinde lenfopeni 10 hastada (%41,7) vardı. Platelet/lenfosit oranı yüksekliği (>150), 12 hastada (%50) ve NLR yüksekliği (>2) 17 hastada (%70,8) olduğu görüldü.

Sonuç: Lokalize hastalığı olan osteosarkomlarda sağ kalım oranlarına benzer sağ kalım oranlarının ne yazık ki halen metastatik osteosarkomlarda elde edilememesi ciddi bir sorun olarak devam etmektedir. Bu yüzden metastatik osteosarkomlu hastalarda yeni tedavi yaklaşımlarına ihtiyaç vardır.

Anahtar Kelimeler: Osteosarkom, çocuk, prognoz

ABSTRACT

Aim: In this study, it was aimed to evaluate the clinical features, treatment approaches and outcomes of patients with childhood osteosarcoma.

Material and Method: From 2006 to 2022, the oncology files of patients with osteosarcoma diagnosed and treated at Selçuk University hospitals between 2006 and 2022 were retrospectively reviewed.

Results: In this period, 24 children with osteosarcoma were included in the study. The male/female ratio was 1/1. The patients' age ranged from 7.8 to 17.2 years (median, 13.9 years). The most common site was the femur (n: 14, 58.3%). The follow-up period of the patients ranged from 9 months to 16.2 years (median, 3.15 years). Eight patients (33.4%) died with progressive disease. Overall and event-free survival rates were 58.6%±11.7% and 61%±10.2%, respectively. A negative effect of lactate dehydrogenase enzyme elevation at the time of diagnosis was observed on the overall survival rate (p=0.021). Although the overall survival rate was low in patients with metastatic disease at the time of diagnosis, the difference was not statistically significant (p=0.059). When the lymphocyte count according to age was evaluated, lymphopenia was present in 10 patients (41.7%). High platelet/lymphocyte ratio (>150) was observed in 12 patients (50%) and increased NLR (>2) in 17 patients (70.8%).

Conclusion: Survival rates similar to those in osteosarcomas with localized disease, unfortunately, still cannot be achieved in metastatic osteosarcomas, which remains a serious problem. Therefore, new treatment approaches are needed in patients with metastatic osteosarcoma.

Keywords: Osteosarcoma, child, prognosis

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GİRİŞ

Çocuklarda, malign kemik tümörleri tüm çocukluk çağı tümörlerinin yaklaşık %6'sını oluşturmaktadır. Ülkemizde ise, kemiğin primer tümörleri tüm çocukluk çağı tümörlerinin yaklaşık %6,5 olarak bildirilmiştir (1, 2). Çocukluk çağı primer kemik tümörlerinin önemli kısmını osteosarkomlar (%56), Ewing sarkom ailesi tümörler (%34) ve diğerleri oluşturmaktadır (1). Diğer primer kemik tümörleri gibi osteosarkomlarda görülme sıklığı genellikle onlu yaşlılarda görülme sıklığı artmaktadır (1, 3). Osteosarkomun sıklığı erkek cinsiyette hafif yüksektir.

Osteosarkomlu hastalarda en sık görülen başvuru şikâyeti tümör bölgesinde ağrıdır (%90). Bunu tümör bölgesinde şişlik, harekette kısıtlılık ve patolojik kırıklar saptanabilir. Daha nadirense etkilenen bölgeye yakın kısımda eklemde efüzyonlar gözlenebilir (1, 3). Patolojik olarak osteosarkomlar beş ana gruba ayrılırlar. Bunlar, klasik (osteoblastik, kondroblastik ve fibroblastik), telanjektazik, küçük hücreli, periosteal ve parosteal ostesarkomlardır (1).

Günümüzde osteosarkomlu hastaların tedavi yaklaşımların neoadjuvan kemoterapi, agressif cerrahi ve adjuvan kemoterapidir. En çok tercih edilen kemoterapi rejimleri sisplatin+adriamisin/yüksek doz metoteraksattır. Yine benzer şekilde sisplatin+adriamisin/ifosfamid + sodium-2-mercaptoethanesulfonate (MESNA) tedavileri de özellikle yetişkin yaşlardaki osteosarkomlarda tedavi seçeneği olarak kullanılmaktadır (1, 3). Cerrahi yaklaşımda ise üç ana temel amaç elde edilmeye çalışılmalıdır. Bunlar: (i) mutlaka güvenli bir cerrahi sınır ile tümörün tam olarak çıkarılması, (ii) mümkün olduğunca fonksiyonların korunması ve (iii) ve kosmetik görüntünün sağlanabilmesidir (3). Tüm bu tedavi yaklaşımları ile beraber metastatik olmayan osteosarkomlu hastalarda yaşam oranları yaklaşık %70'ler civarında iken metastatik olan hastalarda bu oranlar ne yazık ki %10-30'lara düşmektedir.

Bu çalışmada, çocukluk çağı osteosarkomlu hastalarımızın klinik özellikleri, tedavi yaklaşımları ve tedavi sonuçlarının değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM

Bu çalışma için Selçuk Üniversitesi Tıp Fakültesi, Yerel Etik Kurul'undan 26.10.2021 tarihli 2021/479 sayı ile izin alınmıştır. Retrospektif bir çalışma olduğu için hasta ve hasta yakınlarından onam alınmamıştır. Selçuk Üniversitesi hastanelerinde 2006 ile 2022 yılları arasında osteosarkom tanısı alan veya izlenen hastaların dosyaları geriye dönük olarak incelendi. Hastaların dosyalarından:

1. Demografik özellikleri,
2. Başvuru anındaki klinik özellikleri ve laboratuvar bulguları (tam kan sayımı, laktat dehidrogenaz enzim düzeyi). Tam kan sayımlarından nötrofil/lenfosit oranı (NLR) ve platelet/lenfosit oranları hesaplandı. Hem NLR hem de PLR için Vasquez ve arkadaşlarının (4) çalışmasında değerler referans değer olarak alınmıştır.
3. Tümörün yerleşim yerleri: aksiyal kemikler (pelvis, kosta, vertabra, skapula, kafa kemikleri, klavikula), apendiküler kemikler (femur, fibula, tibia, humerus, ayak kemikleri, radius, ulna, el kemikleri), diğer kemikler, ekstraosseoz olarak sınıflandırıldı.
4. Tedavi yaklaşımları
   a. Kemoterapi
      i. 2006-2015 yılları arasında modifiye EURAMOS-1 (5) uygulandı. Metotreaksat dozları 6-8 gr/m2 dozunda ve 24 saat sonrasında Ca-folinat (15 mg/m2/doz, 6 saat ara ile 20 doz uygulandı) ile beraber uygulandı.
      ii. Nekroz oranlarındaki düşüklük nedeniyle 2015 yılından sonra ise sisplatin+adriamisin (EURAMOS-1 dozlarının aynısı) / ifosfamid (2 gr/m2/gün, 1-8 gün) şeklinde uygulandı.
   b. Cerrahi yaklaşım
      i. Ektremite koruyucu cerrahi
      ii. Amputasyon
5. Tedavi sonuçları
   a. Genel sağ kalım oranları
   b. Olaysız sağ kalım oranları hesaplandı.

İstatistiksel Analiz

İstatistiksel analizler için, GraphPad Prisim 9 (GraphPad, San Dieogo, USA) ve SPSS 22.0 paket programı kullanıldı. Tanımlayıcı istatistiklerde, kategorik veriler (nominal ya da ordinal veriler) için frekans ve yüzde değerleri kullanılırken numerik verilerde önce dağılımın normal olup olmamasını değerlendirmede D'Agostino & Pearson testi (GraphPad software'in önerisi) kullanıldı. Eğer dağılım normal ise aritmetik ortalama±standart sapma; dağılım normal değilse en düşük ve en yüksek değerle beraber ortanca değer verildi. Genel ve olaysız yaşam oranları için Kaplan Meier Survival analizi kullanıldı. Sağ kalım analizlerinin karşılaştırılmasında Log Rank testi kullanıldı.

BULGULAR

Bu süre içerisinde, osteosarkomlu 24 hasta çalışmaya dâhil edildi. Erkek/kız oranı 1/1'di. Hastaların yaşı 7,8 ile 17,2 yıl arasında değişiyordu (ortanca, 13,9 yıl).

Şikâyet süresi 15 gün ile 12 ay arasında değişiyordu (ortanca, 2 ay). Hastaların klinik ve laboratuvar bulguları **Tablo 1**'de görülmektedir. En sık başvuru şikâyeti 23 hastada ağrı (%95,8) idi. Ağrıyı sırasıyla şişlik (n: 20, %83,3) ve hareket kısıtlılığı (n: 11, %45,8) takip ediyordu. Tümörün yerleşim yerleri, 18 hastada apendiküler kemiklerde (%75), aksiyal kemik yerleşimi beş hastada (%20,8) ve bir hastada ekstraosseöz yerleşimliydi (%4,2) idi. En çok yerleşim yeri femur idi (n: 14, %58,3).

Tablo 1. Hastaların klinik ve laboratuvar bulguları

	n, (%)
Başvuru anındaki şikâyetleri	
Ağrı	23, (%95,8)
Şişlik	20, (%83,3)
Hareket kısıtlılığı	11, (%45,8)
Kilo kaybı	1, (%4,2)
Ateş	1, (%4,2)
Yerleşim yeri	
Apendiküler kemikler	18, (%75)
Aksiyal kemikler	5, (20,8)
Ektraosseöz	1, (%4,2)
Yerleştiği kemikler	
Femur	14, (%58,3)
Humerus	3, (%12,5)
Tibia	2, (%8,3)
Mandibula	2, (%8,3)
İskium	1, (%4,2)
Vertebra	1, (%4,2)
Ektraossöz	1, (4,2)
Hastalığın yaygınlığı	
Lokalize	16, (%66,7)
Metastatik	8, (%33,3)
Laktat dehidrogenaz düzeyi	
Normal	18, (%75)
Yüksek	6, (%25)
Yaşa göre lenfosit sayısı	
Normal	14, (%58,3)
Düşük	10, (%41,7)
Platelet/lenfosit oranı*	
≤150	12, (%50)
>150	12, (%50)
Nötrofil/lenfosit oranı*	
≤2	7, (%29,2)
>2	17, (70,8)
Uygulanan kemoterapi protokolü	
EURAMOS-1	13, (%54,2)
Sisplatin+adriamisin/ifosfamid	11, (%45, 8)

* Sınır değerleri Vasquez ve arkadaşlarının (4) çalışmasından alınmıştır.

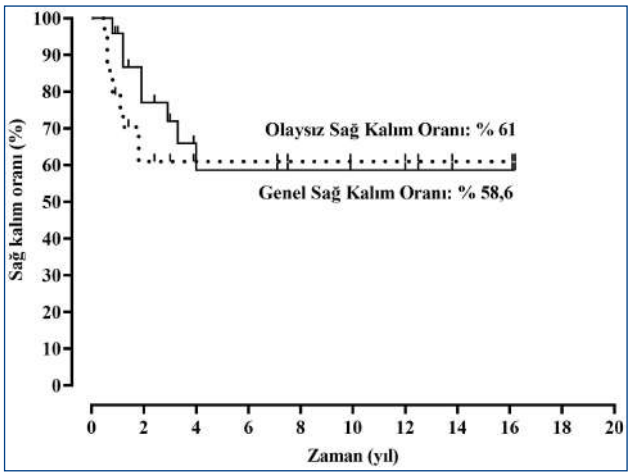
Hastaların tanı anındaki kan sayımları değerlendirildiğinde laktat dehidrogenaz enzim yüksekliği altı hastada (%25) saptandı. Yaşa göre lenfosit sayısı değerlendirildiğinde lenfopeni 10 hastada (%41,7) vardı. Platelet/lenfosit oranı yüksekliği (>150), 12 hastada (%50) ve NLR yüksekliği (>2) 17 hastada (%70,8) olduğu görüldü.

Hastalardan sekizinde (%33,3) tanı anında metastatik hastalık vardı ve hepsinde metastaz yeri akciğerdi.

On üç hastada (%54,2) EURAMOS-1 tedavi protokolü, 11 hastada (%45,8) sisplatin + adriamisin / ifosfamid tedavi protokolü uygulanmıştı. Tüm hastalarda ameliyat edilmişti. Herhangi bir hastada ampütasyon ihtiyacı olmamıştı.

Yaşam Analizi

Hastaların izlem süreleri 9 ay ile 16,2 yıl arasında değişiyordu (ortanca, 3,15 yıl). Sekiz hasta (%33,4) progresif hastalıkla kaybedildi. Genel ve olaysız sağ kalım oranları sırasıyla %58,6±11,7 ve %61±10,2 idi (**Resim 1**). Genel sağ kalım oranı üzerine tanı anındaki laktat dehidrogenaz enzim yüksekliğinin olumsuz etkisi gözlendi (p=0,021). Tanı anında metastatik hastalığı olan hastalarda genel sağ kalım oranı her ne kadar düşük olsa da istatistiksel olarak aradaki fark anlamlı değildi (p=0,059) (**Tablo 2**).



Resim 1.

TARTIŞMA

Osteosarkomlar, tümör hücreleri tarafından osteoid ya da immatür kemiğin üretildiği kemiğin primer malign hastalığıdır. Tüm osteosarkomlara bakıldığında bimodal yaş dağılımı olduğu görülmektedir. Birinci pik ikinci dekatta ve ikinci pik ise 40 yaş üstü yetişkinlerdir (6). Çocuklarda, en sık görülen kemiğin primer malign hastalığıdır. Amerika Birleşik Devletleri'nde primer kemik tümörleri tüm çocukluk çağı tümörlerinin yaklaşık %6'sını oluştururken, ülkemizde bu oran %6,5 civarındadır (1, 2). Erkek cinsiyette hafif bir yükseklik vardır (1,3). Bizim çalışmamızda da hastaların demografik özelliklerine bakıldığında osteosarkomun klasik demografik özelliklerine benzer şekilde ortanca yaşın yaklaşık 14 yıl civarında olduğu görülmektedir. Erkek/kız oranı ise eşit olarak bulunmuştur.

Osteosarkomlu çocuklarda sıklıkla başvuru şikâyetleri tümörün olduğu yerde ağrı ya da şişlik, hareket kısıtlılığı, patolojik kırıklar ve nadiren de tümöre yakın eklemlerde efüzyon görülmesidir. Genellikle hastalıkla ilişkili semptomların ortaya çıkması birkaç aydır (1). Bizim hastalarımızda da semptomlar irdelendiğinde en sık başvuru şikâyeti ağrı iken, ağrıyı şişlik ve hareket kısıtlığı izliyordu. Şikâyet süreleri ise 15 gün ile 12 ay arasında değişiyordu (ortanca, 2 ay).

Tablo 2: Genel ve olaysız sağ kalım oranları üzerine etki eden faktörler

	GENEL SAĞ KALIM ORANI					OLAYSIZ SAĞ KALIM ORANI				
	Genel sağ kalım oranı (%)	Standart hata (%)	Log Rank Testi (Mantel Cox)			Olaysız sağ kalım oranı	Standart hata	Log Rank Testi (Mantel Cox)		
			X2	df	p			X2	df	p
Cinsiyet			0,972	1	0,373			0,079	1	0,779
Kız, (n: 12)	48,2	17,7				57,1	14,6			
Erkek, (n: 12)	68,6	15,1				65,6	14			
Yerleşim yeri			0,63	1	0,73			0,517	1	0,772
Aksiyel kemik, (n: 5)	60,0	21,9				60	21,9			
Apendiküler kemik, (n: 18)	56,4	13,9				58,7	12,1			
Hastalık yaygınlığı			3,557	1	0,059			2,233	1	0,135
Lokalize, (n: 16)	73	14				74,5	11			
Metastatik, (n: 8)	37,5	17,1				37,5	17,1			
Laktat dehidrogenaz düzeyi			5,357	1	0,021			2,998	1	0,083
Normal, (n: 18)	63,9	13,4				70,1	11,2			
Yüksek, (n: 6)	27,8	23,2				22,2	19,2			
Lenfosit sayısı			1,768	1	0,184			1,456	1	0,228
Normal, (n: 14)	73,3	13,2				68,1	13,3			
Lenfopeni, (n: 10)	28	21,6				50,0	15,8			
Platelet lenfosit oranı*			0,128	1	0,720			0,128	1	0,721
≤150, (n: 12)	58,2	16,3				52,9	15,7			
>150, (n: 12)	53,6	18,8				66,7	13,6			
Nötrofil lenfosit oranı*			0,875	1	0,35			0,212	1	0,645
≤ 2, (n: 7)	31,3	24,5				45,7	22,4			
>2, (n: 17)	67,3	12,2				64,7	11,6			

* Sınır değerleri Vasquez ve arkadaşlarının (4) çalışmasından alınmıştır.

Ostesarkomların yerleşim yerleri alt (yaklaşık %75) ve üst ekstremitelerin uzun kemiklerindedir (yaklaşık %11). Hastaların yaklaşık %60'ının yerleşim diz eklemine yakın olan femur distali ile tibia proksimalidir (1). Bizim hastalarımızda da tümörün yerleşim yerlerinin %80'i femur, humerus ve tibiaydı.

Günümüzde osteosarkomda standart yaklaşım kemoterapi ve cerrahidir. Kemoterapide neoadjuvan veya adjuvan tarzında cisplatin, adriamisin ve yüksek doz metotreaksat içeren kemoterapi rejimleri kullanılmaktadır. Diğer etkili ilaçlar ifosfamid ve etopositttir. Cerrahi olarak ise mümkünse özellikle ekstremite koruyucu cerrahi tercih edildiği agresif cerrahi önerilmektedir. Ekstremite koruyucu cerrahini mümkün olmadığı durumlarda ise her ne kadar istenmese de ampütasyon bir tedavi seçeneğidir (1, 3). Bu tedavi yaklaşımları ile günümüzde metastatik olmayan osteosarkomlu hastalarda beklenen hastalıksız yaşam oranları %70'lerdedir. Ülkemizden yapılan çalışmalarda da metastatik olmayan hastalarda bu oranlara yakın genel sağ kalım oranları elde edilmiştir (7-10).

Vasquez ve arkadaşlarının (4) çalışmasında, NLR ve mutlak lenfosit sayısındaki iyileşmenin çocukluk çağı sarkomları için bağımsız prognostik faktör olarak bulunmuştur. Bizim çalışmamızda ilişki saptanmadı. Bu durum hasta sayımızın azlığı ile ilişkili olabilir.

Osteosarkom için iyi bilinen prognostik faktörler, tanı anında metastatik hastalık olması, inkomplet rezeksiyon, neoadjuvan kemoterapiye yanıt olarak nekroz oranlarının düşük olması (<%90), aksiyel kemik yerleşimli olması, tümör boyutunun büyük olması ve ekstremitelerdeki proksimal yerleşimdir (1, 3). Çalışmamızda, tüm hastalar için genel ve olaysız sağ kalım oranları sırasıyla %58,6 ve %61idi. Lokalize hastalığı olan hastalarda genel sağ kalım oranı %73'lerde iken, metastatik hastalığı olan hastalarda bu oran %37,5 idi. Lokalize hastalığı olan hastalarda genel yaşam oranlarının metastatik hastalığı olanlara göre daha yüksek olmasına karşın aradaki fark istatistiksel olarak anlamlı değildi. Hem tüm hastaların olaysız sağ kalım oranın genel sağ kalım oranından yüksek olması, hem de lokalize/metastatik hastalığı olan hastalar arasında istatistiksel olarak fark olmaması hasta sayısının az olması ile ilişkili olduğunu düşündürmektedir. Bizim çalışmamızda univaryant analizde genel sağ kalım oranı üzerine tanı anındaki laktat dehidrogenaz enzim yüksekliğinin olumsuz etkisi gözlendi. Tanı anında normal laktat dehidrogenaz enzim düzeyi normal olan hastalarda genel sağ kalım oranı %63,9 iken, yüksek olan hastalarda bu oran %27,8 idi. Olaysız sağ kalım oranı üzerine etki eden bir faktör saptamadık. Ekstremite yerleşimli olan tüm hastalarımıza ekstremite koruyucu cerrahi yapabildi.

Çalışmamızdaki en önemli limitasyonlar hasta sayısının az olması, özellikle eski hastalarda patolojik alt grupların ve neoadjuvan tedaviye nekroz oranlarının verilmemiş/verilememiş olmasıdır. Patolojiye verilemeyen detaylarda en önemli sorunlardan birisi merkezimize değişik merkezlerden de hasta sevk edilmesidir.

SONUÇ

Çocukluk çağı metastatik olmayan osteosarkomlarda hem kemoterapi hem de özellikle ekstremite yerleşimli olanlarda fonksiyonların mümkün olduğunca korunduğu ekstremite koruyucu cerrahi ile istenilen oranlara ulaşılsa da metastatik hastalığı olan hastalarda bu oran maalesef halen bir sorun olmaya devam etmektedir ve yeni tedavi yaklaşımlarına ihtiyaç duyulmaktadır.

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Aydınlatılmış Onam: Çalışma retrospektif olarak dizayn edildiği için hastalardan aydınlatılmış onam alınmamıştır.

Hakem Değerlendirme Süreci: Harici çift kör hakem değerlendirmesi.

Çıkar Çatışması Durumu: Yazarlar bu çalışmada herhangi bir çıkara dayalı ilişki olmadığını beyan etmişlerdir.

Finansal Destek: Yazarlar bu çalışmada finansal destek almadıklarını beyan etmişlerdir.

Yazar Katkıları: Yazarların tümü; makalenin tasarımına, yürütülmesine, analizine katıldığını ve son sürümünü onayladıklarını beyan etmişlerdir.

Not: Bu çalışma Dr. Sema Yılmaz'ın tıpta uzmanlık tezinden üretilmiştir.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Retrospective Evaluation of Child Cases Followed with the Prediagnosis of Crimean-Congo Hemorrhagic Fever

Kırım Kongo Kanamalı Ateşi Ön Tanısı ile Takip Edilmiş Çocuk Vakaların Retrospektif Değerlendirilmesi

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ABSTRACT

Aim: The aim of our study is to evaluate the clinical, demographic and laboratory findings of the patients who were followed up with the diagnosis of Crimean-Congo hemorrhagic fever (CCHF) in Gaziosmanpaşa University Medical Faculty Child Health and Diseases Service. This study was carried out with the aim of this study was to observe the importance of early diagnosis, observing the effects of the supportive treatment, documenting hospitalization time and the complications during the treatment.

Material and Method: The study was carried out in a single center, Gaziosmanpaşa University Faculty of Medicine, Pediatrics Service in accordance with the Declaration of Helsinki Principles. Medical records of patients who were followed up with a prediagnosis of CCHF between January 2012 and July 2016 were retrospectively reviewed. Epidemiological, demographic and clinical characteristics, laboratory data, treatment methods and results of all cases were evaluated from patient files.

Results: Between January 2012 and July 2016, a total of 100 patients with CCHF were detected. 52 % of the patients came from rural areas. The most applications were in April and June (69 %) months. 100 % of the patients had a history of contact with ticks. The main symptoms and signs were fever (38%), haematological findings (34%), malaise (47 %), abdominal pain (11 %), headache (25 %) and muscle pain (44 %). At the time of admission to the hospital, 6 % of patients had thrombocytopenia, 26 % had leukopenia, 26 % had elevated aspartate aminotransferase (AST), 12 % had elevated alanine aminotransferase (ALT), 44 % had elevated lactate dehydrogenase (LDH), 70 % had elevated creatine phosphokinase (CPK), 8 % had prolonged prothrombin time (PT), prolonged active partial thromboplastin time (aPTT) in 28 % and elevated international normalised ratio (INR) in 13 %. All patients underwent liquid-electrolyte therapy for support, 5 % aphasic platelet suspension, 13 % fresh frozen plasma, 12 % repeated erythrocyte suspension, and 13 % received ribavirin treatment. All of the patients who were included in the study were discharged with recovery.

Conclusion: In conclusion, clinical manifestations of CCHF are similar to adults in children and CCHF is more favorable in children. There is no definitive proven treatment method yet, and most of the treatment is supportive treatment.

Keywords: Crimean-Congo hemorrhagic fever, child, supportive treatment

ÖZ

Amaç: Çalışmamızın amacı Gaziosmanpaşa Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Servisinde Kırım-Kongo kanamalı ateşi (KKKA) tanısı ile takip edilen hastaların klinik, demografik ve laboratuvar bulgularını değerlendirmektir. Bu çalışma erken tanının önemini, uygulanan destekleyici tedavinin hastanede kalış süresini kısaltmaya ve komplikasyon gelişimini önlemeye etkisini gözlemlemek amacıyla yapılmıştır.

Gereç ve Yöntem: Çalışma Helsinki İlkeler Deklarasyonu'na uygun, tek merkezli olarak Gaziosmanpaşa Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları servisinde gerçekleştirilmiştir. Ocak 2012 ile Temmuz 2016 arasında KKKA ön tanısı ile takip edilmiş olan hastaların tıbbi kayıtları geriye dönük olarak incelenmiştir. Tüm olguların epidemiyolojik, demografik ve klinik özellikleri, laboratuvar verileri, tedavi yöntemleri ve sonuçları hasta dosyalarından değerlendirilmiştir.

Bulgular: Ocak 2012-Temmuz 2016 tarihleri arasında KKKA öntanılı 100 hasta tespit edildi. Hastaların %52' si kırsal kesimden geliyordu. En çok başvuru Nisan ve Haziran (%69) ayları aralığında idi. Hastaların %100'ünde kene ile temas öyküsü vardı. Hastaneye başvuru esnasında başlıca semptomlar ve bulgular ateş (%38), hematolojik bulgular (%34), halsizlik (%47), karın ağrısı (%11), başağrısı (%25), kas ağrısı (%44) idi. Hastaneye başvuru esnasında hastalarda %6 trombositopeni, %26 lökopeni, %26 yüksek AST, %12 yüksek ALT, %44 yüksek LDH, %70 yüksek CPK, %8 uzamış PT, %28 uzamış PTT, %13 yüksek INR saptandı. Hastaların tamamı destek amaçlı sıvı-elektrolit tedavisi, %5' i aferezli trombosit süspansiyonu, %13' ü taze donmuş plazma, %12' si tekrarlayan sayıda eritrosit süspansiyonu, %13' ü ribavirin tedavisi aldı. Takibe aldığımız hastalarımız şifa ile taburcu edildi.

Sonuç: Sonuç olarak, KKKA klinik bulguları çocuklarda erişkinlere benzerdir ve ancak KKKA çocuklardaki seyri daha iyidir. Etkinliği kesin olarak kanıtlanmış bir tedavi methodu henüz bulunmamakta olup tedavinin en büyük bölümünü destek tedavisi oluşturmaktadır.

Anahtar Kelimeler: Kırım-Kongo Kanamalı ateşi, çocuk, destek tedavi

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INTRODUCTION

Crimean-Congo Hemorrhagic Fever (CCHF) is a zoonotic Viral Hemorrhagic Fever (VHF) disease, which is an important cause of mortality by causing acute high fever and bleeding and even shock in humans (1). CCHF is a viral infection originating from the Nairovirus species of the Bunyaviridae family, which has been identified in approximately 30 countries in Asia, Africa, Eastern Europe and the Middle East, causing an important public health problem (1,2,3). Although the first case in Turkey was reported in Tokat in 2002, epidemics have been reported in neighboring countries since 1970 (4,5,6). Despite the fact that Turkey is the country with the highest number of cases in the world, the number of publications in pediatric cases regarding CCHF, which is an important public health problem in all seasons, is quite limited. Although human-to-human nosocomial transmission has been reported, the mode of transmission of the virus to humans is usually by contact with infected ticks or by contact with bodily fluids of infected animals. The virus causes a serious clinical course with a mortality of 3-30% in humans (7). Endothelial dysfunction due to vascular damage causes bleeding and this is the most common cause of death due to the disease. Sudden fever, malaise, anorexia, myalgia, cough, headache and abdominal pain are frequently seen in the clinic of the disease. Mortality risk is increased in cases with disseminated intravascular coagulopathy (DIC) and the worst prognosis belongs to this group (8). In laboratory examinations, leukopenia and thrombocytopenia due to bone marrow involvement, elevation in muscle and liver enzymes due to viral cytopathy; elongation is observed in coagulation parameters (9). In order to make the diagnosis, it is important to detect virus isolation, antigen tests or reverse transcriptase polymerase chain reaction (RT-PCR) in the first week of the application, and then detect the antibodies developed against the virus by Enzyme Linked Immuno Sorbent Assay (ELISA) or Indirect Fluorescent Antibody (IFA) method (10).

MATERIAL AND METHOD

The study was carried out in accordance with the Declaration of Helsinki Principles. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was conducted as a single center, retrospective chart review study. Children between 0 and 18 years of age accepted by the tick bite from April 2012 to June 2016 in Gaziosmanpaşa University Medical Faculty Child Health and Diseases Service were evaluated. The data were reviewed retrospectively using the Hospital Information Management System.

Epidemiological data of all patients; age, gender, province, district, contact season, presence of a similar case in the family, extraction of the tick, history of a chronic disease, history of tick contact (tick attachment and/or suspected contact), clinical and laboratory data, fever, anorexia, weakness, headache, nausea-vomiting, abdominal pain, diarrhea, hematological findings as LDH, ALT, AST , CPK, white blood count (WBC), mean platelet volume (MPV), hemoglobin (Hb), platelet (PLT), c-reactive protein (CRP), PT, aPTT, INR, sedimentation; data on treatment; whether oral ribavirin was administered, blood and blood products (fresh frozen plasma, erythrocyte suspension, platelet suspension, random-apheresis) and outcome data; cure or death were analyzed for each patient. Hematological symptoms such as epistaxis, hematuria, melena, gingival bleeding and skin rash were documented.

Statistical Analysis

The statistical data analysis was performed using IBM SPSS for Windows (IBM statistics for Windows version 20, IBM Corporation, Armonk, New York, United States). In descriptive statistics of the data, mean±standart deviation for normally distributed variables and median (min-max) values for non-normally distributed variables were used, categorical variables were given as n (%). The qualitative data were analyzed by chi-square test, as appropriate. $P<0.05$ was accepted as a cutoff value for statistical significance.

RESULTS

100 patients who applied with the complaint of tick bite between April 2012 and June 2016 were included in the study. Polymerase chain reaction (PCR) test positivity was detected in 16 (16%) of these patients and as the 'CCHF group'; Cases that were PCR negative and were not sent PCR in their outpatient follow-up were considered as the 'tick attachment group'. These two groups were compared in terms of demographic, clinical and laboratory characteristics. (**Table 1**).

Considering the distribution, there were 24 patients under 5 years of age (24%), 22 patients between the ages of 5 and 10 years old (22%), and 54 patients older than 10 years old. There was no significant difference between the positive and negative groups with PCR results according to gender and age groups ($p=0.542$, $p=0.052$). Considering the residential areas of the patients, 52 (52%) of 100 patients lived in rural areas. All patients (100%) with positive PCR results lived in rural areas. This relationship was considered significant after it was determined that all PCR-positive cases lived in rural areas ($p<0.001$). In cases whose diagnosis was confirmed by PCR and excluded, CCHF patients were observed to remove the tick by themselves. When the admission periods of the patients were examined, no

significant correlation was found between PCR positive detection (p=0.626). On the other hand, none of our 16 cases whose diagnosis was confirmed by PCR applied to the health institution in the first 24 hours after noticing the tick.

Table 1. Demographic and epidemiological characteristics of patients

	PCR		X2	p
	Positive (n=16,%)	Attachment (n=84,%)		
Gender			0.373	0.542
Female	7 (43.8)	27 (32.1)		
Male	9 (56.3)	57 (67.9)		
Age			5.901	0.052
<5	1 (4.2)	23 (95.8)		
5-10	2 (9.1)	20 (90.9)		
>10	13 (24.1)	41 (75.9)		
Residential			17.582	<0.001
Rural Area	16 (100)	36 (42.9)		
Rural Area Visit	-	24 (28.6)		
Other	-	24 (28.6)		
Extraction			6.547	0.038
By themselves	14 (87.5)	45 (53.6)		
At Hospital	1 (6.3)	28 (33.3)		
Applied without tick penetration	1 (6.3)	11 (13.1)		
Season			1.751	0.626
January – March	-	5 (6)		
April - June	11 (68.8)	58 (69)		
July- September	5 (31.3)	19 (22.6)		
October –December	-	2 (2.4)		
Family History			0.001	0.999
Positive	6 (37.5)	31 (36.9)		
Negative	10 (62.5)	53 (63.1)		
Hospital admission			21.859	<0.001
Immediately	-	37 (44)		
Within three days	5 (31.3)	33 (39.3)		
After three days	11 (68.8)	14 (16.7)		

Pcr : polymerase chain reaction

When the clinical characteristics of the patients at the time of admission are examined in **Table 2**; fever in 38 (38%), headache in 25 (25%), myalgia in 44 (44%), malaise in 47 (47%), abdominal pain in 11 (11%). Since the fever symptom lasted less than 1 week in patients who applied with the complaint of fever, they were not examined for hemophagocytic lymphohistiocytosis (HLH), and fibrinogen triglyceride and ferritin values were not tested. Hematological symptoms such as epistaxis, hematuria, melena, gingival bleeding and skin rash were present in 30 (30%) (**Table 2**). Presence of fever, headache, myalgia, malaise, abdominal pain and hematological symptoms in CCHF clinic were considered statistically significant. (p<0.001, p<0.001, p<0.001, p<0.001, p=0.014, p<0.001).

Table 2. Clinical characteristics of the patients at the time of admission

		Pcr		X2	p
		Positive n=16 (%)	Negative n=84 (%)		
Fever	Present	16 (100)	22 (26.2)	0.282	<0.001
	Absent	-	62 (73.8)		
Headache	Present	12 (75)	(15.5)	-	<0.001
	Absent	4 (25)	71 (84.5)		
Myalgja	Present	16 (100)	28 (33.3)	21.612	<0.001
	Absent	-	56 (66.7)		
Fatigue	Present	16 (100)	31 (36.9)	19.021	<0.001
	Absent	-	53 (63.1)		
Abdominal Pain	Present	5 (31,3)	6 (7.1)	-	0.014*
	Absent	11 (68,8)	78 (92.9)		
Hematological symptom *		12 (75)	18 (25)	47.509	<0.001
Hospitalization Indication	CCHF PCR+	16 (100)	-	86.7722	<0.001
	Tick bite	-	13 (15.5)		
	Other *	-	11 (13.1)		
	Outpatient	-	64 (76.2)		
Hospitalization Time	0-3 days	-	4 (4.8)		
	3-10 days	8 (50)	10 (11.9)	41.42	<0.001
	>10 days	8 (50)	6 (7.1)		

* epistaxis, hematuria, melena, gingival bleeding, rash, CCHF: Crimean-Congo hemorrhagic fever

The patients in the study had thrombocytopenia in 28%, leukopenia in 26%, low Hb in 23%, elevated ALT in 25%, elevated AST in 30%, elevated LDH in %11, elevated CPK in 52%, prolonged PT in 70%, prolonged PTT in 38%, elevated INR in 21% ; 10% of the patients had elevated sediment levels and 21% had elevated CRP levels at initial laboratory data. The definitive diagnosis of the patients was made by PCR test, and there was no significant difference between Hgb and Hct values of PCR+ and PCR- patients (p>0.001), a statistically significant difference was found between the white blood cell measurements, and significant difference was found in the platelet count (p<0.001). With this finding, leukopenia and thrombocytopenia were considered significant in laboratory values of the patient with CCHF diagnosis. Of the 36 hospitalized and followed-up patients, 16 (100%) were included in the group whose CCHF diagnosis was confirmed by PCR. 8 (50%) of the patients with positive PCR analysis were hospitalized for 3-10 days, and the other 8 (50%) were hospitalized for longer than 10 days. Follow-up of 64 patients (76,2 %) who presented with tick bite was performed from the outpatient clinic and emergency service, without admission to the inpatient service.

When we compared the INR values, a statistically significant difference was detected. In these cases, measurement of the INR value within the normal range at discharge suggested that the transient prolongation in coagulation parameters was associated with hematological symptoms. (mean square: 0,778; F: 9,178; p=0,008) (**Table 3**).

Table 3. INR Measurements at Admission and Discharge in Patients with CCHF Diagnosis

(J) Time	Mean Difference (I-J)	Std. Error	Significant.[a]	95% Confidence Interval for Difference[a]	
				Lower bound	Upper bound
Admission	0.29	0.15	0.229	-0.12	0.069
Discharge	0.289*	0.089	0.017	0.048	0.529

CCHF: Crimean-Congo Hemorrhagic Fever, INR:International normalised ratio, Based on estimated marginal means, *. The mean difference is significant at the 05 level. A. Adjustment for multiple comparisons: Bonferroni

When we compared the values of transaminase and muscle enzymes at admission and discharge, there was no significant difference in ALT value, but a significant difference in AST value. (mean square: 228858.336; F: 18.216; p<0.001); Significant difference was also found in CK and LDH values (mean square:1696108.193/1132555.607; F: 15.197/12.593; p<0.001/ p=0.002). For the acute phase reactants CRP and sedimentation, there was no significant difference between PCR positive and negative patients. Oral ribavirin therapy was given to 14 selected patients with bad prognosis. It was confirmed by PCR that 12 (75%) of our selected patients who were started on ribavirin were CCHF. With this finding, we determined that ribavirin was used appropriately in selected patients (p<0.001). It was determined that appropriate supportive treatment was given in all 36 cases followed up by hospitalization, and 13 of the patients were transfused with blood products. (**Table 4**).

Table 4. Ribavirin use in selected cases-Evaluation of support treatment protocol

	PCR		X^2	p
	Positive n=16 (%)	Attachment n=84 (%)		
Ribavirin Usage			-	<0.001
Positive	12 (75)	(2.4)		
Negative	4 (25)	82(97.6)		
Transfusion			-	<0.001
Erythrocyte Suspension	-	-		
Fresh Frozen Plasma	1 (6.3)	-		
Apheresis Platelet	-	-		
Random Platelet	4 (25)	1 (1.2)		
Repeated Transfusion	8 (50)	3 (3.6)		
None	3 (18.8)	80 (95.2)		

Pcr : polymerase chain reaction

DISCUSSION

Studies on CCHF are mostly based on adults all over the world. Studies on the pediatric age group are very rare in the literature. In this study, epidemiological, clinical and laboratory characteristics and results of pediatric patients from the Central Black Sea region, where CCHF is endemic, were evaluated retrospectively. We think that tick contact history is very important in terms of transmission routes of CCHF in our region and that patients with suspected CCHF should be questioned while taking their anamnesis. Our study was carried out in an endemic region and the follow-up of patients who were thought to have CCHF as clinical and laboratory was carried out by hospitalization. Pcr positivity and hemorrhagic symptoms were accepted as hospitalization indications.

Crimean-Congo hemorrhagic fever is known to have seasonal characteristics. June-September is the period when epidemics are common. However, this situation may vary according to the region (11). CCHF is frequently seen in endemic areas in our country, in the spring and summer months when vector ticks become active (12). The most frequent application of our patients was between April and September (most frequently in June).

Tuygun et al. in their retrospective study, which included 50 out of two hundred pediatric patients who applied from the endemic regions of Southern Black Sea, Central and Northeast Anatolia in the spring-summer months between 2005 and 2010, no significant difference was found in terms of age groups and gender (13). Child patients younger than 18 years of age, who are generally in the school age group, were included in our study. Although there was an increase in the number of cases seen in adolescence between pcr positive and pcr negative patients no statistically significant difference was found.

Headache is often reported as the first complaint in CCHF disease. Other clinical findings may include high fever, fatigue, weakness, abdominal pain, widespread muscle and joint pain, and even changes in consciousness at different stages in some patients. Conjunctival hyperemia and ecchymoses of various sizes may occur in patients (14,15). Patients have a tendency to bleed; hemorrhagic symptoms are observed such as hematemesis, epistaxis, melena, hematuria, vaginal bleeding, gingival bleeding, and bleeding into internal organs (5,16). In a study conducted with children in Iran, the most common presentation symptoms and findings were fever (88.2%), nausea (61.8%), myalgia (70.6%), bleeding (70.6%), and headache (64.7%) (17). Our study was concluded in accordance with the literature in terms of clinical findings.

In addition to thrombocytopenia and leukopenia, increased liver enzymes ALT and AST, CPK, LDH and prolonged coagulation parameters can be detected in the laboratory findings of the patients at the time of admission. A general feature of CCHFV infection is thrombocytopenia (2). Dilber et al. reported 70% leukopenia, 50% CPK and ALT elevation, and 65% thrombocytopenia in 21 pediatric patients. Anemia developed in 28.5% of the patients, bleeding from various origins in 42.8% and thrombocytopenia in

23.8% of the patients during follow-up. They reported pulmonary hemorrhage in two of their cases (18). Sharifi-Mood et al. stated that 44% of their cases had elevated transaminase values (17). In our study, at the time of admission, 28% of the patients had thrombocytopenia, 30% had elevated AST, 26% had leukopenia, 38.5% had elevated INR, 35.9% had elevated CPK, 28.2% had elevated ALT, and 70% Prolonged PTT was found in 21% of patients. However, there are no laboratory criteria used to predict the diagnosis for CCHF. In countries where CCHF disease is endemic, such as our country, it is important to recognize the disease early and take the necessary precautions. The only study to interpret the factors affecting mortality in children was conducted in Iran, and it was reported that impaired consciousness is the only independent risk factor associated with mortality at hospital admission (17). Since there was no case lost in our study, the factors affecting mortality could not be evaluated.

The main goal in the management of the disease is general supportive treatment (12). Close monitoring of laboratory parameters is necessary in order to perform blood product replacement when necessary. Apart from general supportive treatment, ribavirin is the only antiviral drug that can be used in the treatment of VHF syndromes. In a study conducted by Sharifi-Mood et al. with 34 children and adolescents from Iran, 26.5% mortality was reported despite ribavirin treatment (17). Izadi et al. reported that the positive effect of ribavirin from the same country is related to the time of initiation of treatment and if it is applied during the viremia period, it will be effective in bleeding and mortality (19). Ergönül et al. reported that ribavirin treatment in the early phase of the disease may reduce mortality (5). Tezer et al. in a study they conducted in our country, they added ribavirin to their treatment options because they had bad prognosis criteria in 7 patients and reported that they did not experience any side effects (20). In our study, 14 patients received ribavirin treatment (14%). 12 patients received supportive treatment in addition to ribavirin treatment (85.7 %). In terms of the limitations of our study, it may not be helpful for cases in the initial period of the disease, as it was conducted in a single-center, retrospective and tertiary healthcare institution.

CONCLUSION

In the Crimean-Congo Hemorrhagic Fever disease, the pediatric age group is a special patient group and precautions for prevention and control must be taken. In order to prevent infection and manage it well, it is important not to be late in diagnosis and treatment. Early diagnosis is important for the patient as well as family members and healthcare professionals who are in contact with the patient. In terms of clinical features, it shares a lot with other viral hemorrhagic fever diseases. In this respect, it is important to remember the diagnosis and make a differential diagnosis. Laboratory findings are valuable in terms of clinical follow-up and prognosis of the patient. In supportive treatment, blood product transfusion with fluid-electrolyte therapy and monitoring of laboratory parameters has an important place. Cases with bad prognosis criteria should be followed closely as critically ill patients in the intensive care unit, and ribavirin treatment should be kept in mind in selected cases. We did not have any patient who applied with repetition of complaints after discharge, but one of our patients living in rural areas applied to our clinic again after two years with a tick bite. We did not lose any patient in our 4-year clinical follow-up. All 100 cases were discharged with cure.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Evaluation of Psychological Effects of COVID-19 Pandemic Process on Cancer Patients

COVID-19 Pandemi Sürecinin Kanser Hastaları Üzerindeki Psikolojik Etkilerinin Değerlendirilmesi

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ABSTRACT

Aim: Coronavirus-19 pandemic poses a threat both physically and mentally for cancer patients (CPs). We aimed to evaluate anxiety and depression levels of CPs during the pandemic period.

Material and Method: In March 2022, CPs treated with chemotherapy and a control group who without a diagnosis of cancer and psychological disorders were evaluated. Volunteer participants completed a questionnaire form included Patient Health Questionnaire (PHQ-9), General Anxiety Scale (GAD-7) and Coronavirus Anxiety and Obsession Questionnaire (CAS, OCS).

Results: 186 (61%) CPs and 119 (39%) control groups were evaluated. 148 (48.5%) were men and 157 (51.5%) were women. 86.1% were married, 50.7% lived in the city center and 40.1% had primary school education. CPs were older, predominantly female, mostly living in the district, had lower education levels, lower working rates and lower income levels. Depression and anxiety scores were higher in CPs (p=0.041, p<0.001). However, there was no difference between the groups in CAS and OCS scores. GAD-7 was increased by cancers other than breast, curative chemotherapy administration, low education level and low daily television watching in CPs (p=0.049, p=0.031, p=0.028 and p=0.04, respectively).

Conclusion: Coronavirus-19 pandemic triggers anxiety and depression in CPs. The PHQ-9 and GAD-7 are simple administered tests, help to evaluate depression and anxiety.

Keywords: Anxiety, cancer, Coronavirus-19, depression, pandemics

ÖZ

Amaç: Koronavirüs-19 pandemisi, kanser hastaları için bedensel ve ruhsal açıdan tehdit oluşturmaktadır. Çalışmamızda pandemi döneminde, kemoterapi uygulanan kanser hastalarındaki kaygı ve depresyon düzeylerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Mart 2022'de kemoterapi ile tedavi edilen kanser hastaları ile kanser hastalığı ve psikolojik rahatsızlık tanısı olmayan bir kontrol grubu değerlendirildi. Gönüllü katılımcılar Hasta Sağlığı Anketi (PHQ-9), Genel Anksiyete Ölçeği (GAD-7) ve Coronavirüs Anksiyete ve Takıntı Anketi (CAS, OCS) içeren bir anket formu doldurdu. Anksiyete ve depresyon skorları incelendi.

Bulgular: 186 (61%) kanser hastası ve 119 (39%) kanser hastalığı olmayan toplam 305 kişi değerlendirildi. 148'i (%48,5) erkek, 157'si (%51,5) kadındı. %86,1'i evli, %50,7'si il merkezinde ikamet etmekte ve %40,1'i ilkokul mezunuydu. Kanser hastaları daha yaşlıydı, ağırlıklı olarak kadındı, çoğunlukla ilçede yaşıyordu, daha düşük eğitim seviyelerine, daha düşük çalışma oranlarına ve daha düşük gelir seviyelerine sahipti. Çalışmaya dahil edilen kanser hastalarının çoğu meme kanseriydi (%34,4). Kanser hastalarında kilo kaybı, günlük televizyon izleme süresi ve nörolojik şikayetler daha yüksekti. Kanser hastalarında depresyon ve anksiyete puanları daha yüksekti (p=0.041, p<0.001). Ancak CAS ve OCS skorlarında gruplar arasında farklılık yoktu. Kanser hastalarında GAD-7, meme dışındaki kanserler, küratif kemoterapi uygulaması, düşük eğitim düzeyi ve düşük günlük televizyon izleyenlerde yüksekti (sırasıyla p=0.049, 0.031, 0.028 ve p=0.040).

Sonuç: Covid-19 salgını, kanser hastalarında kaygı ve depresyonu tetiklemektedir. PHQ-9 ve GAD-7, basit uygulanan testlerdir, depresyon ve anksiyeteyi değerlendirmeye yardımcı olurlar.

Anahtar Kelimeler: Anksiyete, kanser, koronavirus-19, depresyon, pandemiler

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INTRODUCTION

Pandemics such as the Black Plague, the Cholera and the Spanish Flu epidemics have emerged at various times throughout human history. They have caused serious destruction in societies. The world has been struggling with coronavirus pandemic (Covid-19), since December, 2020 (1). Covid-19, which has a very rapid risk of transmission through droplets, can cause severe respiratory symptoms (2).

Cancer patients (CPs) are elderly patients with high comorbidities, heavy smoking, and suppressed immune systems. Periodic hospital admissions are required due to oncological treatments. These patients are at high risk in Covid-19 pandemic (3). It is also known that Covid-19 infection is more severe and mortal in CPs (2).

Isolation measures due to pandemic, social restrictions, intense media exposure, and the number of cases/deaths announced daily, new mutations and unknowns about the virus have led to an increase in psychiatric problems (4,5). Anxiety and depression are more common in CPs than in the normal population. They adversely affect the treatment process and survival in CPs (6). The patient health questionnaire (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) are tests with high sensitivity and effectiveness proven in many countries to evaluate depression and generalized anxiety disorder (6-10). In addition, the Coronavirus Obsession Scale (OCS) and the Coronavirus Anxiety Scale (CAS) are tests that help evaluate obsession and anxiety due to Covid-19 by Lee. (11,12).

In our study, we aimed to determine the anxiety and depression status, coronavirus- related obsessions and anxiety in CPs treated with chemotherapy during Covid-19 pandemic process. Our second aim was to attract clinicians' interest in the anxiety and depression seen in CPs.

MATERIAL AND METHOD

Patients receiving active chemotherapy with a diagnosis of cancer in two centers in March 2022 were evaluated for inclusion in the study.

After obtaining informed written consent from the CPs, a face-to-face questionnaire was filled and a retrospective files and computer records were reviewed.

Criteria for inclusion; 1)age 18-85 years 2)had a cancer diagnosis and was undergoing active chemotherapy treatment, 3)agreeing to fill out the questionnaire, 4) not using psychotropic drugs, being literate, 5)not having an obstacle to communication, 6)not using psychoactive substances and alcohol.

Criteria for exclusion; 1)patients who did not receive oncological treatment, 2)patients using active psychotropic drugs, receiving psychiatric treatment, 3)patients with dementia, mental retardation, 4) patients who did not agree to participate in the questionnaire or patients who reported that they did not want to participate in the study after filling out the questionnaire.

After obtaining informed written consent, the same questionnaire was filled in the control group, which consisted of relatives of patients who applied to the hospital, aged between 18 and 85, without diagnosis of cancer, who did not use psychoactive substances and/or alcohol, who had no communication barriers, and who were literate.

Age, gender, marital status, comorbid diseases, occupation, place of residence, education level, income, coronavirus awareness, neurological symptoms, and presence of epileptic seizures were evaluated. Cancer types of patients and chemotherapy (curative/palliative) treatments were noted. The PHQ-9, GAD-7, CAS and OCS tests translated into Turkish were administered via a questionnaire (5,9,10,13).

Patient health questionnaire (PHQ-9)

PHQ-9 is a scale to determine depression and the severity of depression by questioning the 9 diagnostic criteria in Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV. It was translated into Turkish by Sari et al. and its validity was shown. The cut-off score for PHQ-9 was accepted as nine (7,9). A total of 0-27 points are scored as 1-4 points of minimal depression, 5-9 points of mild depression, 10-14 points of moderate depression, 15-19 points of moderate-severe depression, and 20-27 points of severe depression.

Generalized Anxiety Disorder-7 (GAD-7)

GAD-7 is a test with 89% sensitivity and 82% specificity for evaluating generalized anxiety disorder (8). It is a likert type scale that evaluates what people have experienced in the last 2 weeks with 7-item questions. A total of 0-21 points; cut-off points of 5, 10, and 15 are taken and classified as mild, moderate, and severe anxiety, respectively. The diagnosis of patients with a total score of ten and above should be confirmed by other methods. However, the most acceptable cut-off point was found to be eight in Turkish population (10).

Coranavirus Obsession Scale (OCS)

OCS is a likert-type scale in which people have been asked 4 coronavirus-related questions in the last 2 weeks. An OCS score of bigger and equal seven out of a total of 0-16 points suggests an association between coronavirus and dysfunctional obsession. It has been shown by Kurt et al. that the scale reliably

identifies dysfunctional obsession associated with the pandemic in the Turkish population (13).

Coranavirus Anxiety Scale (CAS)

In addition to its strong psychometric properties, CAS is a test with high sensitivity and specificity that enables discrimination between dysfunctional anxiety and non-anxiety (11). In the scale, participants were asked 5 questions about coronavirus in the last 2 weeks. Out of a total of 0-20 points, the cut-off point was nine (90% sensitivity and 85% specificity) (11). Evren et al. translated the scale into Turkish and the analysis showed that the scale is valid and reliable for assessing the severity of anxiety related to the dysfunctional coronavirus (5).

Individuals who were observed to be at risk for mental illnesses were referred to specialist psychiatrists.

Statistics

SPSS 22.0 (SPSS Inc. Chicago, USA) statistical package program was used in the analysis of the data. Descriptive statistics of evaluation results; numbers and percentages for categorical variables, mean, standard deviation, median, and interquartile range (IQR) for numerical variables. The conformity of the groups to the normal distribution was determined by the Kolmogorov-Smirnov test. When the normal distribution condition was not met in two independent groups, it was evaluated with the Mann Whitney U test. Chi-square test was used to compare qualitative data. Linear regression analysis was performed with logically related predictors of the scales (PHQ-9, GAD-7, CAS, and OCS). Spearman test was used for correlation analysis. Statistical alpha significance level was accepted as $p<0.05$.

RESULTS

A total of 305 participants were included in the study; 186 (61%) CPs and 119 (39%) control group. The median age of the participants was 59 (51.8-65). 148 (48.5%) were male and 157 (51.5%) were female. The demographic and clinical characteristics of patients and control groups are shown in **Table 1**.

CPs were older than the control group (p=0.001). They were female predominant, quit smoking, unemployed, living in a town, low education level, low income and high daily television viewing time (p=0.001, p=0.043, p<0.001, p<0.001, p<0.001, p<0.001 and p=0.001).

125 (67.9%) of CPs had comorbidities and 21.2% of them were multiple. Breast, colorectal, and lung cancer were the most common cancers in the study, respectively. Weight loss and neurological complaints were more common in CPs (p<0.001, p<0.001, **Table 1**).

Table 1. Demographic and clinical characteristics of cancer patients and control groups

	Cancer Patients (%) n= 186 (61.0)	Control Group (%) n= 119 (39.0)	p
Age (median, IQR)	60 (53-68)	56 (50.3-61.8)	0.001*
Gender			0.001†
Female	110 (59.1)	47 (39.5)	
Male	76 (40.9)	72 (60.5)	
Smoking Status, n (%)			0.043†
Non-smoker	92 (50.8)	59 (50.0)	
Active smoker	18 (9.9)	23 (19.5)	
Quit smoking	71 (39.2)	36 (30.5)	
Comorbidities, n (%)			0.055†
Yes	125 (67.9)	19 (50.0)	
No	59 (32.1)	19 (50.0)	
Professional Status, n (%)			<0.001†
Working	37 (24.7)	82 (71.3)	
Non-working	113 (75.3)	33 (28.7)	
Place to live			<0.001†
City	57 (31.5)	95 (79.8)	
District	58 (32.0)	22 (18.5)	
Village	66 (36.5)	2 (1.7)	
Martial Status, n (%)			0.357†
Single	10 (5.6)	6 (5.0)	
Married	148 (83.6)	107 (89.9)	
Widow	17 (9.6)	5 (4.2)	
Divorced	2 (1.1)	1 (0.8)	
Educational Status, n (%)			<0.001†
Illiterate	2 (1.3)	1 (0.8)	
Elementary school	92 (59.0)	18 (15.3)	
Secondary School	26 (16.7)	10 (8.5)	
High School	22 (14.1)	25 (21.2)	
University	14 (9.0)	64 (54.2)	
Weight Loss, n (%)			<0.001†
Absence	93 (53.8)	95 (81.9)	
Presence	80 (46.2)	21 (18.1)	
Daily Television Viewing Time, hour	4 (2-6)	3 (2-5)	0.001*
News Tracking Status, n (%)			0.973†
Absence	15 (8.2)	9 (9.1)	
Presence	168 (91.8)	90 (90.9)	
Coronavirus Anxiety Status, n (%)			0.134†
Absence	27 (15.4)	22 (18.6)	
Some days	89 (50.9)	61 (51.7)	
More than half of the day	11 (6.3)	1 (0.8)	
Everyday	48 (27.4)	34 (28.8)	
Norological Compliant Status, n (%)			<0.001†
Absence	5 (5.3)	42 (40.8)	
Presence	64 (67.4)	33 (32.0)	
Multiple	26 (27.4)	28 (27.2)	
Monthly Revenue Status, n (%)			<0.001†
Minimum wage	87 (51.5)	3 (7.9)	
>6000 Turkish Lira	14 (8.3)	9 (23.7)	
Others	68 (40.2)	26 (68.4)	

*Mann-Whitney U test, †Chi-Square Test

PHQ-9, GAD-7, CAS and OCS scales of the CPs and control group are given in **Table 2**.

Table 2. Depression, anxiety, coronavirus anxiety and obsession scales of cancer patients and control groups

	Total (%) n=305 (100.0)	Cancer Patients (%) n= 186 (61.0)	Control Group (%) n= 119 (39.0)	p
PHQ-9, n=295				<0.001†
minimal depression	110 (57.3)	70 (38.3)	40 (35.7)	
mild depression	104 (35.3)	71 (38.8)	33 (29.5)	
moderate depression	26 (8.8)	22 (12.0)	4 (3.6)	
moderate severe depression	9 (3.1)	5 (2.7)	4 (3.6)	
severe depression	7 (2.4)	5 (2.7)	2 (1.8)	
PHQ-9, n=295				0.041†
≤9	253 (85.8)	151 (82.5)	102 (91.1)	
>9	42 (14.2)	32 (17.5)	10 (8.9)	
PHQ-9, (median, IQR)	4 (2-8) 5.4±5.0	6 (2-8) 6.2±5.0	3 (0-6.8) 4.2±5.0	<0.001*
GAD-7, n=294				0.635†
mild anxiety	257 (87.4)	157 (86.3)	100 (89.3)	
moderate anxiety	27 (9.2)	19 (10.4)	8 (7.1)	
severe anxiety	10 (3.4)	6 (3.3)	4 (3.6)	
GAD7, n=294				0.511†
<8	280 (95.2)	175 (96.2)	105 (93.8)	
≥8	14 (4.8)	7 (3.8)	7 (6.2)	
GAD-7, (median, IQR)	2 (1-3) 2.7±2.9	2 (2-4) 3.0±2.8	1 (1-1.8) 2.1±3.0	<0.001*
CAS, n=300				0.252†
<9	293 (97.7)	176 (96.7)	117 (99.2)	
≥9	7 (2.3)	6 (3.3)	1 (0.8)	
CAS, (median, IQR)	0 (0-0) 0.8±2.2	0 (0-1) 0.9±2.4	0 (0-0) 0.5±1.9	0.097*
OCS, n=301				0.448†
<7	275 (91.4)	169 (92.3)	106 (89.8)	
≥7	26 (8.6)	14 (7.7)	12 (10.2)	
OCS, (median, IQR)	1 (0-3) 2.2±3.0	1 (0-3) 2.1±3.1	1 (0-3) 2.3±3.0	0.311*

*Mann-Whitney U test, †Chi-Square Test, PHQ-9; Patient Health Questionnaire-9, GAD-7; Generalized Anxiety Disorder-7, CAS; Coronavirus Anxiety Scale, OCS; The Obsession with covid-19 Scale

Severe depression was observed in 2.7% of CPs when graded according to PHQ-9. It was more than the control group (2.7% vs 1.8%, p<0.001). Also, CPs had higher PHQ-9 scores than the control group. (p=0.041). Severe anxiety was observed in 3.3% of CPs when classified according to GAD-7. It was similar to control group (3.3% vs 3.6% p=0.635). However, GAD-7 scores in CPs were higher than the control group (p<0.001). No difference was observed in CAS and OCS scores between CPs and control groups (p=0.097, p=0.311). When the correlation between the questionnaires in the whole group was examined, the most significant correlation was found between CAS and OCS (p<0.001).

In the linear regression analysis; factors affecting PHQ-9, GAD-7, CAS and OCS in CPs were evaluated (**Table 3**).

Having cancer type other than breast, administration of curative chemotherapy, lower education level and lower daily television viewing increased GAD-7 (p=0.049, p=0.031, p=0.028, p=0.04). CAS score was higher in active workers than in non- workers (p=0.035).

DISCUSSION

Pandemics are one of the major health problems. In relation to the prevalence, severity and control process of the pandemic, intense financial and moral losses are experienced, and it can cause serious trauma to individuals. In our study, CPs who underwent chemotherapy were affected by Covid-19 pandemic period in terms of mental disorders. CPs were at higher risk for depression and anxiety than the control group. Coronavirus anxiety and obsession scores was similar to the literature. Diagnosed with breast cancer, had palliative chemotherapy, had a high education level, and had a long time to watch television daily were found to have a lower risk of developing anxiety i n CPs during Covid-19 pandemic.

The limitations of our study are; limited number of participants, in the second year of the pandemic, when the severity of Covid-19 infection eased. Persons at risk for mental disorders were referred to specialist psychiatrists, and psychiatrist comments could not be evaluated due to the limited number of patients.

Table 3. Linear regression analysis of depression, anxiety, coronavirus anxiety and coronavirus obsession scales in cancer patients

Variables	PHQ-9		GAD-7		CAS		OCS	
	β (%95 CI)	p	β (%95 CI)	p	β (%95 CI)	p	β (%95 CI)	p
Age (>65 years)	-0.518 (-1.464 - 0.427)	0.246	1.196 (-3.390 – 5.781)	0.574	1.376 (-2.952 – 5.704)	0.490	0.683 (-3.997 – 5.363)	0.752
Gender (female)	-0.367 (-1.284 – 0.550)	0.389	-1.366 (-5.750 – 3.019)	0.504	-1.010 (-5.315 – 3.296)	0.609	-3.709 (-8.184 – 0.767)	0.095
Tumor type (breast cancer)	0.424 (-0.587 – 1.435)	0.367	-5.255 (-10.484 – -0.026)	0.049	1.301 (-3.871 – 6.472)	0.583	1.645 (-3.692 – 6.982)	0.508
Treatment type (Palliative CT)	1.022 (-0.166 – 2.211)	0.083	-6.681 (-12.626 - -0.735)	0.031	3.515 (-2.229 – 9.259)	0.200	0.802 (-5.266 – 6.871)	0.774
Comorbidities (Presence)	0.220 (-0.582 – 1.022)	0.550	-0.584 (-4.634 – 3.465)	0.754	-2.000 (-5.968 – 1.968)	0.284	-0.889 (-5.022 – 3.244)	0.642
Smoking status, (smoker)	-0.419 (-1.578 – 0.740)	0.435	-1.426 (-7.084 – 4.232	0.587	-1.196 (-6.383 – 3.992)	0.615	-2.030 (-7.804 – 3.745)	0.452
Professional status, (Non-working)	-0.384 (-1.296 – 0.528)	0.366	3.103 (-1.673 – 7.879)	0.178	-5.097 (-9.748 - -0.446)	0.035	-1.432 (-6.307 – 3.442)	0.527
Place to live (City)	-0.418 (-1.292 – 0.455)	0.307	-0.196 (-4.415 – 4.023)	0.920	-0.012 (-4.600 – 4.577)	0.996	-1.033 (-5.340 – 3.273)	0.605
Civil status (Married)	-0.584 (-1.680 – 0.511)	0.258	0.363 (-5.368 – 6.094)	0.891	-3.300 (-9.805 – 3.204)	0.281	-3.479 (-9.329 – 2.370)	0.215
Educational status (Middle school and below)	0.159 (-0.456 – 0.775)	0.570	3.626 (0.482 – 6.769)	0.028	2.607 (-0.892 – 6.105)	0.126	2.552 (-0.656 – 5.761)	0.107
Weight loss (Presence)	-0.377 (-1.558 – 0.805)	0.489	-3.054 (-9.209 – 3.101)	0.295	2.262 (-4.034 – 8.558)	0.437	2.913 (-3.370 – 9.195)	0.326
Daily television viewing Time, hour	-0.010 (-0.122 – 0.102)	0.851	-0.618 (-1.202 - -0.033)	0.040	0.161 (-0.404 – 0.726)	0.535	0.052 (-0.545 – 0.649)	0.849
Coronavirus anxiety status (Presence)	-0.128 (-0.962 – 0.705)	0.736	2.330 (-2.036 – 6.695)	0.262	0.732 (-3.979 – 5.443)	0.733	-0.321 (-4.776 – 4.135)	0.876
Neurological compliant status (Presence)	0.172 (-0.453 – 0.797)	0.549	-0.666 (-3.945 – 2.614)	0.661	1.569 (-1.436 – 4.574)	0.268	1.873 (-1.474 – 5.220)	0.241
Monthly revenue status (Minimum wage)	-0.662 (-1.395 – 0.071)	0.072	2.790 (-0.965 – 6.545)	0.129	-0.434 (-4.335 – 3.466)	0.807	-0.850 (-4.682 – 2.983)	0.632

PHQ-9; Patient Health Questionnaire-9, GAD-7; Generalized Anxiety Disorder-7, CAS; Coronavirus Anxiety Scale, OCS; The Obsession with Covid-19 Scale

Cancer disease can negatively affect patients both physically and psychologically. Psychological complaints are high in individuals diagnosed with cancer (14). Especially in an uncertain period such as a pandemic, both the burden of the fight against cancer, the necessity of treatment and the fear of being affected by the pandemic trigger psychological problems in CPs. In addition, there are studies reporting that Covid-19 infection also causes mental disorders (15).

Depression is one of the most common mental disorders that can cause social and economic losses. It has a high prevalence (10-50%) in CPs. Depression may increase mortality by negatively affecting adherence to treatment and treatment outcomes in CPs (6). The rates of depression increased in Covid-19 outbreak. It has been shown that depression is especially higher in patients with advanced age, female gender, and breast cancer (16). In our study, we found significantly higher depression scores compared to the control group in a significant proportion of CPs (94.5%) most of whom had breast cancer and were at an advanced age compared to the control group. This result is thought to be related to the long-lasting pandemic period, which negatively affects cancer patients. In studies, somatic symptoms that may be related to the cancer itself and its treatment can be seen in CPs, and it is discussed whether this will affect the results of the survey. In our study, both weight loss and neurological complaints were more frequent in CPs.

Conditions such as loss of interest, difficulty in controlling stress and sadness, difficulty concentrating, sleep disorders, fatigue, restlessness, tension and irritability are symptoms of anxiety. Anxiety is more common in females and its prevalence increases with age. Covid-19 significantly increases anxiety and stress (17). In our study, in line with the literature, anxiety scores were higher in older CPs in which female gender was dominant. However, there was no difference between the groups in the analysis based on the eight cut-off points determined in the Turkish validity study. It is thought that the cut-off score may differ depending on the sample size or the heterogeneity of the examined groups and may affect the results.

It has been reported that marital status, age and education level may not be associated with depression and post-traumatic stress disorder in pandemics (18). In studies conducted during the Covid-19 period, there are controversial results between factors such as age, marital status, occupation, educational status and parenting status, and the development of anxiety and depression (19). However, the risk of developing depression and anxiety disorder was high in people with female gender and low education level. In our study, anxiety risk was high in CPs with female gender and low education level, and it was compatible with the literature. In addition, the

risk of anxiety increased due to the lack of information about Covid-19 in CPs, whose daily TV viewing time is short, and due to increased stress in those who received curative chemotherapy, in case the treatment process was adversely affected by the infection.

CAS and OCS, were developed to examine the anxiety and obsession problem caused by Covid-19. The score rates in the CAS and OCS, differ between studies. While the rate of high CAS score is between 3.2-4%, high rate of OCS score has been reported between 5.5-13%. In our study, the rates of high CAS and high OCS scores were 3.3% and 7.7% in CPs, respectively. It was consistent with the literature (20). Also, similar to the literature, there was a significant relationship between CAS and OCS in our study (5). In addition, considering that most of the society was vaccinated and faced with Covid-19 infection until the study period, our study shows that anxiety and obsession due to Covid-19 continues even in the later stages of pandemic.

Intensity of depression and anxiety were mostly mild in our study. Severe depression was shown to occur in approximately 5.5% of participants and severe anxiety in 3.4%. In a study conducted in China at the beginning of the pandemic, 16.5% of the participants had severe depression and 28.8% had moderate anxiety (4). The reason for the high rates in the Asian population may be that the pandemic started in this region and rapidly affected many people until the infection was understood, sudden and multiple deaths, intense restrictions by the country's policy, and the trauma experienced was more severe.

CONCLUSION

Covid-19 pandemic affects health systems and the country's economy in different dimensions. In Covid-19 pandemic, the risk of developing depression and anxiety in CPs was found to be high. PHQ-9, GAD-7, CAS and OCS are easily applicable tests and identify people at risk for anxiety and depression.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval was granted by the Ethics Committee of Recep Tayyip Erdoğan Univercity Medical School (Date: 15/03/2022, no: 2022/59).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

A Bibliometric Vision on Triage in the Emergency Department

Acil Serviste Triyaj Konusunda Bibliyometrik Bir Vizyon

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ABSTRACT

Aim: Triage is an indispensable process in the emergency department. Bibliometrics and visual analysis were performed in this study to look at the hotspots and future prospects in triage research, with the aim of giving researchers some useful recommendations.

Material and Method: This study was based on bibliometric methods, which have two main uses: scientific analysis and mapping. The data retrieved on a single day, 15 June 2022. The search keywords, in the title, entered into the database were triage and emergency room or emergency department, and document type was article. From 1970 through 2021, the data were gathered from the Web of Science (WOS) Core Collection database. The retrieved data transferred to Excel 2010 and VOSviewer programs for further analyses.

Results: By searching for the title words in WOS database, firstly a total of 1538 publications were retrieved between 1970–2021. Of these documents, only articles were evaluated due to their high scientific value (n=999; 64.95%). The first article was published in 1970. There was a peak in the number of publications since 2000s. The highest number of publications published in the year 2021. The most prolific countries were the United States of America (USA) (n=317; 31.73%), Canada (n=87; 8.71%) and Australia (n=79; 7.91%). The most prolific institutions were the League of European Research Universities (LERU) (n=82; 8.21%), Harvard University (n=45; 4.51%) and the University of California system (n=34, 3.40%). Although Canadian publications had the most citations per article, the United States had the most publications and the highest H-Index.

Conclusions: This is the first bibliometric study to give comprehensive description on the published emergency triage literature. The number of papers on emergency triage has grown over time, however there have been few research in this area.

Keywords: Bibliometric methods, triage, emergency department

ÖZ

Giriş: Triyaj, acil servislerde vazgeçilmez bir süreçtir. Bu çalışmada, araştırmacılara bazı yararlı tavsiyelerde bulunmak amacıyla, triyaj araştırmalarındaki sıcak noktaları ve gelecekteki beklentileri incelemek için bibliyometri ve görsel analiz yapılmıştır.

Gereç ve Yöntem: Bu çalışma, bilimsel analiz ve haritalama olmak üzere iki ana kullanıma sahip olan bibliyometrik yöntemlere dayanmaktadır. Veriler tek bir günde, 15 Haziran 2022 tarihinde elde edilmiştir. Veritabanına girilen başlıktaki arama anahtar kelimeleri triyaj ve acil servis veya acil servis, belge türü ise makale idi. 1970-2021 yılları arasındaki veriler Web of Science (WOS) Core Collection veri tabanından toplanmıştır. Elde edilen veriler daha ileri analizler için Excel 2010 ve VOSviewer programlarına aktarılmıştır.

Sonuçlar: WOS veri tabanında başlık kelimeleri aranarak, ilk olarak 1970-2021 yılları arasında toplam 1538 yayına ulaşıldı. Bu dokümanlardan sadece makaleler yüksek bilimsel değerleri nedeniyle değerlendirmeye alındı (n=999; %64,95). İlk makale 1970 yılında yayınlanmıştır. Yayın sayısında 2000'li yıllardan itibaren bir zirve yaşanmıştır. En fazla yayın 2021 yılında yayımlanmıştır. En üretken ülkeler Amerika Birleşik Devletleri (ABD) (n=317; %31,73), Kanada (n=87; %8,71) ve Avustralya (n=79; %7,91) olmuştur. En üretken kurumlar Avrupa Araştırma Üniversiteleri Ligi (LERU) (n=82; %8,21), Harvard Üniversitesi (n=45; %4,51) ve Kaliforniya Üniversitesi sistemi (n=34, %3,40) olmuştur. Kanada yayınları makale başına en fazla atıf alan yayınlar olmasına rağmen, Amerika Birleşik Devletleri en fazla yayına ve en yüksek H-İndeksine sahipti.

Sonuçlar: Bu çalışma, yayınlanmış acil triyaj literatürü hakkında kapsamlı bilgi veren ilk bibliyometrik çalışmadır. Acil triyaj konusundaki makalelerin sayısı zaman içinde artmıştır, ancak bu alanda çok az araştırma yapılmıştır.

Anahtar Kelimeler: Bibliyometrik yöntemler; triyaj; acil servis

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INTRODUCTION

The practice of classifying or prioritizing patients depending on their level of acuity is referred to as "triage" in medicine (1,2). The term "triage" is typically linked with the emergency department (ED). Patients' visits to the ED are unplanned and unpredictable, which means that patients with varied treatment needs may show up at the same time or within a short period of time. This necessitates making patient care a top priority (3). Triage is a critical phase that affects not just the patient experience but also ED operations, such as patient flow through the department and resource use (4,5). Failure to properly triage patients could result in their health deteriorating while they wait (4).

This procedure is essential for the efficient operation of the ED. Triage systems are intended to serve as a tool for departmental organization, monitoring, and evaluation as well as to assure clinical justice for patients. Triage systems have been established in a number of nations over the last 30 years, with efforts taken to ensure consistency of application (6). In many industrialized nations, such as Australia, the United Kingdom, Sweden, the United States, and Canada, there is a vast and expanding body of literature that informs the present state and development of ED triage (2,4,5).

We performed bibliometrics and visualizations to investigate the hotspots and frontier prospects of triage studies in the aim of offering researchers some useful recommendations.

MATERIAL AND METHOD

This study was based on bibliometric methods, which have two main uses: scientific analysis and mapping. The data search was conducted on 15 June 2022. To avoid any potential variance due to the database's daily update, the obtained data was collected within one day. The search keywords, in the title, entered into the database were as follows: TS = (triage* and emergency room* or emergency department) and document type: article. Furthermore, there were no restrictions on the countries, journals, or language of publishing.

The Web of Science (WOS)TM is the world's most trusted worldwide citation database that is publisher-independent. Web of Science Core Collection is at the heart of the WOS platform, spanning all subjects and regions. The WOS Core Collection includes only publications that demonstrate high levels of editorial rigor and best practice, as selected by an expert team of in-house editors (7).

The data for the study was retrieved from the WOS database between 1970 and 2021. Because the year 2022 has yet to be completed, publications from this time period were excluded from the analysis.

Analysis Tool

The retrieved data transferred to Microsoft Excel 2010 and VOSviewer programs for further analyses. The data in the tables were converted to absolute values (frequency and percentage). There were no advanced statistical analysis tests employed.

The maps were generated by the VOSviewer program (The VOSviewer 1.6.18 for Microsoft Windows) consisting of citation tree rings and lines. The triage literature maps were created using bibliometric techniques like as co-citation, bibliographic coupling, and keyword co-occurrence. The frequency with which two units are referenced together, demonstrating similarity between them, is known as co-citation analysis (8). The number of references shared by two publications is used as a measure of similarity between them in bibliographic coupling; that is, the more their bibliographies overlap, the stronger their link (9). Co-occurrence, on the other hand, finds word connections when they co-occur, allowing researchers to analyze the conceptual structure of a research field by using the most essential terms or keywords in the texts (10). We analysed the keyword co-occurrence, bibliographic coupling and co-citations of the published documents.

The Hirsch Index (H-Index) has been proposed as a measure of individual research success. Its application has become widespread in the scientific community around the world. Those with a large number of low-impact publications or only a few high-impact articles have little effect on the H-Index (11,12).

RESULTS

Annual Publications

By searching for the title words in WOS database, firstly a total of 1538 publications were retrieved between 1970 and 2021. Of these documents, only articles were evaluated due to their high scientific value (n=999; 64.95%). The first article was published in 1970.13 This article had 12 citations.

There was a peak in the number of publications since 2000s. The highest number of publications published in the year 2021 (**Figure 1**).

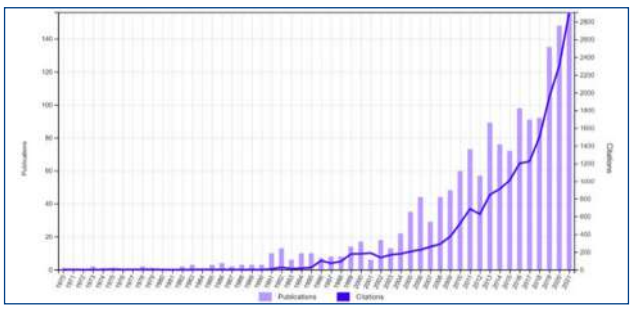

Figure 1. The annual number of publications on triage between 1970 and 2021.

General Features of the Articles

The majority of the articles (92.39%) were written in English language. Spanish (3.10%) and German (1.80%) languages were the other most preferred languages. 79.28% of them published in Science Citation Index Expanded (SCI-E), 22.62% of them published in Social Sciences Citation Index (SSCI) and 17.52% of them published in Emerging Sources Citation Index (ESCI) indexed journals. 448 (44.84%) of the articles had funding sponsors. The leading funding sponsor was United States Department of Health Human Services (5.01%).

Distribution of Countries and Institutions

A total 78 countries contributed the triage literature. The most prolific countries were the United States of America (USA) (n=317; 31.73%), Canada (n=87; 8.71%) and Australia (n=79; 7.91%) (**Table 1**).

Table 1. The list of most prolific countries on triage articles.

Countries/Regions	n	%
USA	317	31.73
Canada	87	8.71
Australia	79	7.91
England	59	5.91
Italy	46	4.61
France	44	4.40
Switzerland	43	4.30
Netherlands	35	3.50
Sweden	35	3.50
Peoples R China	34	3.40
Spain	32	3.20
Iran	30	3.00
Germany	29	2.90
Turkey	27	2.70
South Africa	26	2.60
South Korea	23	2.30
Taiwan	20	2.00
Brazil	18	1.80
Denmark	17	1.70
Belgium	14	1.40

Note: Showing 20 out of 78 countries; Total number of articles: 999

A total 1548 institutions contributed the triage literature. The most prolific institutions were the League of European Research Universities (LERU) (n=82; 8.29%), Harvard University (n=45; 4.51%) and the University of California system (n=34; 3.40%) (**Table 2**).

Publishing Journals

The most of the articles on triage was published in the Emergency Medicine Journal (n=48; 4.81%), Academic Emergency Medicine (n= 36; 3.60%) and the Journal of Emergency Nursing (n=34; 3.40%) (**Table 3**).

Table 2. The list of most prolific institutions on triage articles.

Institutions	n	%
League of European Research Universities (LERU)	82	8.21
Harvard University	45	4.51
University of California System	34	3.40
Udice French Research Universities	23	2.30
University of Toronto	20	2.00
Assistance Publique Hopitaux Paris Aphp	19	1.90
University of Basel	19	1.90
Massachusetts General Hospital	18	1.80
Brigham Women S Hospital	17	1.70
Karolinska Institutet	17	1.70

Note: Showing 10 out of 1548 institutions; Total number of articles: 999.

Table 3. The list of the mostly publishing journals on triage.

Publishing journals	n	%
Emergency Medicine Journal	48	4.81
Academic Emergency Medicine	36	3.60
Journal of Emergency Nursing	34	3.40
Annals of Emergency Medicine	31	3.10
International Emergency Nursing	26	2.60
American Journal of Emergency Medicine	25	2.50
Pediatric Emergency Care	20	2.00
European Journal of Emergency Medicine	19	1.90
Journal of Emergency Medicine	18	1.80
BMC Emergency Medicine	17	1.70
Emergency Medicine Australasia	17	1.70
Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine	17	1.70
Emergencias	15	1.50
Canadian Journal of Emergency Medicine	14	1.40
PLOS One	14	1.40

Note: Showing 15 out of 403 journals; Total number of articles: 999.

Mapping

The keywords analysis was given in **Figure 2**.

The citation analysis between countries was given in **Figure 3**.

The density visualization of bibliographic coupling between countries was given in **Figure 4** with network visualisation.

Citing Analysis

The articles were cited 16880 times (16.9/ per article) and the mean of H-Index was 63. The number of citations had increased over the years, especially after 2013. The highest cited article was published in 1997 (14). This article was cited 817 times. The summary of highly cited articles were given in **Table 4**.

The number of the published articles and citations has increased over the years (**Figure 1** and **Table 5**).

The publications from Canada had the highest number of citations per article, but the USA had the highest number of publications and H-Index (**Table 6**).

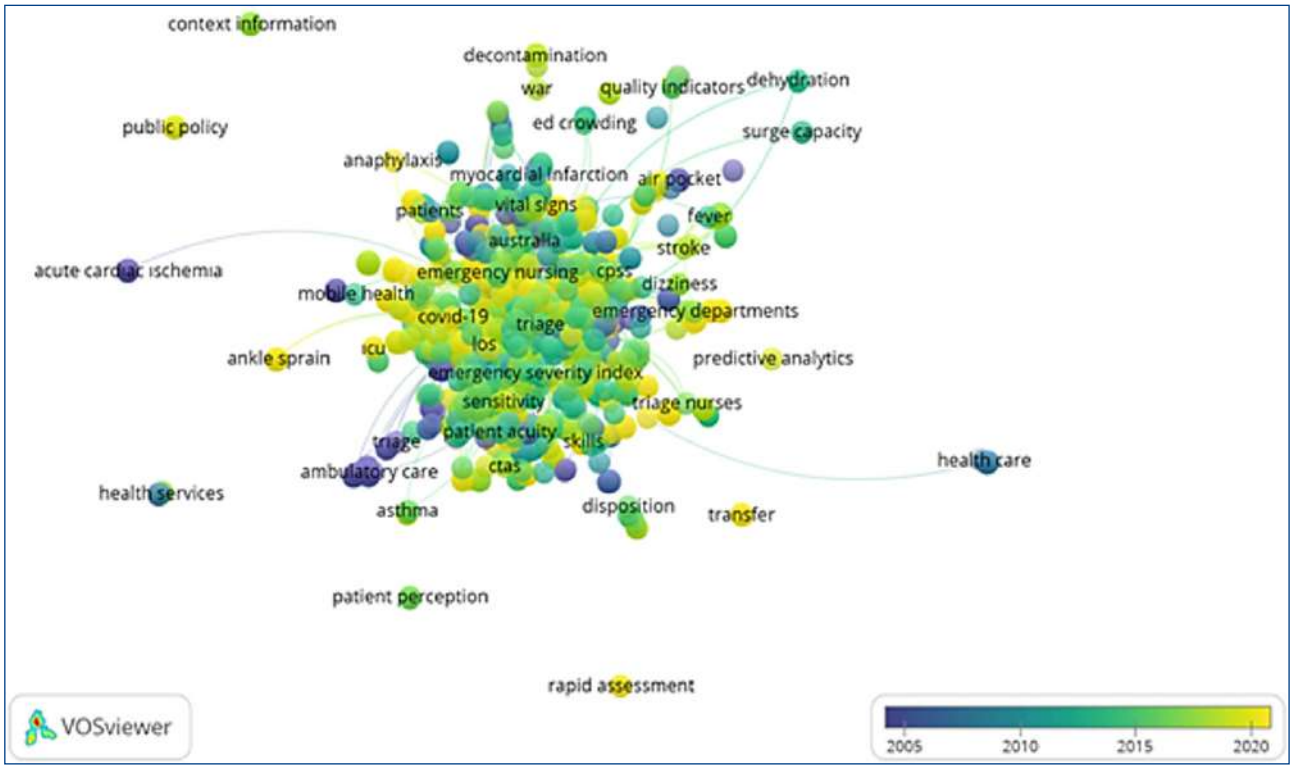

Figure 2. The keywords analysis of the triage articles.

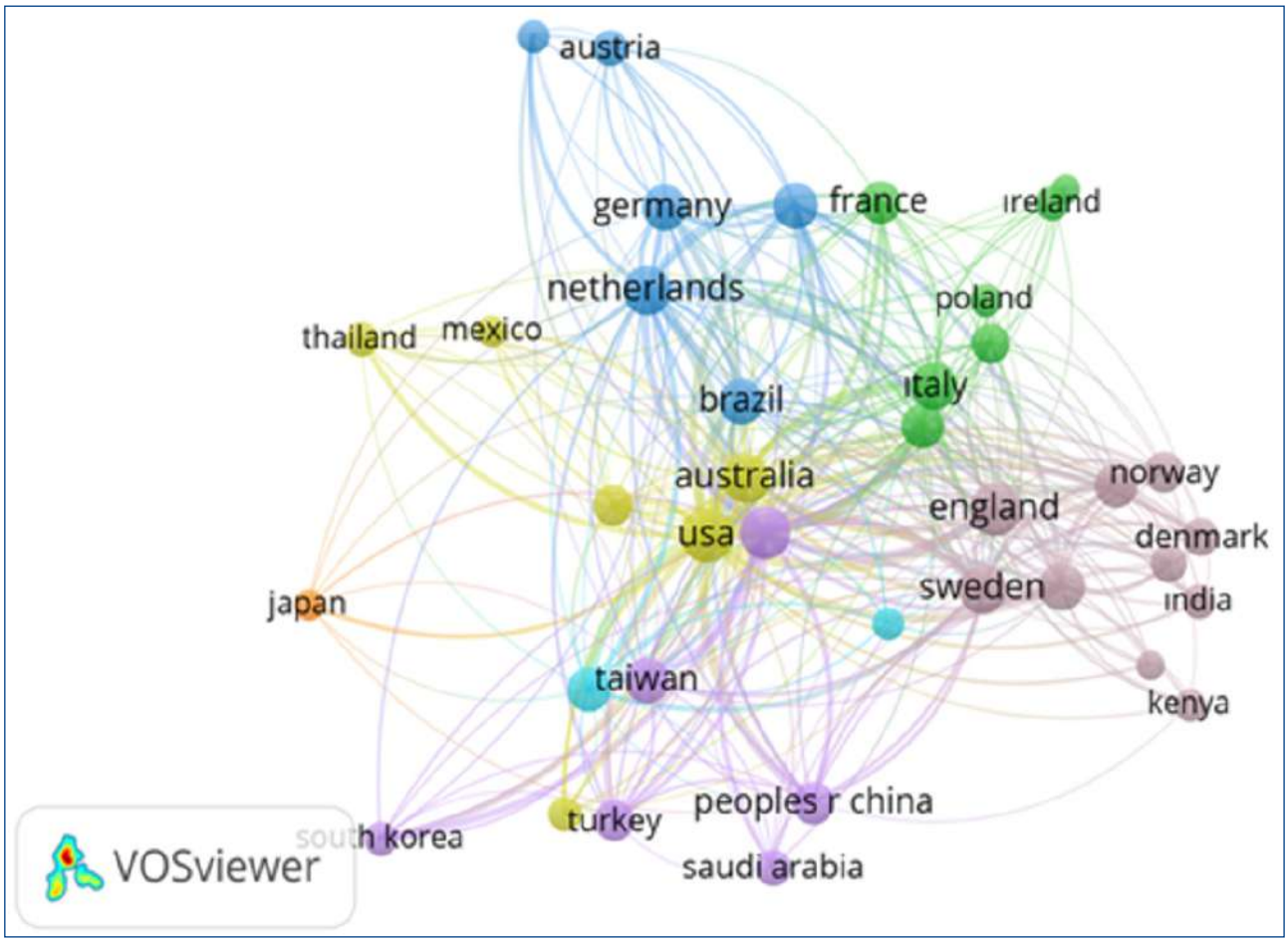

Figure 3. The citation analysis between countries in the context of triage articles.

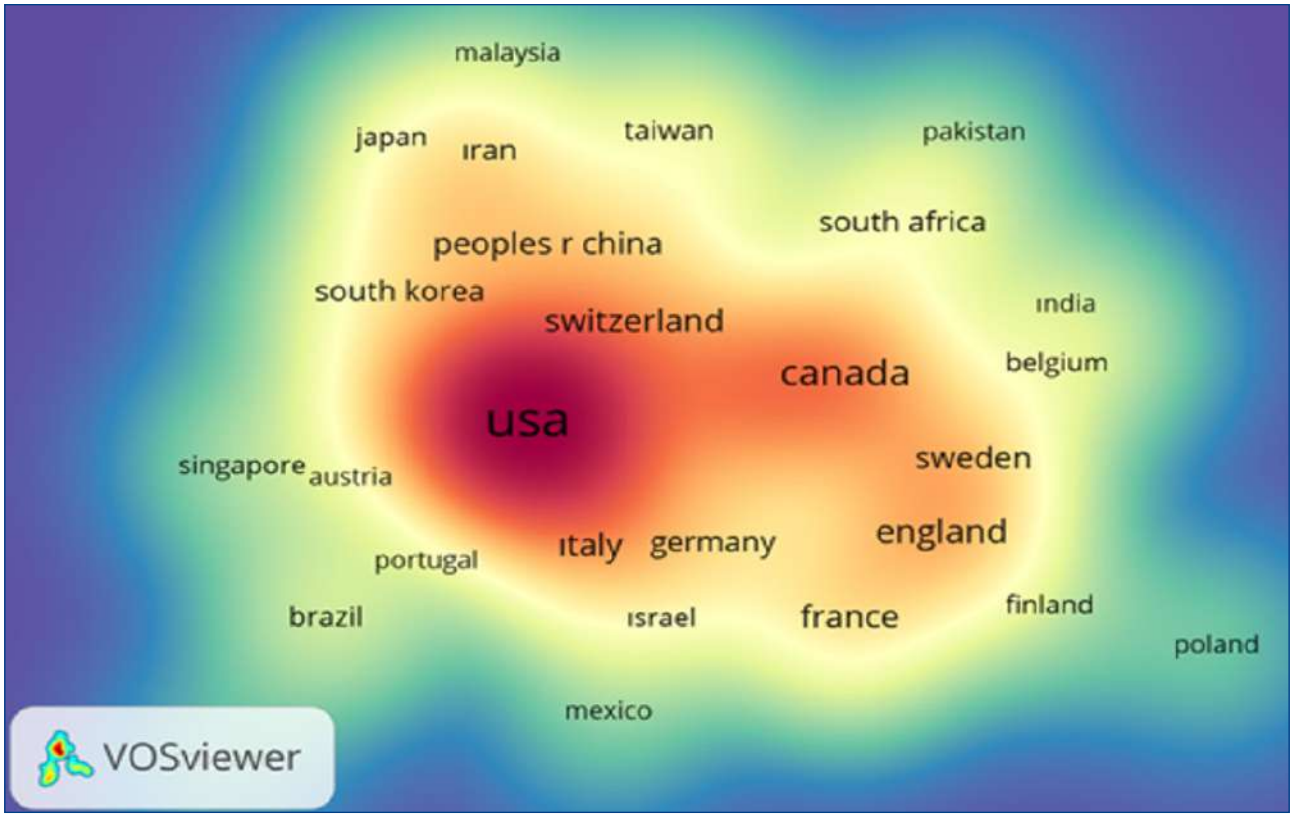

Figure 4. The density visualization of bibliographic coupling between countries in the context of triage literatüre.

Table 4. The summary of the most cited articles.

Reference	Journal	Article name	Citations
Hamm et al. 1997 (14)	New England Journal of Medicine	Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I	817
Eitel et al. 2003 (15)	Academic Emergency Medicine	The emergency severity index triage algorithm version 2 is reliable and valid	206
Molyneux et al. 2006 (16)	Bulletin of the World Health Organization	Improved triage and emergency care for children reduces inpatient mortality in a resource-constrained setting	178
Beveridge et al. 1999 (17)	Annals of Emergency Medicine	Reliability of the Canadian emergency department triage and acuity scale: Interrater agreement	174
Han et al. 2013 (18)	Annals of Emergency Medicine	Diagnosing Delirium in Older Emergency Department Patients: Validity and Reliability of the Delirium Triage Screen and the Brief Confusion Assessment Method	161
Lima et al. 2016 (19)	Stroke	Field Assessment Stroke Triage for Emergency Destination A Simple and Accurate Prehospital Scale to Detect Large Vessel Occlusion Strokes	148
Larsen et al. 2011 (20)	Pediatrics	An Emergency Department Septic Shock Protocol and Care Guideline for Children Initiated at Triage	142
Widgren et al. 2011 (21)	Journal of Emergency Medicine	Medical Emergency Triage and Treatment System (METTS): a new protocol in primary triage and secondary priority decision in emergency medicine	142
Pearson et al. 1995 (22)	Journal of General Internal Medicine	Triage decisions for emergency department patients with chest pain: do physicians' risk attitudes make the difference	141
Horng et al. 2017 (23)	PLOS One	Creating an automated trigger for sepsis clinical decision support at emergency department triage using machine learning	123

Table 5. The number of articles and citations over the years.

Time span	Number of publications	Times cited in WOS	Times cited in all databases
1970-1989	18	122	123
1990-2009	209	7729	7908
2010-2021	772	9029	9305

Table 6. H-Indexes, number of publications, and number of citations of the

Country	H-Index	Number of publications	Number of citations	Number of citations per article
USA	45*	317*	6819*	21.51
Canada	26	87	2078	23.89*
Australia	19	79	1206	15.27
England	20	59	1134	19.22
Italy	12	46	602	13.09

DISCUSSION

The main purpose of the ED is to give prompt assistance to those who have urgent or critical needs. Triage is the initial meeting between healthcare personnel and patients after registering for emergency services (24). In a hospital, the goal of triage is to identify and prioritize individuals with the most urgent requirements so that emergency services can be used first. A proper arrangement of patients to receive emergency care at the most appropriate time for their condition is referred to as an effective triage decision (25). Several researches has looked into the usefulness of triage methods (26-28). But no avaliable bibliometric study on triage research.

A bibliometric study can be used to investigate research hotspots and frontiers in specific subjects by calculating the productivity of institutions, authors, countries and the frequency of keywords (29). Researchers can use bibliometric analysis to describe the present state of research domains or specific diseases, as well as propose recommendations and ideas for future study. In recent years many bibliometric studies conducted on various topics in medicine (30-35). But, the current study is the first bibliometric study of emergency triage research, and it may give useful references for investigators looking to delve deeper into current topics in the field.

We performed a preliminary search in the WOS database using terms linked to ED triage. For the extraction, we used the WOS database because it is a scientific database in the biomedical field with a precise and specific search engine. Also we chose articles as they had high scientific impact. A total of 999 papers on emergency triage were evaluated for this study. Although the number of published articles has risen exponentially since 2000, it can be said that there has not been enough valuable work in this field in total. In addition, the number of articles in the emergency medicine literature has increased a lot in recent years, but it seems like there has been less shooting in the field of triage (36,37). According to the findings of a Pubmed Medline search, the first publication on emergency triage was published in the year 1947. However, the WOS database only goes back to 1970.

Furthermore, an ED network may be developed to debate and give recommendations on how to use the triage system across the country. The network clears up any ambiguities regarding the triage process, and a standardized triage training program for all EDs across the country might be developed. A triage training instructor's qualification can be generated through network communication. Furthermore, the network can provide recommendations to the research team of the triage system in order to improve the system's future development. The network can establish an acceptable triage rate for the nation to improve overall triage performance (25). Our results showed that a total of 78 countries contributed to the triage literature. The most prolific countries were the USA (31.73%), Canada (8.71%), and Australia (7.91%). The first prolific countries were American, Europan and Asian countries. This demonstrated the priority focused on scientific research and the fact that the USA has numerous scientific institutions. No countries other than South Africa were listed in the top 25 country rankings, among African countries.

The bibliometric visualization programs CiteSpace and VOSviewer are widely used for data processing and visualization (26,28,33-35). In this study we used VOSviewer for visualization. We analyzed keywords, citation analysis between countries and bibliographic coupling between countries. The co-occurrences of author keywords show that these concepts have been examined extensively by the researchers (32,36-38). We also studied this parameter in our study.

Limitations

The study only examined at documents from the WOS database. So the period prior to 1970 cannot be analyzed using the current database. We also expect that exploring multiple databases will turn up further works.

CONCLUSION

This is the first bibliometric study to give comprehensive description on the published emergency triage literature. Throughout time, the number of papers on the emergency triage has increased but there were limited studies. As there are few studies concentrating on triage, further research is needed to discover and assess its usefulness in improving triage accuracy. In conclusion, this study gives potential collaborators and institutions, as well as hot topics, so providing a perspective on the growing trend of triage on the ED, which may assist academics explore new research routes in this field.

ETHICAL DECLARATIONS

Ethics Committee Approval: There were no human or animal subjects in this retrospective bibliometric analysis study. The data for this study was taken directly from the WOS database. Therefore, there was no need for ethical approval.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Systemic Immune Inflammatory (SII) Index in Evaluating the Severity of Multitrauma Patients in the Emergency Department

Acil Serviste Multitravma Hastalarının Şiddetinin Değerlendirilmesinde Sistemik İmmün İnflamatuvar (SII) İndeksi

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ABSTRACT

Aim: In the emergency department, healthcare providers face the critical task of assessing and managing patients with multitrauma, a condition characterized by multiple injuries sustained simultaneously. In this study, we evaluated the power of the systemic immune inflammatory index in predicting the prognosis and severity of patients admitted to the emergency department with multitrauma

Material and Method: Patients aged 18 years and older who presented to the adult emergency department of the hospital and were diagnosed with Multitrauma 1 January 2022 and 31 December 2022 were included in the study. Demographic characteristics (age and gender), initial laboratory test results including neutrophil (N), lymphocyte (L), and platelet counts, as well as NLR, PLO and SII will be calculated according to laboratory results; (NLR=neutrophil count / lymphocyte count ratio; PLR=platelet count / lymphocyte count ratio; SII=platelet count x neutrophil count / lymphocyte count ratio), hospital admission or intensive care unit (ICU) admission status, and patient outcomes were recorded from the medical records.

Results: According to ROC analysis, NLR, PLR and SII parameters were statistically significant for the distinction between hospitalization and discharge (P<0.001, P:0.016 and P<0.001, respectively). When the data were categorized according to the cut-off values determined in the ROC analysis, NLR over 2.84 and SII over 777 were found to be significant for hospitalization according to the Chi-square analysis, while PLR over 108 was not significant (respectively P. <0.001, P:0.111 and P<0.001)

Conclusion: These markers provide valuable insights into the systemic inflammatory response and have the potential to aid in risk stratification, prognosis assessment, and treatment decision-making. However, further research is warranted to validate their utility in diverse patient populations and clinical scenarios.

Keywords: Systemic immune inflammatory index, multitrauma, early alert, emergency medicine

ÖZ

Giriş: Acil serviste, sağlık hizmeti sağlayıcıları, aynı anda birden fazla yaralanma ile karakterize edilen bir durum olan multitravmalı hastaları değerlendirme ve yönetme gibi kritik bir görevle karşı karşıyadır. Bu çalışmada acil servise multitravma ile başvuran hastaların prognozunu ve ciddiyetini öngörmede sistemik immün inflamatuar indeksin gücünü değerlendirdik.

Gereç ve Yöntem: Hastanenin erişkin acil servisine başvuran ve 1 Ocak 2022 ile 31 Aralık 2022 tarihlerinde Çoklu Travma tanısı alan 18 yaş ve üstü hastalar çalışmaya alındı. Demografik özellikler (yaş ve cinsiyet), nötrofil (N), lenfosit (L) ve trombosit sayılarını içeren ilk laboratuvar test sonuçları ile NLR, PLO ve SII laboratuvar sonuçlarına göre hesaplanacaktır; (NLR = nötrofil sayısı / lenfosit sayısı oranı; PLR = trombosit sayısı / lenfosit sayısı oranı; SII = trombosit sayısı x nötrofil sayısı / lenfosit sayısı oranı), hastaneye yatış veya yoğun bakım ünitesine (YBÜ) yatış durumu ve hasta sonuçları kaydedildi. tıbbi kayıtlar.

Bulgular: ROC analizine göre NLR, PLO ve SII parametreleri hastaneye yatış ve taburculuk ayrımında istatistiksel olarak anlamlı bulundu (sırasıyla P<0.001, P:0.016 ve P<0.001). Veriler ROC analizinde belirlenen cut-off değerlerine göre kategorize edildiğinde Ki-kare analizine göre NLO 2,84 üzeri ve SII 777 üzeri anlamlı bulunurken PLO 108 üzeri anlamlı bulunmadı (sırasıyla P <0,001, P:0,111 ve P<0,001)

Sonuç: Bu belirteçler, sistemik inflamatuar cevaba ilişkin değerli bilgiler sağlar ve risk sınıflandırması, prognoz değerlendirmesi ve tedavi kararı vermeye yardımcı olma potansiyeline sahiptir. Bununla birlikte, çeşitli hasta popülasyonlarında ve klinik senaryolarda faydalarını doğrulamak için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Sistemik immün inflamatuar indeks, çoklu travma, erken uyarı, acil tıp

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INTRODUCTION

In the emergency department, healthcare providers face the critical task of assessing and managing patients with multitrauma, a condition characterized by multiple injuries sustained simultaneously (1). Multitrauma cases often present a complex and dynamic clinical scenario, requiring prompt decision-making and swift interventions to save the patient's life. In such high-stress situations, it becomes crucial to identify reliable and efficient methods that can aid in determining the severity of injury and guide appropriate treatment strategies (2).

The time-sensitive nature of multitrauma demands swift and accurate assessment to optimize patient outcomes. Prompt recognition of severe injuries, identification of associated complications, and timely interventions can significantly impact a patient's survival and long-term functional recovery (1). Clinicians and researchers continually seek innovative tools and markers that can aid in the rapid evaluation of multitrauma patients, providing valuable insights into their overall condition and guiding appropriate clinical management (3).

One promising avenue of investigation in assessing the severity of multitrauma patients involves the use of the Systemic Immune Inflammatory (SII) index (4). The SII index is a derived parameter that integrates peripheral blood cell counts, including platelet, lymphocyte, and neutrophil counts. It has been proposed as a potential marker of systemic inflammation and immune response, with emerging evidence suggesting its utility in various disease states, including cancer, infectious diseases, and cardiovascular disorders (5).

The rationale behind exploring the application of the SII index in multitrauma cases lies in its ability to provide insights into the intricate relationship between inflammation, immune response, and trauma severity (6). Trauma triggers a cascade of immune and inflammatory processes that play a vital role in determining the extent of tissue damage, organ dysfunction, and overall prognosis. By leveraging the SII index, clinicians can potentially assess the severity of systemic inflammation and immune dysregulation, thus aiding in risk stratification and therapeutic decision-making for multitrauma patients (7).

The critical need for swift assessment and intervention in multitrauma cases, exploring the potential utility of the SII index in evaluating trauma severity becomes essential. In this study, we evaluated the power of the systemic immune inflammatory index in predicting the prognosis and severity of patients admitted to the emergency department with multitrauma.

MATERIAL AND METHOD

Study Design and Setting

This was a single-center retrospective cross-sectional study conducted in the emergency medicine clinic of a tertiary care hospital located in a metropolitan area with an approximate population of 4.5 million. The study was carried out with the permission of Izmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (Decision No: 0050, Date: 23.02.2023).

Study Population

Patients aged 18 years and older who presented to the adult emergency department of the hospital and were diagnosed with Multitrauma (such as in-vehicle traffic accidents and out-of-vehicle traffic accidents, falling from a height, loss of limb, assault etc.)1 January 2022 and 31 December 2022 were included in the study. Patients under the age of 18 and Cases under the age of 18, Burns, Persons with a history of cancer, autoimmunity, allergy, inflammatory or infectious disease in the last 3 months, Patients with missing data, and Unable to follow-up (cases referred or refused treatment) were excluded from the study.

Data Collection and Processing

Demographic characteristics (age and gender), initial laboratory test results including neutrophil (N), lymphocyte (L), and platelet counts, as well as NLR, PLO and SII will be calculated according to laboratory results; (NLR=neutrophil count / lymphocyte count ratio; PLR=platelet count / lymphocyte count ratio; SII=platelet count x neutrophil count / lymphocyte count ratio), hospital admission or intensive care unit (ICU) admission status, and patient outcomes were recorded from the medical records.

Outcome Measures

To determine the superiority of NLR, SII and PLR values in diagnosing meningitis and encephalitis, as well as predicting the severity and clinical outcomes of the disease, these parameters were compared with other variables that could be associated with disease severity and clinical outcomes. Additionally, N/L ratio, SII values, and other associated parameters were compared between the group with mortality and the group who survived in both diseases.

Data Analysis

Data obtained in the study were analyzed using IBM SPSS Statistics for Macos, Version 26.0. Armonk, NY: IBM Corp. Categorical variables were expressed as numbers and percentages, while numerical variables were expressed as mean and standard deviation when presenting the descriptive statistics. Shapiro-Wilk test was used as the normality test. Since the data did not follow a normal distribution, Mann-Whitney U test was used for comparisons between two group means. Chi-square test was used for comparisons of categorical variables. A p-value of <0.05 was considered statistically significant. Results were presented with a 95% confidence interval.

RESULTS

A total of 179 patients were included in the study. The mean age of the patients was 37±16. Thirty-five (20%) of the patients were female and 144 (80%) were male. While 95 (53%) patients were discharged from the emergency room, 66 (37%) patients were admitted to the service and 18 (10%) patients to the intensive care unit. Eight of the patients included in the study died. The average of the laboratory results of the patients is presented in **Table 1**.

Table 1. General characteristics of the patients

	N	Minimum	Maximum	Mean	Std. Deviation
Neutrophil	179	2.51	40.46	8.5	5.3
Lymphocyte	179	.350	6.840	2.4	1.2
Platelet	179	51	443	260	70
NLR	179	.6	56.2	5.6	7.6
PLR	179	18.0	700.0	142	103
SII	179	69.4	14208.0	1453	2015
Age	179	17	92	37	16

According to ROC analysis, NLR, PLR and SII parameters were statistically significant for the distinction between hospitalization and discharge (P<0.001, P:0.016 and P<0.001, respectively). When the data were categorized according to the cut-off values determined in the ROC analysis, NLR over 2.84 and SII over 777 were found to be significant for hospitalization according to the Chi-square analysis, while PLR over 108 was not significant (respectively P. <0.001, P:0.111 and P<0.001) (**Table 2**)

Table 2. Hospitalization-discharge ratios

	AUC	Sensitivite	Spesifite	PPD	NPD	P
NLR >2.8	0.762	71	64	58	76	<0.001
PLR >108	0.611	59	54	45	65	0.111
SII >777	0.732	68	68	59	76	<0.001

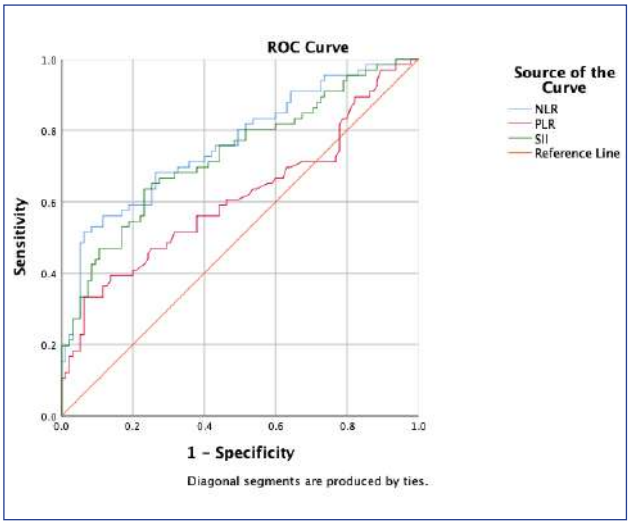

Figure 1. ROC analysis of NLR, PLR and SII in predicting ICU and service hospitalisation

According to the ROC analysis, while NLR and SII parameters were statistically significant for the distinction between hospitalization and ICU (P=0.045 and P=0.047, respectively), PLR was not significant (p=0.187).

When the data were categorized according to the cut-off values determined in the ROC analysis, according to the Chi-square analysis performed, NLR above 9.5, PLR above 156 and SII above 1397 were found to be significant for ICU (Respectivly P=0.002, P= 0.021, P=0.028) (**Table 3**).

Table 3. Service-ICU hospitalization rates and comparison

	AUC	Sensitivite	Spesifite	NPD	PPD	P
NLR>9.5	0.655	61	77	42	88	0.002
PLR>156	0.602	67	64	33	88	0.021
SII>1397	0.653	76	62	32	87	0.028

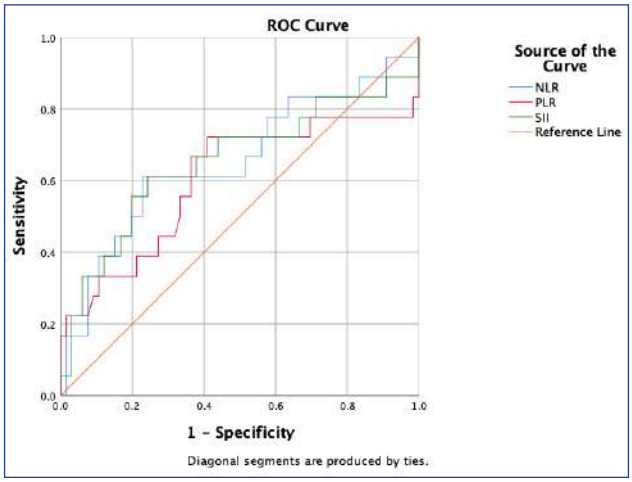

Figure 2. ROC analysis of NLR, PLR and SII in predicting mortality

In the ROC analysis performed to evaluate the success of the tests in predicting mortality, it was seen that NLR, PLR and SII failed to predict mortality (p=0.235, p=0.831 and p=0.507, respectively).

DISCUSSION

The aim of our study was to investigate the predictive value of blood count-derived inflammatory markers and systemic immune-inflammation indices in various clinical outcomes. Let's discuss and comment on our results, incorporating the references provided.

In our study, we observed that elevated levels of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) were associated with adverse outcomes, such as longer hospital stays and increased risk of complications. These findings align with previous research (8-10) and highlight the potential clinical utility of these markers as prognostic indicators. However, it is important to note that our study had a relatively small sample size, which may limit the generalizability of the findings.

In line with studies by Calleja et al. (2020) and Ciechanowicz et al. (2020), our findings emphasize the importance of effective information transfer and comprehensive management strategies for multitrauma patients. Early identification of injuries, such as completely transected common hepatic duct injury (3), is crucial for successful management and improved patient outcomes. Our study contributes to the understanding of the systemic immune response to trauma, which plays a pivotal role in tissue damage and organ dysfunction (4, 7).

Furthermore, the association between inflammatory markers and clinical outcomes extends beyond trauma-related conditions. Studies by Esenboğa et al. (2022) and Simon et al. (2016) demonstrate the predictive value of systemic immune-inflammation indices and plasma brain-derived neurotrophic factor levels in predicting outcomes in cardiovascular and traumatic brain injury patients, respectively (5,11).

While our study adds to the existing literature, it is essential to acknowledge the limitations. The retrospective nature of our study introduces the possibility of bias, and prospective studies with larger cohorts are needed to establish a causal relationship between inflammatory markers and clinical outcomes (12).

The systemic immune-inflammation index (SII), a marker combining platelet, neutrophil, and lymphocyte counts, has been investigated in different clinical settings. Studies have shown its prognostic value in pediatric burned patients (13), as well as in patients with acute appendicitis (14), gastric cancer (15), urologic cancers (16), and COVID-19 (17-19). These studies demonstrate the broad applicability of SII as a prognostic marker across different disease entities.

Additionally, the neutrophil-lymphocyte ratio (NLR), another inflammatory marker, has been extensively studied in various clinical conditions. It has been associated with adverse outcomes in polytrauma patients (2), thoracic trauma patients (8), and patients with traumatic brain injury (9). Moreover, the platelet-lymphocyte ratio (PLR) has been investigated in patients with hip fracture (10) and primary percutaneous coronary intervention (5), showing its potential prognostic value in these populations.

The relevance of inflammatory markers in trauma extends beyond their predictive value. Inflammatory responses play a pivotal role in the pathophysiology of trauma and surgery, affecting the systemic inflammatory response syndrome (SIRS) and subsequent organ dysfunction. Understanding the mechanisms underlying SIRS and the protective strategies to mitigate its detrimental effects is essential for improving patient outcomes. Margraf et al. provide a comprehensive overview of the mechanisms and protective measures against SIRS after surgery (20).

In summary, our study provides valuable insights into the potential clinical utility of blood count-derived inflammatory markers and systemic immune-inflammation indices in predicting clinical outcomes in various conditions. These markers have the potential to aid in risk stratification, prognosis assessment, and treatment decision-making. However, further research is warranted to validate their utility in diverse patient populations and clinical scenarios.

Limitation

The retrospective nature of our study introduces inherent limitations, including the possibility of selection bias and incomplete or missing data. The reliance on medical records and data collected for clinical purposes may lead to inconsistencies and inaccuracies in the variables analyzed. Moreover, the retrospective design limits our ability to establish causality between inflammatory markers and clinical outcomes. Prospective studies with standardized data collection protocols are needed to overcome these limitations and provide more robust evidence.

CONCLUSION

This study contributes to the growing body of evidence supporting the clinical utility of blood count-derived inflammatory markers and systemic immune-inflammation indices as prognostic indicators in various clinical conditions. These markers provide valuable insights into the systemic inflammatory response and have the potential to aid in risk stratification, prognosis assessment, and treatment decision-making. However, further research is warranted to validate their utility in diverse patient populations and clinical scenarios.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Izmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (Decision No: 0050, Date: 23.02.2023).

Informed Consent: Informed consent form did not obtained from the participants due to the nature of the study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Aile Sağlığı ve Toplum Sağlığı Merkezinde Çalışan Hemşirelerin İletişime Gönüllülük Durumları ve İletişim Doyumlarının Belirlenmesi

Determination of Communication Volunteer Status and Communication Satisfaction of Nurse Working in Family Health and Community Health Center

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ÖZ

Amaç: İletişim, bir bireyin başka bir bireye yaptığı herhangi bir etki olmasının ötesinde bir paylaşma eylemi olarak nitelendirilmektedir. Günlük yaşamda temel vazgeçilmez bir unsur olarak ifade edilen iletişim bir amacın gerçekleştirilmesi hususunda önemli yapı taşlarından biridir. Sağlık alanında iletişim olgusu ise; hasta ve sağlık personeli arasında gerçekleşen düşünce ve duygu alışverişi olarak ifade edilmektedir. Hasta ve hemşire arasındaki iletişim bağı ne kadar kuvvetli olursa alınan hizmet de daha verimli, kaliteli ve tatmin edici olacaktır. Araştırma; Aile Sağlığı ve Toplum Sağlığı Merkezleri'nde görev yapan hemşirelerin iletişime gönüllülük durumlarının ve iletişim doyumlarının belirlenmesi amacıyla tanımlayıcı olarak yapılmıştır.

Gereç ve Yöntem: Şubat 2018-Mart 2018 tarihleri arasında; Erzurum ili merkez ilçelerine görev yapmakta olan Aile Sağlığı ve Toplum Sağlığı Merkezleri'nde görev yapan araştırmaya gönüllü olarak katılıp anket sorularını eksiksiz yanıtlayan 95 hemşire ile yapıldı. Veriler; Şubat 2018-Mart 2018 tarihleri arasında Sosyo-Demografik Durum Anketi, İletişime Gönüllülük Ölçeği ve İletişim Doyum Ölçeği ile toplandı. Verilerin analizinde ; SPSS 15.0 for Windows programı, frekans ve yüzde, ortalama ve standart sapma, t testi, Tek Yönlü Varyans Analizi, Kruskal Wallis, Mann Whitney U Testi, Cronbach alfa güvenilirlik analizi kullanıldı.

Bulgular: Araştırmamıza katılan hemşirelerin yaş ortalaması 29.66±7.31 olarak tespit edilmiştir. Katılımcıların meslekte ortalama 8.77±7.06 yıldır çalıştıkları ve son bir yılda %32.6 oranında çalıştıkları işten ayrılmayı düşündükleri belirtmişlerdir. Hemşirelerin iletişime gönüllülük durumlarına bakıldığında ortalama 50.22±2.12'si yani yarısı iletişime gönüllü olduklarını ve çalıştıkları işteki iletişim doyumlarının ortalama 91.54±12.19 oranıyla yüksek düzeyde olduğu saptanmıştır.

Sonuç: Araştırmaya katılan hemşirelerin orta düzeyde iletişime gönüllü oldukları fakat çalıştıkları kurumdaki iletişim doyumlarının yüksek olduğu saptanmıştır.

Anahtar Kelimeler: Hemşire, iletişime gönüllülük, iletişim doyumu

ABSTRACT

Aim: Communication is characterized as a demonstration to conclude any impact a community has made on another individual. Communication, which is expressed as a basic indispensable and unique in daily life, is one of the important building blocks of the realization rooms of a purpose. The communication phenomenon in the field of health is; It is expressed as the exchange of thoughts and feelings between the patient and the health personnel. It has been perceived that there is a purposeful and positive relationship between the volunteering of consultation and communication satisfaction of the nurses as they think.

Material And Method: Between February 2018 and March 2018; The study was conducted with 95 nurses who voluntarily participated in the study and answered the questionnaire questions, working in the Family Health and Community Health Centers working in the central districts of Erzurum. Data; It was collected between February 2018 and March 2018 with the Socio-Demographic Status Questionnaire, Volunteering for Communication Scale and Communication Satisfaction Scale. In the analysis of data; SPSS 15.0 for Windows program, frequency and percentage, mean and standard deviation, t test, One Way Analysis of Variance, Kruskal Wallis, Mann Whitney U Test, Cronbach alpha reliability analysis were used.

Results: The mean age of the nurses participating in our study was 29.66±7.31. The participants stated that they had been working in the profession for an average of 8.77±7.06 years and that they were considering quitting their job at a rate of 32.6% in the last year. When the volunteering status of the nurses for communication was examined, it was determined that an average of 50.22±2.12, that is, half of them, volunteered for communication and their communication satisfaction in their job was at a high level with an average of 91.54±12.19.

Conclusion: It was determined that the nurses participating in the study were willing to communicate at a medium level, but their communication satisfaction in the institution they worked in was high.

Keywords: Nurse, volunteering to communication, communication satisfaction,

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GİRİŞ VE AMAÇ

İletişim; bireylerin duygu, düşünce ve bilgilerini simgeler aracılığıyla aktarması olarak tanımlanmaktadır. Bireyler duygu ve düşüncelerini iletişim yoluyla paylaşarak mutlu oldukları için iletişim, insanlar arası etkileşimin temelini oluşturur (1-18). Çünkü bireyler iletişim sayesinde fikirlerini paylaştığı, değerlendirdiği ayrıca iletişim sayesinde hem etkileyip hem de etkilendiği için hayattan ayrı tutulamaz (2). Temel yaşam becerilerinden biri olan iletişim, doğumdan ölüme kadar öğrenilen, bireyi şekillendiren, hayatı sağlıklı bir şekilde devam ettirmeyi amaçlayan bir süreçtir (3). Bireylerin hayatında vazgeçilmez olan iletişim diğer alanlarda olduğu gibi sağlık alanında da önemli bir faktördür. Sağlıkta iletişimin güçlü olabilmesi için dürüst, destekleyici, açık olunmalıdır. Sağlık kurumlarını düşündüğümüzde bireyler ile en fazla iletişim halinde bulunan sağlık çalışanı hemşirelerdir (4). Bu yüzden sağlık ihtiyacı olan bireye bu ihtiyacı anlayıp karşılayabilmesine olanak sağlayan kişidir (5). Her birey iletişim kurmaktadır ancak bu süreçte bazıları bunu kolay bir şekilde gerçekleştirmekte, bazıları ise iletişim kurmakta güçlük yaşamaktadır (18). Kendisini karşısındaki insana ifade etmede zorluk yaşayan kişi; karşısındaki kişiyi tanıyamaz, düşüncelerini anlayamaz ve kişiyi kendi kafasında nereye koyduğunu tahmin edemez. Bu durumda bireyde sürekli bir tedirginlik ve güvensizlik duygusu yaşamasına neden olmaktadır (6). Bu yüzden hemşireler çeşitli iletişim tekniklerini öğrenmeli ve sağlıklı ikili iletişim kurabilmelidir. Hemşirelik mesleği bakım verme ve yardım etme olarak benimsense de her alanda iletişim sürecini kapsamaktadır (17). Bu süreçte hemşirelere düşen en önemli görev; bireylerle daha sağlam ilişkiler kurup, sağlıklı iletişim ortamı oluşturmaktır (1). Birey ve hemşirenin etkili iletişim kurup birbirini anlayabilmeleri kaliteli sağlık hizmeti için önem arz etmektedir (7). Bu nedenle hemşirelerin kurumsal iletişim etkinliğinin saptanmasında ve kurumsal amaçlara ulaşmada önemli olan etmen iletişim doyumlarının değerlendirilmesidir. İletişim doyumu Battey ' e göre "organizasyonda meydana gelen iletişimin tüm halleri ile çalışanın bunlardan duyduğu bireysel memnuniyeti" olarak tanımlamaktadır (8). Sağlık kurumlarında çalışan hemşirelerin iletişim doyumlarını arttırmak için sağlık hizmetlerindeki eğitimlerin, işlevselliğin ve hizmet kalitesinin artırılması önemli bir faktördür (9). İletişim doyumu doğrudan iş doyumuna katkı sağlamaktadır. Sağlık personelinin özelliklerinin ve beklentilerinin bilmek ve kurumca karşılamak onları doyuma ulaşmaktadırlar (8). Fakat doyum tek başına bireylerin daha yüksek performans göstermelerini teşvik etmeyebilir (9). Doyumun yanında gönüllülük de esastır. Bireylerin iletişime gönüllü olmaları onların hem sosyal yaşamına etki eden hem de toplum içindeki yerini belirleyen önemli bir faktördür. Doğru ve etkili bir iletişimin gerçekleşmesi için bireylerin birbirlerini anlaması ve ardından da istenen yönde anlaşması gerekmektedir. Böylece bireyler arasındaki iletişim ne kadar güvenli ve iyi olursa onların kişisel mutluluğu da o oranda yüksek olur (3). İletişime gönüllü hemşirelerin kurumu daha çok benimsemeleri ve verimliliklerinin artması gönüllü olmayanlara göre daha fazladır (10). İletişime gönüllü hemşireler bireylerin iletişim kurmada yaşadıkları korku, utanma, çekinme, kaygı gibi duyguları yenmelerini sağlamaktadır (3). İletişim doyumları yüksek ve gönüllü olan hemşireler birey ve topluma sunduğu sağlık hizmetlerinde daha etkili olacaklardır (10). Ülkemizde ve Dünyada, günümüzde sağlık hizmetleri kapsamının genişlemesi sebebiyle kaliteli, verimli ve tatmin edici iş gücü gereksinimi artmıştır. Bu gereksinimlerin sağlanmasında genel anlamda da tüm yaşam demek olan iletişim faktörünün rolü büyüktür. Sağlık hizmetlerinin belkemiğini oluşturan hemşirelik mesleği üyeleri çalışma koşullarındaki meslekte yetersizlik, fazla iş yükü, hemşire sayısına oranla hasta sayısındaki artış gibi sıkıntılar sağlık bakım hizmetini etkilemektedir. Çalışmalar incelendiğinde hemşirelerin aynı problemleri yaşadıkları görülmüştür. Ülkemizde giderek artmakta olan iletişim probleminin sağlık alanındaki hemşirelerin iletişime ne kadar gönüllü olduklarını saptamak ve iletişim doyumlarını belirlemek ve incelenmek amaçlanmaktadır.

GEREÇ VE YÖNTEM

Bu araştırma; Aile Sağlığı ve Toplum Sağlığı Merkezleri'nde görev yapan hemşirelerin iletişime gönüllülük ve iletişim doyumlarının belirlenmesi amacıyla tanımlayıcı olarak yapılmıştır. Çalışmanın evreni Nisan 2019 ve Haziran 2019 tarihleri arasında, ana kütlesini Türkiye' nin doğusunda merkez ilçelerindeki ASM ve TSM'lerde çalışan 100 hemşire oluşturmaktadır. Bu ana kütleden %95'lik güvenilirlik sınırları içerisinde %5'lik bir hata büyüklüğü öngörülerek örneklem büyüklüğü 80 kişi olarak hesaplanmasına rağmen 95 kişiye ulaşılmıştır. Bununla birlikte bazı hemşirelerin cevap veremeyeceği ve olası cevaplama hataları dikkate alınarak 95 hemşireye anket formları dağıtılmıştır. 95 hemşirenin dahil edilme nedenleri ise; hemşirelerden 2'si yıllık izinde, 1'i ölüm izninde 2'si de süt izninde olduğunun tespit edilmesidir. Araştırmaya katılım oranı %95'dir. Verilerin toplanmasında anket tekniğinden yararlanılmıştır. Bu çalışmada değişkenler, sağlık alanında iletişim, hemşirelerin iletişime gönüllülük durumları ve iş doyumlarının belirlenmesi konularına dayanan geniş literatür taramasından sonra oluşturulan bir anket ve iki ölçekten oluşan veri toplama araçları ile ölçülmüştür. Veri toplama aracı olarak; "Sosyodemoğrafik Bilgi Formu", "İletişim Gönüllülük Ölçeği" ve "İletişim Doyum Ölçeği" yararlanılmıştır. Araştırmacı tarafından hazırlanan hemşirelerin tanıtıcı özelliklerini içeren 14 sorudan oluşan "Sosyodemoğrafik Bilgi Formu" anketi verileri genel anlamda; yaş, cinsiyet, medenidurum,

eğitimdurumu, meslek, çalışma süresi gibi sorulardan oluşmaktadır. Diğer bir ölçek ise, 1992 yılında James J.Croskey tarafından geliştirilmiş olan ölçeğin Türkiye'de geçerlik ve güvenirlik çalışması, 2016 yılında Karadağ, Ş. Kaya D, Uludağ A tarafından yapılan "İletişim Gönüllülük Ölçeği" isimli Likert ölçeğidir. Bu ölçekte katılımcılar sorulara 0 – Asla, 100 – daima puan aralığında kendilerini değerlendirerek cevaplandırırlar. İletişime gönüllülük ölçeği (İGÖ) toplam 20 maddeden oluşmaktadır. Bu maddelerden 8'i doldurucu, 12'si ise ölçeğin kendisini oluşturmaktadır. İGÖ puanlama sistemi bir toplam puan ve 7 alt puandan oluşmaktadır. Alt puanlar 4 iletişim koşulundan ve 3 tip örneklemin iletişimde gönüllülüğü ile ilgilidir. Ölçekten alınabilecek en düşük puan 0, en yüksek puan ise 100'dür. Diğer ölçek olan 1977 yılında Downs ve Hazen tarafından geliştirilen 25 sorudan oluşan "İletişim Doyum Ölçeği" Türkçe uyarlaması Bal (2013) tarafından hemşireler üzerinde yapılmıştır. Ölçek; İletişim İklimi, Üstle İletişim, Yatay İletişim, Kurum Bilgisi, Bireysel Geri Bildirim olmak üzere 5 alt boyuttan oluşmaktadır. Yüksek olması iletişime gönüllülüğünün yüksek olduğunu göstermektedir. İDÖ'de her sorunun puanı 1 ila 5 arasında değişmekte olup soruların tamamı düz puanlanmaktadır. Her biri 5 sorudan oluşan alt boyutlarda toplam puan; 5 ila 25 arasında değişmektedir. Ölçekte toplam puan; 25 ila 125 arasında değişebilmektedir. Toplam puanın yüksekliği, bireyin çalışma ortamındaki iletişim doyumunun yüksek olduğunu ifade etmektedir. Sadece araştırmacı tarafından kullanılacaktır. Araştırma da Nisan 2019 ve Haziran 2019 tarihleri arasında Erzurum merkez ilçelerindeki Aile Sağlığı ve Toplum Sağlığı Merkezi'nde çalışan hemşireler ele alınacaktır. Hemşirelerden formları sorularda belirtilen durumlarda iletişime gönüllülük düzeylerini değerlendirerek doldurmaları istenmiştir. Verilen cevaplar tümüyle katılımcıların kişisel beyanlarına dayanmaktadır. İletişim Gönüllülük Ölçeği'nin geliştiricisi olan James J.Croskey 2012 yılında vefat etmiştir. Ancak çalışmaları kendi adına oluşturulan web sitesi üzerinden araştırmacıların kullanımına açılmıştır. Çalışma için Ölçek için çalışmacılardan gerekli izinler alınmıştır. Ayrıca Atatürk Üniversitesi Sağlık Bilimleri Enstitüsü'nden etik kurul izni alınarak yapılmıştır. Katılımcılar için Halk Sağlığı Kurumu'ndan da gerekli izinler ve katılımcılardan da bilgilendirilmiş onam alınmıştır. Verilerin analizinde; SPSS 15.0 for Windows programı, frekans ve yüzde, ortalama ve standart sapma , t testi, Tek Yönlü Varyans Analizi, Kruskal Wallis, Mann Whitney U testi, Cronbach alfa güvenilirlik analizi kullanılmıştır. Anket formlarının Cronbach Alpha güvenirlik katsayısı İletişime Gönüllülük Ölçeğinde ,93 ve İletişim Doyum Ölçeğinde ise ,86 olarak bulunmuştur. Cronbach Alfa katsayısının değerlendirilmesinde uyulan kriterlere göre bu veri, anketlerin oldukça güvenilir olduğunu göstermektedir.

Araştırmanın Sınırlılıkları

Araştırma, il merkez ilçelerindeki Aile Sağlığı ve Toplum Sağlığı Merkezi'nde çalışan hemşirelerle sınırlı olduğundan sonuçlar buralara genellenebilir. Araştırmaya aşağıda belirtilen kriterlere uyan bireyler alınmıştır.

- Aile Sağlığı Merkezi ve Toplum Sağlığı Merkez'lerinde hemşire olarak çalışan ,
- İletişim ve mental sorunu olmayan,
- Türkçe konuşabilen, okuyabilen ve yazabilen,
- Araştırmaya katılmayı kabul eden bireyler, olarak belirlendi.

BULGULAR

Sosyo-demografik özelliklere ilişkin bulgular

Araştırmaya katılan hemşirelerden toplanan verilerin değerlendirilmesi sonucu aşağıdaki bulgular elde edilmiştir. Çalışmamıza katılan 95 hemşirenin %100'ü kadın, %63.2'si evlidir. Ankete katılan hemşirelerin %40'ının lisans mezunu olduğu ve genel eğitim durumuna oranla daha az olan %3.2 'lik bireylerin ise yüksek lisans yapmış olduğu sonucuna varılmıştır. Araştırmamıza katılan hemşirelerin yaş ortalaması 29,63±7.16 olarak tespit edilmiştir. Katılımcıların meslekte ortalama 8,76±6.83 yıldır çalıştıkları ve son bir yılda %31,6 oranında çalıştıkları işten ayrılmayı düşündüklerini belirtmişlerdir. Hemşirelerin %72,6 'sı ASM'de çalışmaktadır. Hemşirelerin Sosyo-Demografik özellikleri **Tablo 1**'de özetlenmiştir.

Tablo 1: Araştırmaya Katılan Hemşirelerin Sosyo-Demografik ve Mesleki Özelliklerinin Dağılımı (N= 95)

	Ort	SS
Yaş	29.63	7.16
Meslekte Toplam Çalışma Yılı	8.76	6.83
	N	%
Medeni Durum		
Evli	60	63.2
Bekar	35	36.8
Eğitim Durumu		
Lise	30	31.6
Önlisans	24	25.3
Lisans	38	40.0
Y. Lisans ve üstü	3	3.2
Bulunduğunuz kurumdan ayrılmayı düşündünüz mü?		
Evet	30	31.6
Hayır	65	68.4
Çalışılan birim		
ASM	69	72.6
TSM	26	27.4

İletişim gönüllülük ölçeğine baktığımızda hemşirelerin ölçek alt boyutu olan tanıdık ve arkadaşlarla konuşmak 30.99 ± 20.66 ile ortalama olarak en düşük olarak bulunmuştur. Ölçek toplam puanına baktığımızda 100 üzerinden ortalama değer olarak 50.08 ± 20.07 olduğu saptanmıştır. Bu sonuç hemşirelerin iletişim gönüllülüklerinin orta düzeyde olduğunu göstermektedir (**Tablo 2**).

Hemşirelerin İletişim Doyumu Ölçeğinde "Üstle İletişim" alt boyutu puan ortalaması 19,01 ± 3.77 olarak en fazla iletişim doyumu sağladıklarını en az ise 15.04 ± 3.02 ortalaması ile çalıştıkları kurumun iletişim ikliminin olduğunu belirtmişlerdir (**Tablo 2**).

Tablo 2: ASM ve TSM'de çalışan Çalışan Hemşirelerin İletişime Gönüllülük Ölçeği ile İletişim Doyum Ölçeği Alt Boyutlarından Aldıkları Puanlar ve Standart Sapmaları (N= 95)

Ölçekler	Alt Boyutlar	Ort.	SS
İletişime gönüllülük Ölçeği	Tanıdık ve arkadaş gruplarına sunum yapmak	50.94	20.23
	Yabancılarla konuşmak	40.83	20.32
	Tanıdık ve arkadaşlarla konuşmak	30.99	20.66
	Toplam	50.08	20.07
İletişim Doyum Ölçeği	İletişim İklimi	15.04	3.02
	Yatay İletişim(Resmi olmayan iletişim)	17.96	2.24
	Üstle İletişim	19.01	3.77
	Kurum Bilgisi	17.62	2.74
	Bireysel Geribildirim (Kendi performansı)	17.64	3.72
	Toplam	95.46	12.46

Hemşirelerin iletişime gönüllülük ölçeği ile iletişim doyum ölçeği alt boyutları ve toplam puanları arasındaki ilişkiye baktığımızda; çalışılan kurumun iletişim iklimi ($p<0,05$), tanıdık ve arkadaş gruplarına sunum yapmak ($p<0.05$), tanıdıklarla konuşmak ($p<0,05$), iletişime gönüllülük toplam puanı ($p<0,05$) arasında istatistiksel olarak anlamlı bir ilişki olduğu saptanmıştır (**Tablo 3**).

Ayrıca, İletişim doyumu alt boyutu bireysel geribildirim alt boyutu ile iletişime gönüllülük ölçeği alt boyutları yabancılarla konuşmak ($p< 0,01$), tanıdık arkadaşlarla konuşmak ($p<0,01$) ve toplam puan ($p<0,05$) arasında istatistiksel olarak anlamlı pozitif ilişki saptanmıştır (**Tablo 3**).

İletişim doyum ölçeği toplam puan ve iletişime gönüllülük ölçeği alt boyutları arasında yabancılarla konuşmak ($p<0,05$)tanıdıkla konuşmak($p<0,01$) arasında istatistiksel olarak ilişki saptanmıştır (**Tablo 3**).

Tablo 3'te görüldüğü gibi; her iki ölçek ve alt boyutları arasında pozitif yönde ve anlamlı ilişki olduğu tespit edildi ($p<0.013$).

TARTIŞMA

Bu araştırmada; sağlık alanında çalışan hemşirelerin iletişime gönüllülük durumları ile iletişim doyumları arasında bir ilişkinin var olup olmadığını saptamak amaçlanmıştır. Analizler sonucunda, araştırmaya katılan hemşirelerin iletişime gönüllülükleri ile çalıştıkları kurumdaki iletişim doyumları arasında anlamlı ve benzer doğrultuda bir ilişkiye sahip oldukları görülmüştür. Farklı bir ifadeyle hemşirelerin iletişime gönüllülükteki artış/azalış, katılımcıların iş doyumunu artırıp azaltmaktadır (1).

Hemşirelerin %68,4'ü son 1 yılda işten ayrılmayı düşünmemeleri, hemşirelerin mesleğe bağlılığının orta düzeyde olduğunu göstermektedir (**Tablo 1**). Korkmaz ve Görgülü'nün (2010) çalışmasında hemşirelerin %70.0'nin işten ayrılmayı düşünmedikleri bulunmuştur ve bu düşüncelerinin başlıca nedeni olarak da hemşireliği sevdiğini (%70.7) ifade etmişlerdir (11).

İletişim gönüllülük ölçeği toplam puana bakıldığında 100 üzerinden ortalama değer olarak (50,08±20.07) olduğu saptanmıştır. Bu da hemşirelerin iletişim gönüllülüklerinin orta düzeyde olduğunu göstermektedir. Baysal (2014) tarafından sağlık çalışanları üzerinde yapılan çalışmada sağlık işletmelerinde yaşanan iletişim problemlerinin tespit edilmesi amaçlanmış ve sağlık çalışanlarının yaklaşık yarısının daha önce hasta veya yakınıyla olumsuz iletişime girdiği, çoğu hasta yakınının sağlık personeline kötü ve çok kötü tepki verdiklerini belirtmişlerdir (12). Hemşirelerin iletişim doyum ölçeğinde alt boyut puan ortalaması en az 15.04±3.02 çalıştıkları kurumdaki iletişim iklimi olduğu bulunmuştur. Bu sonuç Öztürk ve Babacan'ın çalışmasını desteklemektedir. Öztürk ve Babacan (2014) tarafından sağlık personelleri ve hastalar üzerinde yapılan çalışmada sağlık personelinin çoğunluğu, hastaların ise çok az bir kısmı sağlık personeline sözlü olarak şiddet uygulandığını belirtmiştir. Bu şiddetin sebebinin de ana

Tablo 3: Aile Sağlığı ve Toplum Sağlığı Merkezinde Çalışan Hemşirelerin İletişime Gönüllülük Ölçeği ve İletişim Doyum Ölçeği Alt Boyutları Arasındaki İlişki (N=95)

			İletişime Gönüllülük Ölçeği Alt Boyutları			İletişime gönüllülük Ölçeği Toplam
			Tanıdık ve arkadaş gruplarına sunum yapmak	Yabancılarla konuşmak	Tanıdık ve arkadaşlarla konuşmak	
İletişim Doyumu Ölçeği alt Boyutları	İletişim İklimi	r	,227*	.185	.224*	.242
		p	.027	.073	.029	.018
	Yatay İletişim	r	-.069	.054	.056	.007
		p	.507	.603	.593	.946
	Üstle İletişim	r	.140	.076	.135	.134
		p	.175	.467	.192	.194
	Kurum Bilgisi	r	.162	.167	.173	.190
		p	.117	.107	.094	.065
	Bireysel Geribildirim	r	.158	.261*	.291**	,261*
		p	.127	.011	.004	.011
İletişim Doyumu Ölçeği Toplam			.178 085	.236* .021	.267** .009	.253* .013

kaynağının sistem olduğuna (bekleme süresi, kişilerin sabırsızlanmaya başlaması gibi) vurgu yapılmıştır. Bu iki çalışmanın bulgularına baktığımızda hemşirelerin iletişim doyumu çeşitli sebeplerden dolayı etkilenebilmektedir (13).

Hemşirelerin iletişim doyumları (95.46±12.46) yüksek olduğu saptandı.. Mart'ın (2014) çalışmasında da hemşirelerin iletişim doyumu iyi düzeyde (82.67±16.46) bulunmuştur. Hemşirelik mesleğinin doğasında iletişime dayalı olması ve hem ekip arkadaşlarının hem de hasta profilinin iletişiminin iyi olması bunu etkileyebilir (**Tablo 2**) (14).

İletişim Doyum Ölçeği alt boyutu Bireysel geri bildirim ile iletişime gönüllülük ölçeği alt boyutları yabancılarla konuşmak ($p<0.01$), tanıdık arkadaşlarla konuşmak ($p<0.01$) ve iletişime gönüllülük toplam puan ($p<0.05$) arasında istatistiksel olarak pozitif yönde anlamlı bir ilişki bulunmuştur. Kim ve diğerleri (2008) tarafından yapılan çalışmada iletişimde başarılı olan hemşirelerin iletişimde etkili olmaya çalıştığı, iş arkadaşlarından gelen geri bildirimlere dikkat ettiği ve kendilerini bu şekilde motive ettikleri saptanmıştır (15).

Hemşirelerin iletişim doyum ölçeğinde alt boyut puan ortalaması en fazla 19,01±3.77 üstle iletişim olduğu bulunmuştur. Çıtak ve diğerleri (2011) tarafından yapılan çalışmada ise bu çalışmadaki bulguların tam tersi olan iletişim sıkıntısının temel noktasının yönetimin problem çözemediği ve bununla birlikte yönetime güvenmemesi olduğu ortaya çıkmıştır. Genel olarak araştırmaya katılan hemşirelerin orta düzeyde iletişime gönüllü oldukları fakat çalıştıkları kurumdaki iletişim doyumlarının yüksek olduğu saptanmıştır (16).

SONUÇ

Çalışmanın sonucunda; evrenin tamamını oluşturan hemşirelerin kadın; çoğunun genç yaş grubunda, bulundukları kurumdan ayrılmayı düşünmeyen, orta derecede iletişime gönüllü ve çalıştıkları kurumdaki iletişim doyumlarının yüksek olduğu bulunmuştur. Hemşirelerde iletişim doyumu ve iletişim gönüllülüğü arasında pozitif ilişki bulunmuştur.

Daha sonraki araştırmalarda iletişim doyumu ve iletişime gönüllülük değişkenleri dikkate alınarak çalışmamızda örneklem olarak seçtiğimiz hemşirelerin yerine farklı kamu kuruluşlarında çalışan bireyler alınabilir. Bu sayede farklı alanlardaki bireylerin iletişim gönüllülükleri ve iletişim doyumları karşılaştırılarak literatüre yeni kaynak sağlanmış olabilir. Kişilerarası ve çevresel iletişim sorunlarının çözülerek iletişimdeki mevcut doyumun ve gönüllülüğün korunması, hatta daha da güçlendirilmesi önerilmektedir.

ETİK BEYANLAR

Etik Kurul Onayı: Atatürk Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurul Başkanlığından 2019 etik izin alınmıştır.

Aydınlatılmış Onam: Çalışma retrospektif olarak dizayn edildiği için hastalardan aydınlatılmış onam alınmamıştır.

Hakem Değerlendirme Süreci: Harici çift kör hakem değerlendirmesi.

Çıkar Çatışması Durumu: Yazarlar bu çalışmada herhangi bir çıkara dayalı ilişki olmadığını beyan etmişlerdir.

Finansal Destek: Yazarlar bu çalışmada finansal destek almadıklarını beyan etmişlerdir.

Yazar Katkıları: Yazarların tümü; makalenin tasarımına, yürütülmesine, analizine katıldığını ve son sürümünü onayladıklarını beyan etmişlerdir.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

A Questionnaire-Based Study to Evaluate the Benefits of Summer Internships for Anesthesia Technician Intern Training in Turkey: Internship Programme of Anaesthesia Technicians

Türkiye'de Anestezi Teknisyen/Teknikerlerinin Stajyer Eğitimi İçin Yaz Stajının Faydalarının Değerlendirilmesine Yönelik Anket Tabanlı Bir Çalışma: Anestezi Teknisyen/Teknikerlerinin Staj Programı

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ABSTRACT

Aim: Quality training of anesthesia technicians must be high. To provide this crucial high quality, summer internship programs are important. This questionnaire-based study aimed to evaluate the benefits of summer internships for anesthesia technician intern training in Turkey.

Material and Method: The study was approved by the ethical committee. An internet questionnaire on Google docs was formed containing participants' demography data, internship applications and their observations. Finding standard questionnaire to investigate technicians' training is difficult; we create a form to investigate our purpose. The descriptive and cross-sectional study included anesthesia technician students and graduates who did summer internships in Turkiye. Questionnaire was replied by 1,179 technicians.

Results: The average age is 23 ± 4.87 years. 84.4% of the participants are women and 77.8% work for 0-1 year. Only 89.2% of the participants did an internship, and 97.8% thought that a summer internship was necessary. Essentials trainings like intubation (39.1%) and monitoring (15.5%) were never performed by nearly half of the technicians. The preparation of alternative airway devices was the least performed application (0.3%). As other applications were in low percentages, these findings could not be accepted as success.

Conclusion: In literature, to our knowledge, there isn't a standard evaluation scale for anesthesia technician training. Thus, we could not define success or failure of internships precisely. However and because of lacking applications in various percentages, we speculate that it is difficult to explain internships as success. To solve this problem, success criteria and "critical numbers" for "training success" must be validated.

Keywords: Nurse Anesthetists, internship, professional practice

ÖZ

Amaç: Anestezi tekniker/teknisyenlerinin eğitim kalitelileri yüksek olmalıdır. Bu çok önemli yüksek kaliteyi sağlamak için yaz stajı programları önemlidir. Ankete dayalı bu çalışma, Türkiye'de anestezi teknisyeni stajyer eğitimi için yaz stajının faydalarını değerlendirmeyi amaçladı.

Gereç ve Yöntem: Çalışma etik kurul tarafından onaylandı. Katılımcıların demografi verilerini, staj başvurularını ve gözlemlerini içeren Google docs üzerinden internet anketi oluşturulmuştur. Teknisyenlerin eğitimini araştırmak için standart anket bulmak zordur; amacımızı araştırmak için form oluşturduk. Tanımlayıcı ve kesitsel tipteki çalışmaya Türkiye'de yaz stajı yapan anestezi teknisyenliği öğrencileri ve mezunları dahil edilmiştir. Anket 1.079 teknisyen tarafından yanıtlanmıştır.

Bulgular: Yaş ortalaması 23 ± 4,87'dir. Katılımcıların %84,4'ü kadın ve %77,8'i 0-1 yıl çalışıyor. Katılımcıların sadece %89,2'si staj yapmıştı ve %97,8'i yaz stajının gerekli olduğunu düşünmekte. Entübasyon (%39,1) ve monitörizasyon (%15,5) gibi temel eğitimler teknisyenlerin yaklaşık yarısı tarafından hiç uygulanmadı. Alternatif hava yolu cihazlarının hazırlanması en az yapılan uygulama (%0,3) idi. Diğer başvurular düşük oranlarda olduğu için bu bulgular başarı olarak kabul edilememiştir.

Sonuç: Literatürde bilgimize göre anestezi teknisyenliği eğitimi için standart bir değerlendirme ölçeği bulunmamaktadır. Bu nedenle stajların başarısını veya başarısızlığını tam olarak tanımlayamadık. Ancak çeşitli oranlarda eksik uygulama olması nedeniyle stajları başarı olarak açıklamanın zor olduğunu düşünüyoruz. Bu sorunu çözmek için başarı kriterleri ve "eğitim başarısı" için "kritik sayılar" doğrulanmalıdır.

Anahtar Kelimeler: Hemşire Anestezist, anestezi teknisyen/teknikerleri. staj, mesleki uygulama

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INTRODUCTION

Vocational colleges must be one of the practical educational institutions in reaching the knowledge required for professional expectations. These associate degree schools and colleges are educational institutions that train qualified human resources for different business sectors such as health. They play a significant role in developing personal abilities and skills, especially with practical training for health care providers other than doctors.

Vocational associate degree schools of health services have been established in higher education in Turkiye since 1983 (1). Those who graduated from the anesthesia department of health high schools and those who graduated from the anesthesiology associate degree programs of Health Services Vocational Schools are authorized as technical staff assisting the anesthetists in the induction, maintenance, and emergence of anesthesia. (2). All the technical staff is supposed to have sufficient pharmacological knowledge, the ability to use multiple materials, and the management of multiple tasks regarding the vital importance of anesthesia procedures. Also, expectations include it is necessary to have good working in harmony as a team and have a good sense of responsibility (3,4). Internship programs are indispensable to accomplish these goals however, to our knowledge, detailed evaluations of training effectiveness has not been investigated in Turkiye.

This questionnaire-based study aimed to evaluate the benefits of summer internships for anesthesia technician intern training in Turkey.

Also, we aimed to define, if possible, the term "Minimum Number of Practices" as the mean of setting a standard that could be useful throughout the country for consistent training practice.

MATERIAL AND METHOD

Study Design

The study is a descriptive and cross-sectional study. Ethical approval was obtained from the Ethics Commission of our hospital. The questionnaire method was preferred in order to reach all anesthesia staff. Therefore, randomization was based on participations of technicians. The survey form was prepared on "Google docs" form, and the form was reached through social media platforms or e-mail. Design of the study and purpose was described in the introduction section of questionnaire, and highlighted that filling the questionnaire would be accepted as consent to participation of the study. Gender, age, education degree, work time, satisfaction, sufficiency, relevancy factors, night shift internships and working stations were asked. Also applications that they were involved in their internships were asked.

Participation

By making power analysis, a sample group of 382 people is predicted with a confidence interval of 95%, with a margin of error of 0.05. As the study was the very first of its kind, it attracted a lot of attention, so 1123 men and women responded to the call for the questionnaire.

Inclusion-Exclusion Criteria

When participants evaluated, 44 people who were neither anesthesia technicians nor students were excluded. A total of 1079 people were included in the study. There were other exclusion or inclusion criteria.

Data Evaluation and Statistics

There were no standard types of evaluations for anesthesia technicians' training. So, we designed a form that could widely consist the desires of technicians in. As all the participants were in the study, there was no control group. Because of this reason statistic will not meet the need of the study. Also, as there is not any standard evaluation method, comparison with similar studies becomes sophisticated. Therefore the study determined the participants circumstances to be functional data for further studies.

RESULTS

Participants

The distribution of the participants on the sociodemographic structure is shown in (**Table 1**). There were 911 women participated in the survey. Most participants (n=971, (90%)) have associate degrees. Also, most (n=840) are in their first year of the profession.

Table 1. Demography of participants

	n	%
Gender		
Male	168	15.6
Female	911	84.4
Age		
0 - 21 years	509	47.2
22 - 29 years	473	43.8
30 years and above	97	9.0
Profession Education Degree		
Health Vocation School	21	1.9
Associate Degree	971	90.0
Bachelor graduate	82	7.6
Graduate	5	0.5
Work time in profession		
0 - 1 year	840	77.8
2 - 3 years	111	10.3
4 - 5 years	29	2.7
6 years and above	99	9.2

Participant Opinions on Internship

Opinions for summer internship efficacy were demonstrated in (**Table 2**). Most participants (n=963) (89.2%) succeeded in their internship. The satisfaction rate slightly decreases among these participants (84.8%). Training in internships was found insufficient in 46.4%. They primarily defined (52%) that being temporary interns was the main reason for insufficient training.

Unfortunately, 6.2% of them worked on irrelevant sections during the internship.

Table 2. Evaluations of the participants for summer internship

	n	%
Did you satisfy? (n=968)		
Yes	813	84.8
No	145	15.2
Was it sufficient?		
Not replied	17	1.6
Sufficient	316	29.3
Must be longer	731	67.7
Must be shorter	15	1.4
Did you have night shift?		
Not replied	16	1.5
Yes	767	71.1
No	296	27.4
What does summer internship mean to you?		
Getting close to profession	830	76.9
Comparison lectures and practice	798	74.0
Cliche to be graduate	158	14.6
Mandatory in curriculum	173	16.0
Who supervised your internship?		
Anesthesia technicians/technicians	914	84.7
Anesthesia Lecturer	145	13.4
Anesthesia Resident	192	17.8
Anesthesia Consultant	505	46.8
Vocational School Directors or Deputies	87	8.1
Were practices enough in internship? (n=960)		
Sufficient	515	53.6
Not Sufficient	445	46.4
If not sufficient, why?		
Workload	431	39.9
Staffs' behaviors interns as temporary worker	561	52.0
Being ignored	483	44.8
Behaving interns as untrusted staff	519	48.1
Even staff has insufficient practice	86	8.0
Seeing interns as unskilled labor	425	39.4
In which unit you worked?		
Preoperative Preparation Unit	375	34.8
Operating Theatre	925	85.7
Anesthesia stockroom and archives	189	17.5
Postoperative recovery room	469	43.5
Intensive Care Unit	75	7.0
Patient Referral and Transport	68	6.3
Algology	33	3.1
Non-operating room Anesthesia	262	24.3
Emergency and Blue Code Management	94	8.7
Did you work in an irrelevant unit? (n=947)		
Yes	67	6.2
No	880	81.6

Applications Attendances

The number of applications made by the participants during their summer internship is shown in (**Table 3**). There were a significant percentage of participants that did not perform different applications. The group of participants that "Never Did Applications" was remarkable, and 15 to 81 per cents of the total group did not attend those applications (**Table 3**). These applications are all essential to be performed, so the numbers of "never did applications" are discouraging.

DISCUSSION

In this study, efficacy of the training program in our country was investigated. Participants mostly (84.3%) defined the internship training satisfying. However, most of them found internships insufficient (70.7%).Participants also gave details about reasons of insufficiency such as permanent staff behavior against interns (52.0%), being targeted as untrusted person(48.1%). Also, in the study, we investigated attendance of interns to applications. Among 12 applications replies about "Never did" are concerning because the least "never did"s were 17.7% and the most "never did"s were 81.3%. It is hard to conclude these results as training success because of few data, however it could be speculated that individual training is important so we accepted the result discouraging. Anesthesia workload is one of the complex, dynamic and time dependent burdens for its staff (4). In addition to hard conditions, number of anesthetists to succeed all these workload is short. For example, in Ethiopia very few anesthetists are serving in the country compared to total population (3). There are only 258 anesthetists for 80 million populations (3). Anesthetists' shortage forces governments to take precautions (3). As many countries do, the best path to solve this problem is recruiting mid-level educated anesthesia technicians (3). However, in some instances, roles of anesthesia technicians are underestimated, and, even their clinical training hours were not reported as it is done for anesthesiologists (5).

Table-3. Number of summer internship application of participants

Application Name/ n(%)	Never Did	1 -19 applications	20 - 59 applications	60 and above applications
Monitoring	167 (15.5)	145 (13.4)	428 (19.6)	339 (31.4)
Intravenous Catheter	191 (17.7)	445 (41.2)	326 (15.1)	117 (10.8)
General Anesthesia Preparation	176 (16.3)	223 (20.7)	447 (20.2)	233 (21.6)
Regional Anesthesia Preparation	345 (32.0)	375 (34.8)	299 (14.3)	60 (5.6)
Airway Application	266 (24.7)	466 (43.2)	285 (12.4)	92 (8.5)
Mask Ventilation	189 (17.5)	475 (44.0)	304 (13.5)	111 (10.3)
LMA Application	502 (46.5)	458 (42.4)	106 (4.4)	13 (1.2)
Alternative Airway Devices	877 (81.3)	174 (16.1)	25 (1.3)	3 (0.3)
Tracheal Intubation	422 (39.1)	463 (42.9)	144 (7.7)	50 (4.6)
Orogastric Application	537 (49.8)	396 (36.7)	118 (5.3)	28 (2.6)
Infusion Pomp Preparation	523 (48.5)	372 (34.5)	141 (6.7)	43 (4.0)
Suction	260 (24.1)	434 (40.2)	270 (12.5)	115 (10.7)

LMA: Laryngeal Mask Airway

Anesthesia technician training started towards the end of the 1800s (6).In the modern sense, anesthesia technician education started in the 1970s (6). Our country's term anesthesia technician is equivalent to "Anesthesia Nurses" in different countries (7, 8). It is stated that with the curriculum applied at the University of Pittsburgh, anesthesia technicians are given 120 hours of simulation training, at least 800 case training, and more than 2000 hours of training on documents (6). This training is stated to be 36 months (6). Like anesthesia nurses' education programs, anesthesia technicians have education programs usually constructed on a 24-month curriculum. Also, Turkiye's total time for associate degree training is 24 months.

In the evolution of anesthesia technician education, cooperation between professional groups is increasing (9). The increase in morbidity and mortality in perioperative or acute care requirements was why health provider groups cooperate (9). So it is realized that within this period of evolution, the only aim is not to increase knowledge and skills but also to strengthen joint harmonious work (9). As a result, over time, the duties of the anesthesia support units have gained a hybrid feature as both direct patient care and taking the necessary measures to provide anesthesia (10).

The current role of clinical educators is essential training of anesthesia technicians (11). Consequently, internship applications are applied mainly in summer periods, as we do, or various types of time schedules are used for a half-day for one month (9). Studies show that technician trainees who participate in such training benefit from every aspect (9).

However, standardization failures of education and training programs threaten anesthesia technicians. A study stated that there are 22 different education models in Africa (12). In a study completed in 2013 about the education levels of anesthesia technicians, especially in Ethiopia, it was found that the education level was not good (12). A study conducted in China in 2022 stated that there is no standard practice regarding anesthesia technicians (13). It is said that the basis of the training content and duration needs to be clarified (13). For this, it was stated that after the International Federation of Nurse Anesthetists standards were established in China; the Nanjing Health Commission was assigned to standardize education throughout the country (13). In the 10-year study conducted with this method, it was stated that although anesthesia technician practices have progressed, a significant number of anesthesia technicians need new training (13).

In our country, according to the law named "Regulation on Principles and Procedures Regarding Practices and Internships," it is determined as "The internship period will start at the beginning of July and continue for a minimum of 30 and a maximum of 60 working days as a summer internship". However, in the Turkish Republic Presidential Internship Mobilization Implementation Directive, it is recommended that the internship period be at least twenty working days within the scope of the internship mobilization project. In the practices of universities, it is seen that different periods are applied especially after the COVID-19 Pandemic. Similar to our curriculum, it was reported that some other summer internship was completed in 30 days (14).

In the literature, efficacy assessments of internship curricula are few. The reason for rare reports might be because of used terms like "other health personnel," which meant that there were no specific determinations for professional branches and evaluating health providers, including anesthesia technicians, under a simple name. In this study, we specifically studied anesthesia technicians.

We found that most anesthesia technicians participate in the summer internship practice. Although summer internship is compulsory to graduate from the vocational school of health, face-to-face training was suspended due to the COVID-19 Pandemic in 2021 and many practical pieces of training, including internships, were discontinuous. For this reason, universities performed document training instead of internship requirements. In our study, participants had their internships not suspended.

The question for the necessity of an internship responded as "Necessary" in our study, as in the literature (14-16). Internship training is an essential practice for students to have the opportunity to practice. Clinical experiences have essential effects on the awareness of anesthesia technicians, critical thinking, psychomotor efficiency, and professionalism (17). When there is compliance with Clinical trainers, education is satisfactory. Still, problems such as non-continuous feedback and evaluation, indifference, poor perception of education skills, limited perception of education, inappropriate communication, and intimidation reduce the quality of education (17). Attitudes of clinical educators were found to be very important for forming students' educational experiences (17). What is expected from anesthesia technician students is not only to learn skills related to their profession but also to produce solutions to professional and ethical problems and uncertainties in areas such as the operating room (18). In terms of many anesthesia technician students, unethical behavior and lack of cooperation in the operating room were described as lacking moral trust (18). The training should be carried out in the determined equipped to service, school, or work environments (10).

In our study, the questionnaire also asked about the presence of "night shift" in summer internships. Two-thirds of them responded with "Yes." Most participants found shifts useful, and this entity is an expected

parameter. This may be because they can practice more. After all, there are fewer health personnel on night shifts.

The vast majority of respondents wrote that they had been satisfied with their internship program. Most of them stated the meaning of a summer internship as "Getting to know the profession closely," and a few stated it as "a formality to graduate." In contrast to these statements, nearly half of the participants stated that the information provided during the internship was insufficient, which could be considered unsatisfactory. Also, it was stated that the reason for this is the temporary workings of interns. Kepekci et al., when asked about the training of anesthesia technicians/technicians in their study with anesthesiologists, 60.6% of them reported that their training was insufficient (19). There is an inability to acquire sufficient skills due to inadequate practice in vocational schools. In the study of Delibaş L. et al., "lack of trust in interns" was stated as the reason for insufficient knowledge (15).

The majority of the participants answered the question about the location of internship as "Operating Room." Few participants did internships in pain rooms where "Algology" procedures, a sub-branch of anesthesia, are performed. Unfortunately, some participants stated that they did internships in places unrelated to anesthesia (blood taking, administrative work, et cetera.) which might be avoided in future practices.

In a study conducted in the USA, the work of anesthesia technicians is mainly in the direction of maintenance and follow-up of anesthesia devices and providing logistic support (20). It is also stated in the study that 67% of anesthesia technicians are responsible for machine maintenance as their primary task, while 35% perform tasks such as blood gas analysis (20). In training, it was stated that the best-learned procedure is executive intubation (12). For this reason, it has been stated that intubation practices on the manikin are related to their behavior (12). For this reason, the importance of doing these practices during internship periods has increased even more. Our study examined the rate of performing the 12 most basic applications in anesthesia during a summer internship. The most applied application was determined as "Monitoring," and the least was determined as "Alternative Airline Vehicle Application." Regular monitoring is the first step to starting anesthesia, and knowledge of monitoring is the cornerstone of anesthesia, so it is the most common practice of all trainees. At the same time, since monitoring is a non-invasive and harmless practice for the patient, it can be quickly done by the interns. However, even in this procedure, there is a discouraging percentage of the "never did" group in our study.

Tracheal intubation and Laryngeal Mask application are anesthesia's most commonly used airway control methods. Anesthesia technicians are mainly at the forefront of airway control. For this reason, the blue code system is usually created by anesthesia staff. Our study determined that almost half of the participants did not perform tracheal intubation and Laryngeal Mask application. These applications are vital since the airway of every patient who is administered general anesthesia must be kept under control. For this reason, the experience gained will help save the lives of many patients in the coming years, as much as possible, to apply in appropriate patients and situations.

With the developing technologies, the devices used in anesthesia are also changing daily. Infusion pumps, which ensure the delivery of liquids and drugs to patients at specified times, are among the most used devices in anesthesia. It has been reported that training is given according to age, anatomical regions, anesthesia methods, and vascular access practices (6). In the USA, while the drug preparation rate was 3%, arterial line placement is performed at a rate of 6% (20). Intravenous access is committed by only 14% of anesthesia technicians (20). However, it was stated that there was an increasing tendency in the evaluated group to take direct action and take responsibility for the patient (20). In our study, nearly half of the participants said they needed to prepare the infusion pump. Especially being close to technological devices and instruments increase the comfort of anesthesia. Therefore, working closely with these devices during internship periods is necessary.

We have limitations on evaluating the trainings of anesthesia technicians. On-the-job training for anesthesiologist is first-level preparation (20). Evaluating the quality of trainings can affect positively the education protocols. Asking trainees if "they liked" the internships, extent of their learning, the performances of trainers and effectively of the organizations will be helpful for policy makers (4). Nevertheless, trainers have deficiencies and differences regarding standardization and consistency of training processes (11). The most important reason for this is the problems related to the definition and standardization of the training items used(11). In order to provide this goal, councils and accreditation boards were usually established (11). These aforementioned insufficiencies are all present in our country.

-. Also formal education, however, is an education that requires time and resources and can always allow mistakes to be made (10). Another that has to be taken into account is preparing students for emotional, physical and psychological stresses (8). These factors were not evaluated which limited the studyfor basic problems in all over the world that has to be solved.

Also, there are rare studies evaluating education qualities. Therefore, we could not be able to compare our country circumstances with others. There are

studies, as mentioned in the manuscript, defining needs for anesthesia technician for countries but these studies did not fully cover our aim.

CONCLUSION

For students in Vocational Schools of Health, the most effective way to get to know the field and learn about their future profession is to do summer internships. When training programs were evaluated disappointing results could come up. In our country, we monitored training failures in various percentages To minimize non-practicing groups, sharing the objectives of the summer internship planned at the universities with the education supervisors in the institutions where the internship is held and preparing joint plans. It may be provided by increasing internship periods as much as possible, and the number of practicing parameters should be increased.

We, on the other hand, speculated that minimum number of applications during internships should be determined in all Health Vocational Schools in our country because the percentages and numbers of applications were lower than expected, especially for the most important ones. With the forms to be made, a certain standard should be provided. For this purpose, the internship of students who have made a certain number of applications can be considered successful, and the quality of practical training can be increased throughout the country.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Yozgat Bozok University Ethics Committee (Date: 24.06.2022 Decision No: 34/22).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Evaluation of the Relationship between Laboratory Parameters and Allergy Tests in Children with Atopic Dermatitis

Atopik Dermatit Tanılı Çocuklarda Laboratuvar Parametrelerinin Alerji Testleri ile İlişkisinin Değerlendirilmesi

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ABSTRACT

Aim: The aim of this study was to evaluate the relationship between neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), eosinophil lymphocyte ratio (ELR), serum total IgE values and allergy test positivity among children with atopic dermatitis (AD).

Material and Method: The study is a case-control type study in a retrospective design. Children aged 0-18 years with ADand applied to the pediatric allergy and immunology outpatient clinic of our hospital were included as the patient group. Children aged 0-18 years, who did not have any chronic diseases and applied to the pediatrics outpatient clinic of our hospital, were included as the control group. Children's sociodemographic characteristics, hemogram parameters, total IgE values, allergy history and allergy test positivity were evaluated. $p<0.05$ was accepted as the statistical significance level.

Results: The data of 193 children with AD were evaluated. 100 children were included as the control group. Eosinophil, lymphocyte, total IgE, ELR values were significantly higher in the patient group ($p<0.05$). The median values of PLR and ELR were higher in patients with allergy test positivity, but there was no statistical significance between the groups ($p=0.268$ and $p=0.251$, respectively). As the total IgE values were examined, the median total IgE value of the patients with a positive allergy test was 168.0 (2.0-6098.0), while this value was 37.0 (0-3577.0) in patients with a negative test ($p<0.001$).

Conclusion: Although there is no statistical significance, the fact that PLR and ELR values were higher in patients with AD with positive allergy test suggest that these values can be used as a marker to predict allergy test positivity. Evaluation of hemogram parameters, which is an easily accessible test among AD patients, is extremely important for physicians working in this field.

Keywords: Atopic dermatitis, children, allergy test, eosinophil lymphocyte ratio

ÖZ

Amaç: Bu çalışmanın amacı, atopik dermatitli (AD) çocuklarda nötrofil lenfosit oranı (NLO), trombosit lenfosit oranı (TLO), eozinofil lenfosit oranı (ELO) ve serum total IgE değerleri ile alerji testi pozitifliği arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Çalışma retrospektif dizaynda vaka kontrol tipi bir çalışmadır. Çalışmaya çocuk alerji ve immünoloji polikliniğine başvuran 0-18 yaş arası AD tanılı çocuklar dahil edildi. Kontrol grubu olarak hastanemiz çocuk polikliniğine başvuran, kronik hastalığı olmayan 0-18 yaş arası çocuklar alındı. Çocukların sosyodemografik özellikleri, hemogram parametreleri, total IgE değerleri, alerji öyküsü ve alerji testi pozitifliği değerlendirildi. $p<0,05$ istatistiksel anlamlılık düzeyi olarak kabul edildi.

Bulgular: Atopik dermatitli 193 çocuğun verileri değerlendirildi. Kontrol grubu olarak 100 çocuk dahil edildi. Eozinofil, lenfosit, total IgE, ELO değerleri hasta grubunda anlamlı olarak yüksekti ($p<0,05$). Alerji testi pozitif olan hastalarda ortanca TLO ve ELO değerleri daha yüksekti ancak gruplar arasında istatistiksel anlamlılık yoktu (sırasıyla $p=0,268$ ve $p=0,251$). Total IgE değerlerine bakıldığında alerji testi pozitif olan hastalarda ortanca total IgE değeri 168,0 (2,0-6098,0) iken, testi negatif olan hastalarda bu değer 37,0 (0-3577,0) bulundu ($p<0,001$).

Sonuç: İstatistiksel olarak anlamlı olmamakla birlikte, alerji testi pozitif olan atopik dermatitli hastalarda TLO ve ELO değerlerinin daha yüksek olması, bu değerlerin alerji testi pozitifliğini öngörmede bir belirteç olarak kullanılabileceğini düşündürmektedir. AD hastalarında kolaylıkla ulaşılabilen bir test olan hemogram parametrelerinin değerlendirilmesi bu alanda çalışan hekimler için son derece önemlidir.

Anahtar Kelimer: Atopik dermatit, çocuklar, alerji testi, eozinofil lenfosit oranı

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INTRODUCTION

Atopic dermatitis (AD) is the most common chronic inflammatory skin disease (1). AD is a recurrent and highly itchy dermatitis. Dryness of the skin, eczematous lesions and lichenification are also the clinical findings of AD (2). The prevalence of AD is increasing worldwide (3-5). Besides, the frequency of AD generally decreases with advancing age (6).

There is an impaired skin barrier in the pathophysiology of AD (7,8). Due to the disrupted skin barrier, irritants and allergens penetrate the skin. IL-4, IL-5, IL-12 cytokines and IFN-gamma are released through the overactive Th2 and Th1 response in acute and chronic lesions, respectively, due to the defective skin barrier. Thus, the inflammation process begins (2, 9). This inflammation is a neutrophilic and eosinophilic inflammation (10,11).

In a study conducted in pediatric patients with AD; total IgE, eosinophil, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), eosinophil lymphocyte ratio (ELR) levels were found to be higher in AD patients compared to the control group (12). In addition, in another study, it was reported that the relative eosinophil count and NLR values could be used to evaluate the severity of AD (13). Neutrophils, lymphocytes and platelets are important blood parameters involved in inflammation and can be quantified easily with accessible hemogram tests. Today, these laboratory parameters are used in many infectious and tumoral lesions. According to literature, these parameters are also extremely important both for the diagnosis and follow-up of patients with AD (12).

In the literature, it has been suggested to use NLR as a new marker for the presence of systemic inflammation (14). An increase in total IgE levels has also been reported in AD patients (15). In this context, it was aimed to evaluate the laboratory parameters of pediatric patients diagnosed with AD. Besides; the aim of this study was to examine the relationship between allergy test positivity and NLR, PLR, ELR and serum total IgE values that can be measured in peripheral blood.

MATERIAL AND METHOD

Research Design, Type and Sample

The study is a case-control study in a retrospective design. Data on pediatric patients aged 0-18 years with AD who applied to the Umraniye Training and Research Hospital Pediatric Allergy and Immunology outpatient clinic were examined retrospectively from the hospital's database. All patients with AD who applied to our clinic within the year 2022 (between January 2022-December 2022) were included in the study. In addition, children aged 0-18 years who applied to the pediatrics outpatient clinic of our hospital without any chronic disease or AD were also included in the study as the control group.

Measures

The sociodemographic characteristics (age, gender) of the children, hemogram parameters (neutrophil, eosinophil, lymphocyte, platelet), total IgE values, allergy history and allergy test positivity were evaluated within the scope of the study. Patients with positive allergen-specific IgE and/or skin tests were considered positive for the relevant allergen test.

Statistical Analysis

SPSS (Statistical Package for Social Sciences for Windows 25.0 program was used for the analysis and the recording of data. Descriptive data was presented wtih median, minimum, maximum values, numbers (n) and percentages (%). For the analysis of categorical data, Chi-square test was used. For the comprasion of continuous variables that non-normally distrubuted; Mann Whitney U test was used. The statistical significance level was set at $p<0.05$.

Ethics

Ethics committee approval was obtained from the Health Sciences University Ümraniye Training and Research Ethics Committee on 24/04/2023 with decision number 113.

RESULTS

The data of 193 children aged 0-18 years with AD were evaluated in the study. And, 100 children were included as the control group. Of the children with AD, 56.5% (n=109) were boys and 43.5% (n=84) were girls. Of the children in control group, 59.0% (n=59) were boys and 41.0% (n=41) were girls. Gender distribution of the patients and the control group was statistically similar (p=0.679). The median values of the age of the children with and without AD was 3 years (0-17) and 5 years (0-17), respectively (p=0.053).

When the laboratory values of the patients were examined; median values of white blood cell (WBC) and neutrophils were 8440.0 103mm3 (4240.0 ve 18900.0) and 3070.0 103/uL (610.0-13870.0), respectively. Absolute eosinophil and eosinophil (%) median values were 350.0 103/uL (10.0-2470.0) and 4.1% (0.2-25.8), respectively. The median values of lymphocytes, platelets and total IgE were 4110.0 103/uL (1280.0-13810.0), 329000.0 1103mm3 (51000.0-656000.0), 86.0 IU/mL (0-6098.0), respectively. In patients; eosinophil, lymphocyte and total IgE values were significantly higher than the control group (**Table 1**).

Table 1. Laboratuary parameters of the patients and control group

	Patients	Control group	P value
	Median (min-max)	Median (min-max)	
WBC (10^3 mm^3)	8440.0 (4240.0-18900.0)	8370.0 (3050.0-21580.0)	0.529
Neutrophil (10^3/uL)	3070.0 (610.0-13870.0)	2970.0 (300.0-8180.0)	0.261
Eosinophil (10^3/uL)	350.0 (10.0-2470.0)	220.0 (0-4160.0)	0.002
Eosinophil (%)	4.1 (0.2-25.8)	3.0 (0-21.0)	0.001
Lymphocyte (10^3/uL)	4110.0 (1280-13810.0)	3470.0 (1300.0-7870.0)	0.019
Platelet (10^3 mm^3)	329000.0 (51000.0-656000.0)	329000.0 (190000-734000)	0.832
Total IgE (IU/mL)	86.0 (0-6098.0)	31.0 (1.0-3633.0)	<0.001

WBC: White blood cell

When the allergy test positivity of the patients was examined; house dust mite allergy was positive in 26.4% (n=51) of the patients. Egg allergy test was positive in 22.8% (n=44) of the patients, milk allergy test was positive in 9.3% (n=18) and peanut allergy test was positive in 6.7% (n=13) of the patients. The test positivity of the patients for other allergens is also shown in **Table 2**.

Table 2. Allergy test positivity of patients

Allergy test positivity	n	%
House dust mite	51	26.4
Egg	44	22.8
Cat	20	10.4
Cow's milk	18	9.3
Pollen	17	8.8
Peanut	13	6.7
Hazelnut	11	5.7
Walnut	3	1.6
Pistachios	1	0.5

When allergy test results of the AD patients were evaluated, 52.3% (n=101) of the patients had a positive test for at least one allergen. NLR, PLR, ELR and total IgE values of patients with and without allergy test positivity were compared. While NLR median values were the same in both groups; the median values of PLR and ELR were higher in patients with allergy test positivity, but there was no statistical significance between the groups (p=0.268 and p=0.251, respectively). As the total IgE values were examined, while the median total IgE value of the patients with a positive allergy test was 168.0 IU/mL (2.0-6098.0), this value was 37.0 IU/mL (0-3577.0) in patients with a negative allergy test. This elevation in total IgE value in patients with positive allergy test was statistically significant (p<0.001) (**Table 3**).

Table 3. NLR, PLR, ELR and total IgE values of patients with and without test positivity

	AD with test positivity (n=101)	AD without test positivity (n=92)	P value
	Median (min-max)	Median (min-max)	
NLR	0.67 (0.19-7.74)	0.67 (0.20-4.19)	0.807
PLR	89.62 (8.06-268.75)	84.24 (22.59-219.44)	0.268
ELR	0.09 (0.01-0.60)	0.07 (0-0.82)	0.251
Total IgE (IU/mL)	168.0 (2.0-6098.0)	37.0 (0-3577.0)	<0.001

AD: Atopic dermatitis, NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, ELR: eosinophil lymphocyte ratio

NLR, PLR, and ELR values were calculated by dividing neutrophil, platelet, and eosinophil values by lymphocyte values, respectively. The median NLR, PLR, and ELR values of the patients were 0.67 (0.19-7.74), 87.30 (8.06-268.75), and 0.08 (0-0.82), respectively. The median NLR, PLR, and ELR values of the control group were 0.78 (0.0.06-5.53), 92.75 (43.91-365.52), and 0.06 (0-0.53), respectively. ELR values of AD patients were significantly higher than the control group (p=0.044). PLR value was also significantly higher in the control group (p=0.011) (**Table 4**).

Table 4. NLR, PLR and ELR values of the patients and control group

	Patients	Control group	P value
	Median (min-max)	Median (min-max)	
NLR	0.67 (0.19-7.74)	0.78 (0.06-5.53)	0.880
PLR	87.30 (8.06-268.75)	92.75 (43.91-365.52)	0.011
ELR	0.08 (0-0.82)	0.06 (0-0.53)	0.044

NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, ELR: eosinophil lymphocyte ratio

DISCUSSION

In cases where inflammation accompanies chronic diseases, an increase in laboratory parameters indicating inflammation can be observed. Easily accessible and practical laboratory tests such as hemogram are used in the follow-up of many diseases. Hemogram markers such as WBC, neutrophils, and eosinophils have a great role both in the diagnosis and follow-up of AD patients. Evaluation of the level of NLR, ELR, and PLR parameters, which can be evaluated by hemogram in AD patients, will provide a practical approach in the diagnosis and follow-up process of the disease. The study carried out in this context and evaluated the relationship between laboratory parameters and allergy test positivity in AD, which is one of the most common allergic diseases in childhood and accompanied by inflammation. At the same time, NLR, PLR and ELR values were compared with the healthy control group.

In the literature, increased eosinophil values in both blood and tissue have been determined in patients with AD (16). Similarly, an increase in total IgE levels can be observed in AD patients, as in other allergic

diseases (17, 18). The patients with AD in our study had significantly higher eosinophil, lymphocyte and total IgE values compared to the control group. In a similar study conducted in pediatric patients with AD in our country, eosinophil and total IgE values of AD patients were found to be significantly higher than the control group (12). In another study, children with AD had significantly higher eosinophil values than the control group (17).

In our study, when the allergen sensitivity of AD patients was examined; house dust mite allergy was positive in 26.4% (n=51) of the patients. Of the patients, 22.8% (n=44) had egg allergy, 9.3% (n=18) had cow's milk, 6.7% (n=13) had peanut allergy. Similarly, positivity in house dust mite specific IgE value was observed most frequently in AD patients in the literature (19). In our study, there was no statistical significance between NLR, PLR and ELR values of AD patients with and without allergy test positivity. In addition, as expected, total IgE values were found to be significantly higher in patients with a positive allergy test. Although there is no statistical significance, the fact that PLR and ELR values were higher in patients with AD with positive allergy test suggests that these values can be used as a marker to predict test positivity. Further studies are needed in this regard.

There are data in the literature that NLR, ELR and PLR values can be used as inflammatory markers in many diseases such as cardiovascular diseases and inflammatory diseases (17, 20). In our study, the ELR value of AD patients was significantly higher than the control group. The PLR value of the control group was also significantly higher. No significant difference between the two groups was determined for the NLR value. In the literature, NLR and ELR values of pediatric patients with AD have been reported to be significantly higher than the control group (17). In the same study, no statistically significant difference was observed between the groups in terms of PLR values. The higher PLR values of the control group in our study may be due to potential confounding factors that may play a role in the study. In further studies evaluating also the severity of the disease, the utility of PLR as a clinical inflammatory marker in AD patients should be examined.

Limitations and Strengths

Conducting the study in a single center creates a limitation in terms of the generalizability of the study results. Another limitation of the study is that the clinical severity of the disease could affect the laboratory parameters, however the clinical severity of AD patients was not evaluated in the study. In addition, studies comparing NLR, PLR and ELR values in pediatric patients with AD are limited in the literature. This can be considered as the strength of our study.

CONCLUSION

In our study, laboratory parameters of pediatric patients with AD were evaluated. Eosinophil, lymphocyte and total IgE values were significantly higher in patients with AD when compared to the control group. In addition, the ELR value of AD patients was also significantly higher than the control group. Evaluation of laboratory parameters is extremely important in the diagnosis and follow-up of AD patients. Specific IgE values and skin prick tests are tests that can not be performed in every clinical center. Although there is no statistical significance, the fact that PLR and ELR values are higher in patients with AD with positive allergy test suggest that these parameters can be used as a marker predicting allergy test positivity. Evaluation of hemogram parameters, which is an easily accessible laboratory test in AD patients, is extremely important for physicians working in this field. In AD patients, further studies with large samples should be planned in which inflammatory markers, clinical severity of the disease, and response to treatment are evaluated.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was obtained from the Health Sciences University Ümraniye Training and Research Ethics Committee (Date: 24.04.2023 Decision No: 113).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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ORIGINAL ARTICLE
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Mitral Valve Repair with Isolated Ring Annuloplasty: Mid-term Results of 43 Patients

İzole Ring Anüloplasti ile Mitral Kapak Onarımı: 43 Hastanın Orta Dönem Sonuçları

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[10]Regrettably, our esteemed professor, who served as the supervisor of the thesis from which this study was adapted, passed away during the COVID-19 pandemic. We respectfully commemorate his memory and the enduring values he imparted to us

ABSTRACT

Aim: Repair techniques are recommended for mitral regurgitation in appropriate cases. Although there are many different mitral valve repair techniques described, data on the outcomes of patients undergoing isolated ring annuloplasty are limited. In this study, we analyzed the operative and postoperative results of isolated ring annuloplasty.

Material and Method: Forty-three patients who underwent isolated ring annuloplasty for mitral regurgitation were included in the study and the results were analyzed retrospectively. Patients were followed up for 18.4±13.4 months.

Results: The mean age of the patients was 53.9±10.8 years (25 (58.1%) males). According to Carpentier functional classification, 21 (48.8%) patients had type I and 22 (51.2%) patients had type IIIb dysfunction. While 7 (16.3%) patients were planned to undergo intervention for mitral valve only, the majority of patients (36 patients, 83.7%) underwent combined procedures. When the preoperative and postoperative values of our patient group were compared, a statistically significant improvement was observed in functional capacity according to NYHA (p<0.001). In addition, the mitral regurgitation grade of the patients decreased from a mean of 2.37±0.49 to 0.73±0.52 (p<0.001). Improvements in left ventricular end-diastolic diameter, left ventricular end-systolic diameter, pulmonary artery pressure and left atrial size measured at follow-up were statistically significant compared to preoperative data (p<0.001, p=0.001, p=0.001, p=0.007 and p=0.005, respectively).

Conclusions: Isolated ring annuloplasty technique can be safely performed in patients with normal leaflets and subvalvular structures and only annular dilatation. In addition, if the mitral valve anatomy is appropriate, only ring annuloplasty can be performed to correct valve pathology to avoid prolonging cross-clamp and cardiopulmonary bypass time in operations where other long procedures will be performed in addition to mitral valve intervention.

Keywords: Annuloplasty, mitral valve, repair, ring

ÖZ

Amaç: Mitral yetmezlikte uygun vakalarda tamir tekniklerinin uygulanması önerilmektedir. Tanımlanmış birçok farklı mitral kapak onarım tekniği mevcut olmakla birlikte sadece ring anuloplasti yapılan hastaların sonuçlarına dair veriler sınırlıdır. Bu çalışmada sadece ring kullanılarak gerçekleştirilen anuloplasti olgularının operatif ve postoperatif sonuçları incelenmiştir.

Gereç ve Yöntem: Mitral yetmezlik nedeniyle izole ring anuloplasti yapılan 43 hasta çalışmaya dahil edilmiş ve sonuçları retrospektif olarak incelenmiştir. Hastalar ortalama 18.4±13.4 ay takip edilmiştir.

Bulgular: Hastaların ortalama yaşları 53.9±10.8'dir (25 (%58.1) erkek). Carpentier fonksiyonel sınıflandırmasına göre hastalar değerlendirildiğinde 21 (%48.8) hastanın tip I ve 22 (%51.2) hastanın tip IIIb disfonksiyona sahip olduğu izlenmiştir. 7 (%16.3) hastaya sadece mitral kapak nedeniyle girişim planlanırken hastaların büyük çoğunluğuna (36 hasta, %83.7) kombine prosedürler uygulanmıştır. Hasta grubumuzun preoperatif ve postoperatif değerleri kıyaslandığında NYHA göre fonksiyonel kapasitelerinde istatistiksel olarak anlamlı iyileşme görülmüştür (p<0.001). Ayrıca hastaların mitral yetmezlik dereceleri ortalama 2.37±0.49'dan 0.73±0.52'ye gerilemiştir (p<0.001). Hastaların kontrollerinde ölçülen sol ventrikül diyastol sonu çapı, sol ventrikül sistol sonu çapı, pulmoner arter basıncı ve sol atriyum büyüklüğündeki iyileşmeler de preoperatif verilerle kıyaslandığında istatistiksel olarak anlamlıdır (sırasıyla p<0.001, p=0.001, p=0.007 ve p=0.005).

Sonuç: Lifletlerin ve subvalvuler yapıların normal olduğu ve sadece anuler dilatasyonun izlendiği hasta grubunda izole ring anuloplasti tekniği güvenle uygulanabilir. Ayrıca mitral kapak girişimine ek olarak başka uzun prosedürlerin de yapılacağı operasyonlarda kros klemp ve kardiyopulmoner bypass süresini uzatmamak için eğer mitral kapak anatomisi uygunsa sadece ring anuloplasti yapılarak kapak patolojisi düzeltilebilir.

Anahtar Kelimeler: Anuloplasti, mitral kapak, onarım, ring

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INTRODUCTION

Although prosthetic valves have been the preferred choice in mitral valve surgery for many years, the concept of mitral valve repair has emerged and made significant advancements, particularly with the introduction of annuloplasty rings. Mitral valve repair aims to address the underlying pathology while preserving the patient's native valve, thereby preserving left ventricular function and eliminating the need for anticoagulation therapy. This approach also mitigates complications such as bleeding, thrombosis, infective endocarditis, and prosthetic valve dysfunction that are associated with valve replacement (1,2). Current guidelines strongly recommend mitral valve repair as the primary treatment for mitral regurgitation (MR), assigning it a class-1 indication and prioritizing it over valve replacement in suitable cases (3,4).

While various techniques have been described for mitral valve repair, it is recommended that all repair procedures incorporate an appropriate annuloplasty method to reshape and/or stabilize the mitral annulus. The concept of annuloplasty emerged in 1968 with the introduction of the first remodeling annuloplasty technique, and since then, prosthetic rings have undergone significant development and are now widely utilized (5). Although annuloplasty techniques are often employed in conjunction with other repair methods, they may suffice as standalone interventions in select cases. Despite the abundance of studies on mitral valve repairs in the literature, there is a limited number of publications focusing specifically on isolated ring annuloplasty. In this retrospective, single-center study, we present the mid-term outcomes of patients who underwent "isolated ring annuloplasty" as a technique for mitral valve repair.

MATERIAL AND METHOD

This retrospective study included a cohort of forty-three consecutive patients who underwent mitral ring annuloplasty procedure performed by the same surgeon at the Türkiye Yüksek İhtisas Training and Research Hospital between 2006 and 2013. The study adhered to the principles outlined in the Declaration of Helsinki, and informed consent was obtained from all patients prior to surgery. Patients' demographic, clinical, and operative data was retrieved from the hospital's anonymous database under the supervision of the data protection officer, guaranteeing the confidentiality of patients' identities. This study is derived from the first author's doctoral dissertation and was approved by the Educational Planning Committee of the Türkiye Yüksek İhtisas Training and Research Hospital. The patients were followed up for an average duration of 18.4±13.4 months. Early mortality was defined as the first 30-day period following surgery, while late mortality encompassed the subsequent period.

Transthoracic echocardiography (Vivid 7 Dimension, GE Medical Systems, Horten, Norway) was employed for both preoperative and postoperative assessments to determine the MR grading. Parameters such as mitral regurgitant volume, effective regurgitant orifice area, and vena contracta width obtained through Doppler echocardiography were utilized to grade the severity of mitral regurgitation. The severity of mitral regurgitation was assessed and classified into four grades (Grade 1 to Grade 4) based on the progressive extent of the regurgitant jet filling the left atrium.

The mitral valve insufficiency in our study was classified into three functional types based on the established Carpentier and colleagues' classification system (6). According to this classification, MR was categorized as type I when there is normal leaflet motion, type II when there is excessive leaflet motion such as prolapse, or type III when there is restrictive leaflet motion due to valve and subvalvular apparatus restriction and thickening (IIIa) or left ventricular remodeling (IIIb). Furthermore, in our study, we comprehensively assessed and described the various anatomical and functional abnormalities associated with mitral regurgitation using the Carpentier's Mitral Regurgitation Classification. This classification system allows for a detailed characterization of the specific characteristics of MR, aiding in the understanding of the underlying pathology and guiding treatment decisions in a precise and tailored manner.

Surgical Procedure

After the initiation of general anesthesia and median sternotomy, anticoagulation was achieved by administering a dosage of 400 IU/kg of heparin. Ascending aorta and bicaval selective venous cannulation were performed. Cardio-pulmonary bypass was initiated. Cardiac arrest was achieved with antegrade and retrograde cardioplegia (Plegisol®, Abbot, IL, USA) after cross-clamping. Maintenance cold cardioplegia was given retrogradely. The optimum cooling temperature was 32 °C. Mitral valve intervention was performed through the Sondengaard's atrial groove in 38 (88.4%) patients and through the transseptal approach into the left atrium in 5 (11.6%) patients. The mitral valve was carefully examined with the help of hooks. The reactive endocardial thickening zone due to the jet of regurgitant volume into the left atrium was tried to be detected. Mitral regurgitation was classified according to the Carpentier's functional classification based on preoperative echocardiographic data and intraoperative valve inspection. Twenty-one (48.8%) patients had Carpentier type I and 22 (51.2%) had type IIIb mitral regurgitation. Subsequently, annuloplasty was performed using a St. Jude Medical Rigid Saddle Ring (St. Jude Medical, Inc., St. Paul, MN, USA) for the patients with Carpentier type IIIb,

and a Carpentier-Edwards Physio Annuloplasty Ring (Edwards Lifesciences, Irvine, CA, USA) was chosen as a flexible ring for patients with Carpentier type I MR. Following the mitral ring annuloplasty, intraoperative assessment of valve coaptation was performed by the surgeon using a saline test. In cases with a larger anatomical size exceeding 5 cm, reduction of the left atrium was achieved through plication. Warm blood cardioplegia was administered, and subsequently, the cross clamp was removed. Protamine sulfate was used to neutralize anticoagulation in a 1:1 ratio. Mitral valve regurgitation was evaluated postoperatively through transesophageal echocardiography. A total of 36 patients (83.7%) underwent combined procedures involving simultaneous coronary bypass, ascending aortic surgery, and aortic or tricuspid valve surgery. In the remaining 7 patients (16.3%), isolated mitral valve surgery was performed.

As part of our standard clinical protocol, patients were regularly monitored at specific intervals following their surgery, including on the 10th day, 3rd, 6th, 12th, and 18th month postoperatively. For the purpose of this study, the data from the patients' last follow-up visit was included as part of the postoperative data analysis.

Statistical Analysis

The statistical analysis was conducted using the SPSS v20.0 software package (SPSS Inc., Chicago, IL, USA). The normality of the data distribution was assessed both analytically (Kolmogorov-Smirnov/Shapiro-Wilk test) and visually (histogram plots). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The comparison between preoperative and postoperative data was performed using paired sample t-tests for variables with a normal distribution and Wilcoxon tests for variables without a normal distribution. A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

Preoperative demographic data and echocardiographic characteristics of the patients are presented in **Table 1**. The mean age of the patients was 53.9±10.8 years (25 males (58.1%)). In the preoperative period, 5 (11.6%) patients were in atrial fibrillation (AF) rhythm, while the other patients had normal sinus rhythm. The preoperative functional capacity of the patients was class-I in 3 patients, class-II in 30 patients and class-III in 6 patients according to New York Heart Association (NYHA) classification. The etiology of mitral regurgitation was rheumatic in 2 patients, degenerative in 19 patients, congenital in 1 patient, infective endocarditis in 1 patient and ischemic in 20 patients.

Table 1. Demographic characteristics and preoperative echocardiographic data of the patients

Number of Patients	43
Follow-up period (month)	18.4±13.4
Age (years)	53.9±10.8
Gender (male)	25 (%58.1)
Functional capacity according to NYHA	
Class I	3 (%7)
Class II	30 (%69.8)
Class III	6 (%14)
Body mass index (kg/m^2)	27.1±3.9
Hypertension	20 (%46.5)
Hyperlipidemia	6 (%14)
Diabetes mellitus	7 (%16.3)
Smoking	6 (%14)
Chronic obstructive pulmonary disease	16 (%37.2)
Electrocardiography	
Normal sinus rhythm	34 (%79.1)
Atrial fibrillation	5 (%11.6)
Mitral Insufficiency	
Grade 2	24 (%55.8)
Grade 3	17 (%39.5)
Grade 4	2 (%4.7)
Ejection fraction (%)	50.3±10.7
Left ventricular end-diastolic diameter (cm)	5.7±1
Left ventricular end-systolic diameter (cm)	4.3±1
Pulmonary artery pressure (mmHg)	39.7±14.9
Left atrium (cm)	4.7±1.1

Out of the total patient cohort, seven patients (16.3%) underwent surgery solely for mitral valve pathology, while 36 patients (83.7%) underwent combined procedures. The additional procedures performed are outlined in **Table 2**. The average cross-clamp time was 103.5±25.3 minutes, and the cardiopulmonary bypass time was 139.2±33.4 minutes. In all patients included in the study, the ring annuloplasty technique was employed, with 22 patients receiving a rigid ring and 21 patients receiving a flexible ring. No operative mortality was observed during the study period.

Table 2. Procedures performed in addition to mitral ring annuloplasty

Additional procedure	n (%)
Coronary artery bypass grafting	24 (55.8%)
Aortic valve surgery	15 (34.9%)
Ascending aorta surgery	10 (23.3%)
Tricuspid valve surgery	4 (9.3%)
Atrial septal defect repair	3 (7%)
Left atrium reduction	1 (2.3%)
Right atrium reduction	2 (4.7%)
Left ventricular aneurysm repair	3 (7%)

Table 3 presents the postoperative data of the patients. Among the patients, 23 (53.5%) required inotropes and 2 (4.7%) required intraaortic balloon pump support during the postoperative period. The average duration of intubation was 14.1±6.3 hours, the mean length of intensive care unit (ICU) stay was 1.9±0.8 days, and the

mean hospitalization duration was 8.2±3.5 days. Two patients underwent revision surgery due to bleeding. Additionally, one patient (2.3%) developed mediastinitis, and one patient experienced pneumonia.

Table 3. Postoperative data of the patients	
Positive inotrope requirement	23 (53.5%)
Intraaortic balloon pump	2 (4.7%)
Extubation time (hours)	14.1±6.3
Duration of intensive care stay (days)	1.9±0.8
Duration of hospitalization (days)	8.2±3.5
Drainage (ml)	708±411
Revision due to bleeding	2 (4.7%)
Postoperative arrhythmia	4 (9.3%)
Pace maker requirements	1 (2.3%)
Mediastinal infection	1 (2.3%)
Pneumonia	1 (2.3%)

The patients were followed up for an average of 18.4±13.4 months in the postoperative period. Substantial improvement was observed in the functional capacity of the patients during the postoperative follow-up. Based on the NYHA classification, 29 patients (67.4%) were classified as class I, and 2 patients (4.7%) were classified as class II. Postoperative echocardiographic assessments revealed that 9 patients (20.9%) had no detectable mitral regurgitation, while 20 patients (46.5%) had grade 1 mitral regurgitation, and 1 patient (2.3%) had grade 2 mitral regurgitation. Detailed information regarding the postoperative follow-up of the patients can be found in **Table 4**.

Table 4. Postoperative follow-up parameters of the patients	
Functional capacity according to NYHA	
Class I	29 (67.4%)
Class II	2 (4.7%)
Electrocardiography	
Normal sinus rhythm	28 (65.1%)
Atrial fibrillation	4 (9.3%)
Mitral regurgitation	
No regurgitation	9 (20.9%)
Grade 1	20 (46.5%)
Grade 2	1 (2.3%)
Ejection fraction (%)	49.5±11.3
Left ventricular end-diastolic diameter (cm)	5.2±0.7
Left ventricular end-systolic diameter (cm)	3.8±0.7
Pulmonary artery pressure (mmHg)	31.5±5.4
Left atrium (cm)	4.3±0.6

The comparison of preoperative and postoperative values in our patient group (**Table 5**) revealed a statistically significant improvement in functional capacity according to NYHA classification (p<0.001). Furthermore, there was a significant decrease in the mean MR grade from 2.37±0.49 to 0.73±0.52 (p<0.001). However, no statistically significant difference was observed in mean ejection fraction between the preoperative period (50.27%±10.72) and the postoperative period (49.47%±11.33) (p=0.56). Notably, significant improvements were observed in left ventricular end-diastolic diameter, left ventricular end-systolic diameter, pulmonary artery pressure, and left atrial size during the postoperative follow-up when compared to the preoperative data (p<0.001, p=0.001, p=0.007, and p=0.005, respectively).

Table 5. Comparison of preoperative and postoperative characteristics of the patients			
	Preoperative	**Postoperative**	**p value**
NYHA classification	2.06±0.44	1.06±0.25	<0.001
Mitral regurgitation	2.37±0.49	0.73±0.52	<0.001
Ejection fraction (%)	50.27±10.72	49.47±11.33	0.56
Left ventricular end-diastolic diameter (cm)	5.69±0.97	5.24±0.69	<0.001
Left ventricular end-systolic diameter (cm)	4.25±1.02	3.83±0.72	0.001
Pulmonary artery pressure (mmHg)	39.73±14.94	31.5±5.37	0.007
Left atrium (cm)	4.73±1.12	4.3±0.56	0.005

During the postoperative period, we observed early mortality in 2 patients and late mortality in 1 patient. One patient experienced low cardiac output and passed away on the 12th day after the operation. Another patient developed pneumonia and died on the 20th day postoperatively. Additionally, one patient had mediastinal infection six months after the operation. Furthermore, one patient developed severe mitral regurgitation at the sixth postoperative month, requiring a reoperation and mitral valve replacement.

DISCUSSION

Mitral regurgitation is the second most prevalent valvular disorder requiring intervention, following aortic stenosis. Over the years, the etiology of mitral regurgitation has shifted, with a decline in rheumatic causes and an increase in ischemic and degenerative causes. In the treatment of mitral regurgitation, there is a growing trend towards mitral valve repair as opposed to mitral valve replacement in numerous medical centers. This shift can be attributed to several advantages associated with mitral valve repair, including lower morbidity and mortality rates, improved preservation of left ventricular function, reduced incidence of thromboembolic events, and increased resistance to endocarditis (7). A meta-analysis comparing mitral valve replacement and repair demonstrated that repair had lower early postoperative mortality but necessitated more re-interventions in the long term (8).

The recurrence of mitral valve regurgitation following mitral valve repair surgery is a significant concern for both surgeons and patients. Regardless of the underlying cause of mitral regurgitation, the ring annuloplasty is the sine qua non of a successful mitral

valve repair. The mitral annulus is a crucial component of the mitral valve complex and is integral to the heart's fibrous skeleton. It consists of a dense connective tissue between the left and right fibrous trigones in the anterior leaflet and a thinner band of connective tissue in the posterior region, which is prone to circular dilatation. In its normal state, the mitral annulus is predominantly circular during diastole and assumes an elliptical shape during systole. Ring annuloplasty serves to restore the annulus to its normal structure, ensuring long-term and durable valve repair. By preventing annular dilatation, ring annuloplasty helps maintain the geometric integrity of the annulus and minimizes stress on the leaflets during systole. Prosthetic rings were first introduced in 1968 with the advent of the concept of remodeling annuloplasty and have since become widely utilized (9). The selection of an appropriate ring is crucial, as an improper choice can contribute to recurrent mitral regurgitation in the postoperative period.

Carpentier's studies have demonstrated that a normal mitral valve exhibits a balanced 3:4 ratio between the anteroposterior and transverse distances. This ratio becomes disrupted when annular dilatation occurs, leading to the development of mitral regurgitation. The aim of ring annuloplasty is to restore this ratio. However, in cases of Barlow's disease characterized by excessive tissue in the leaflets, there can be a discrepancy between the anteroposterior diameter and tissue redundancy, resulting in a phenomenon known as systolic anterior motion (SAM). SAM can narrow the left ventricular outflow tract. To prevent this, larger rings or specially designed rings that mitigate SAM can be utilized (10).

While annular dilatation is commonly associated with Carpentier type I and type IIIb regurgitation according to the Carpentier classification, it can occur in all etiologies, particularly as a secondary mechanism to delayed mitral regurgitation. In a study by de Marchena et al. (11), Carpentier type I regurgitation was found to be the least common type, while type III regurgitation was the most prevalent among the adult population in the United States. In our clinic, where mitral repair patients with various etiologies were included, annular dilatation alone was observed in only 6% of cases. In this study, we treated 43 patients using ring annuloplasty as the sole method of repair. Among them, 21 patients exhibited annular dilatation (Carpentier type I dysfunction), while 22 patients had systolic restriction of leaflet motion (Carpentier type IIIb dysfunction). Although there are alternative repair techniques available for type IIIb lesions, we opted for ring annuloplasty alone when additional procedures, such as coronary bypass or aortic valve surgery, were required alongside mitral valve surgery. This approach aimed to minimize cross-clamp and cardiopulmonary bypass time and avoid complex repair techniques. For patients with degenerative etiology and isolated annular dilatation, a flexible annuloplasty ring was selected, whereas a rigid annuloplasty ring was used for patients with ischemic etiology. Although there is no complete consensus in the literature regarding ring selection, some studies have shown that the choice of ring does not significantly impact repair outcomes (12). Furthermore, despite the controversy surrounding the potential adverse effects of rigid rings on left ventricular function, studies by Rayhil et al. (13) and Castro et al. (14) found no significant difference in left ventricular systolic performance between patients with rigid or flexible rings.

In the study conducted by Geidel et al. (15), it was found that the correction of mitral insufficiency with ring annuloplasty alone, along with coronary bypass surgery, significantly contributed to left ventricular remodeling and ventricular performance in patients with ischemic mitral regurgitation. For patients with ischemic mitral regurgitation, surgeons often opt for a smaller annuloplasty ring (16). While this approach has been shown to effectively alleviate mitral regurgitation, recent studies have indicated that it does not have a substantial impact on long-term survival. Therefore, in some cases, additional procedures such as papillary muscle repositioning and secondary chordae resection may be necessary (17,18).

Several studies have indicated a link between annular dilatation and AF. Otsuji et al. (19) from Japan reported that annular dilatation can occur due to AF. They suggested that incomplete leaflet closure, mismatch between annulus and leaflet areas, flattening of the annulus leading to loss of its saddle shape, and left atrial dysfunction are all indicative of AF-induced mitral annulus dilatation (20). The prevalence of mitral annular dilatation in patients with AF has been reported to range between 3-15% (20). Additionally, Glower et al. (21) demonstrated that isolated mitral annular dilatation is associated with female gender, hypertension, and low left ventricular ejection fraction.

When evaluating the postoperative follow-up results of our patient group at an average of 18.4±13.4 months after the operation, a significant improvement was observed in the functional capacity of the patients. The degree of mitral regurgitation showed a statistically significant improvement when compared to preoperative echocardiographic values. Favorable improvements were also observed in left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left atrial size, and pulmonary artery pressures. There was a slight decrease in postoperative ejection fraction compared to preoperative values, but this difference was not statistically significant. In our study, mortality was observed in 3 patients (6.9%), and reoperation was required in 1 patient (2.3%). It should be noted that our

patient group was heterogeneous due to the additional surgical procedures performed, and therefore, direct comparisons of mortality and reoperation rates with the existing literature may not be accurate.

Our study acknowledges several limitations that need to be considered. The first limitation of this study pertains to its retrospective design, which may introduce inherent biases and limitations associated with the collection and analysis of retrospective data. Furthermore, this study solely focuses on a single technique without any comparative analysis against alternative techniques, thereby limiting the comprehensive evaluation of different approaches. Another limitation stems from the inclusion of patients with both Carpentier's type I and type IIIb mitral regurgitation, leading to heterogeneity within the study population. Additionally, the lack of long-term follow-up for MR assessments due to difficulties in reaching all patients is another constraint of this study. Finally, the relatively small sample size of this trial may reduce its statistical power and generalizability.

CONCLUSION

The preservation of the mitral valve's native tissue and the avoidance of chronic anticoagulation have made mitral valve repair surgery an attractive option for many surgeons. Various types of rings have been developed as an integral part of mitral valve repair surgery, and they continue to be the most effective method for annuloplasty. Our study has demonstrated that the isolated ring annuloplasty technique can be safely performed in patients with normal leaflets and subvalvular structures, and when there is only annular dilatation present. Furthermore, our study has shown that in cases where other complex procedures such as coronary bypass, aortic valve replacement, or ascending aortic surgery need to be performed in addition to mitral valve surgery, if the mitral valve anatomy is suitable, performing only ring annuloplasty can effectively correct the valve pathology without prolonging the cross-clamp and cardiopulmonary bypass time. This approach allows for the correction of mitral pathology while avoiding undesirable morbidity and mortality associated with prolonged and complicated combined procedures.

ETHICAL DECLARATIONS

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Evaluation of COVID-19 Vaccination In Healthcare Professionals

Sağlık Çalışanlarında COVID-19 Aşılamasının Değerlendirilmesi

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ABSTRACT

Aim: Vaccination is one of the most successful and cost-effective healthcare initiatives for preventing infectious diseases, and vaccines are of exceptional importance to control and prevent COVID-19.

Material and Method: In our study, the results of the COVID-19 vaccine applications, which started in healthcare workers after determining the priority groups, were evaluated. The study population, which was planned as a retrospective cohort study, consists of healthcare professionals working in Kayseri city center. 24.421 healthcare workers from file records were included in this study. This study consists of two independent phases. Only the retrospective registry was not scanned, and the demographic information, vaccination status, and source case information of the healthcare workers who were found positive were questioned by phone.

Results: The rates of PCR (+) healthcare workers in the pre-vaccination period were 5.96% and 2.53% in the post-vaccination period. Considering the vaccination status of all healthcare workers, 5.14% of the unvaccinated ones were found to be PCR (+), while 2.04% of those vaccinated were PCR (+) (p<0.001).

Conclusion: The rate of protection against infection in the field of the inactivated vaccine administered to healthcare workers was found to be 52.86%. In our study, in which we evaluated the inactivated CoronaVac vaccine, it seems that the vaccine contributes to the service providers and the society in the fight against the epidemic, and it seems appropriate to be among the available vaccine options in line with the data obtained.

Keywords: COVID-19, inactive vaccine, healthcare workers

ÖZ

Amaç: Aşı uygulaması, bulaşıcı hastalıkları önlemek için en başarılı ve maliyet-etkin sağlık hizmeti girişimlerinden biridir ve COVID-19'u kontrol etmek ve önlemek için olağanüstü bir öneme sahiptir.

Gereç ve Yöntem: Çalışmamızda öncelik grupları belirlenerek sağlık çalışanlarında başlanan COVID-19 aşısı uygulamalarının sonuçları değerlendirilmiştir. Retrospektif kohort çalışması olarak planlanan çalışmanın evrenini Kayseri il merkezinde görev yapan sağlık çalışanları oluşturmaktadır. Dosya kayıtlarından 24.421 sağlık çalışanı bu çalışmaya dâhil edilmiştir. Bu çalışma iki bağımsız aşamadan oluşmaktadır. Sadece geriye dönük kayıt taranmamış, pozitif bulunan sağlık çalışanlarının demografik bilgileri, aşılanma durumları ve kaynak vaka bilgileri telefonla sorgulanmıştır.

Bulgular: Aşılama öncesi dönemde PCR (+) sağlık çalışanı oranı %5,96 ve aşılama sonrası dönemde %2,53 olarak gerçekleşti. Tüm sağlık çalışanlarının aşılama durumuna bakıldığında aşı olmayanların %5,14'ünün PCR (+), aşı olanların ise %2,04'ünün PCR (+) olduğu saptandı (p<0,001).

Sonuç: Sağlık çalışanlarına uygulanan inaktive aşının sahada enfeksiyondan koruma oranı %52,86 olarak bulundu. İnaktif CoronaVac aşısını değerlendirdiğimiz çalışmamızda aşının salgınla mücadelede hizmet sunucuları ve topluma katkı sağladığı, elde edilen veriler doğrultusunda mevcut aşı seçenekleri arasından yer almasının uygun olduğu görünmektedir.

Anahtar Kelimeler: COVID-19, inaktif aşı, sağlık çalışanları

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INTRODUCTION

The COVID-19 pandemic caused by SARS-CoV2 is the most important health problem of our century. The high contagiousness of the virus, its negative effects on countries' economies and health systems, and the lack of adequate treatments that affect the prognosis since the beginning of the epidemic have made it very important to develop an effective and safe vaccine against this disease. Vaccination is one of the most successful and cost-effective healthcare initiatives for preventing infectious diseases, and vaccines are of exceptional importance to control and prevent COVID-19 (1,2). Considering that the basic reproduction number for SARS-CoV-2 is 2.5-3.5 (R0), it has been stated that 60-72% (1-1 / R0) of the population should be vaccinated to prevent the spread of the virus and end the epidemic through community immunity (3).

The safety, tolerance, dosage, and vaccination scheme of the inactivated COVID-19 vaccine presented as a vaccine candidate by a company of Chinese origin were determined by the Phase 1/2 studies conducted in China with the approval of the Chinese National Medical Products Administration (NMPA) on 13.04.2020 and the information obtained has been published in a highly prestigious peer-reviewed journal (4–6). After the high seroconversion values were obtained, four independent Phase 3 studies were initiated in China, Turkey, Brazil, and Indonesia. As a result, authorities in Brazil declared that the safest vaccine among the five vaccines tested in Phase 3 studies is the inactivated vaccine of Chinese origin (CoronaVac) (4).

Although vaccine development studies continue, there are 13 vaccines in Phase 3, and according to the World Health Organization, there are 12 vaccines under development in Turkey (7). The COVID-19 vaccine, which was approved for emergency use by China in July 2020 and is in Phase 3 in our country, was started to be applied after obtaining emergency use approval following the agreement of the Ministry of Health for 50 million doses (4).

Four separate Phase 3 studies were carried out with 13,060 volunteers over the age of 18 in Brazil in July 2020, 1,620 volunteers aged 18-59 in Indonesia in August 2020, 13,000 volunteers aged 18-59 in Turkey in September 2020, and 1,040 volunteers over the age of 18 on 31 October in China (7). In studies on the efficacy of inactivated COVID-19 vaccine, it was determined that the vaccine reached sufficient antibody titers for immunization 14 days after the second dose. Furthermore, it has been reported that the vaccine provides 83.70% protection from medical intervention, the rate of preventing hospitalization is 85%-100%, and the rate of preventing deaths is 80% (8–11).

Phase 4 studies of vaccines administered will provide us soon with very important real data on the efficacy and safety of these vaccines. In this context, in our study, the results of the COVID-19 vaccine applications, which started in healthcare workers after determining the priority groups, were evaluated. In our study, the healthcare workers in Kayseri province, the vaccination rates of the workers in the process before the start of vaccination and after the application of the first-second doses of the vaccination, when they were vaccinated, the status and frequency of being infected with COVID-19 before and after vaccination were examined to evaluate the COVID-19 vaccination and its effects in healthcare workers.

MATERIAL AND METHOD

Study Design and Setting

The study population, which was planned as a retrospective cohort study, consists of healthcare professionals working in Kayseri city center.

24,421 healthcare workers are working in the province, and since all of them were planned to be included in the study, no sampling was made. In line with the instructions of the Ministry of Health of the Turkey, information such as the number of people vaccinated daily and weekly, the number of positive cases, the occupation of those who have been vaccinated are monitored and recorded in the electronic environment by the Provincial Health Directorate. Coronavirus vaccination in the province started on 14.01.2021 with healthcare workers.

Study Participants - Data Screening Process

This study consists of two independent phases:

The 1st phase covers the dates between 14.12.2020 and 15.04.2021. Information was scanned and evaluated retrospectively in the electronic environment. Also, healthcare workers who had or did not have the COVID-19 vaccine and those found to have PCR positivity before and after vaccination were examined with the data of the general provincial population.

In the second phase, information in the Public Health Management System (HSYS) of 1334 healthcare workers found positive as of 14.01.2021, the beginning of the vaccination calendar, was obtained by scanning daily records. Also, a phone call was made between 14.01.2021 and 22.02.2021. In this date range, 493 people found positive but whose vaccination status was unknown, who could be

reached, and whose verbal consents were obtained were included in the study. Also, age, gender, source case information, and vaccination status of positive healthcare workers were questioned.

Our study consisted of two independent phases because not all healthcare workers are vaccinated with the start of the vaccination calendar. Another reason is the continuation of the vaccination process. Therefore, only the retrospective registry was not scanned, and the demographic information, vaccination status, and source case information of the healthcare workers who were found positive were questioned by phone.

Statistical Analysis

The data obtained were analyzed in the computer by evaluating the sociodemographic characteristics of the participants, their vaccination status and their COVID-19 stories together. Numbers and percentages were used to represent frequency tables and graphs. Chi-square tests were used in the comparative analysis of categorical data, and relative risk calculation was used to compare the risk status for COVID-19 in vaccinated and unvaccinated individuals. To evaluate the vaccine's effectiveness while calculating the relative risk, the data after the second dose of vaccination 14 days and later were analyzed. A p-value<0.05 was considered statistically significant.

RESULTS

24,421 healthcare workers from file records were included in this study. Before vaccination, in the period 14.12.2020-13.01.2021, 8641 (21.68%) PCR (+) in the general population, 3028 (7.59%) PCR (+) in the period of the 1st dose of vaccine, 6057 (15.19%) PCR (+) in the period of the 2nd dose of vaccine, and after two doses of vaccination (14.03.2021-15.04.2021 period) 22318 (55.54%) PCR (+) cases were detected. While there were 515 (38.60%) PCR (+) cases in the pre-vaccination period in healthcare workers, 101 (7.57%) PCR (+) cases were detected during the first dose vaccination period, 132 (9.90%) PCR (+) cases during the second dose vaccination period, and 586 (43.93%) PCR (+) cases after two doses of vaccination. The rates of PCR (+) healthcare workers in the pre-vaccination period were 5.96% and 2.53% in the post-vaccination period. The ratio of vaccinated PCR (+) healthcare workers/vaccinated healthcare workers was 1.02%. Unvaccinated PCR (+) healthcare worker/Unvaccinated healthcare worker was 2.13(%) (**Table 1**) (**Figure 1**) (**Figure 2**). The first date of the second dose of vaccination is 11.02.2021. Fourteen days after this date, PCR results were evaluated based on the vaccination status between 25.2.2021-15.4.2021. Considering the vaccination status of all healthcare workers, 5.14% of the unvaccinated ones were found to be PCR (+), while 2.04% of those vaccinated were PCR (+) (p<0.001) (**Table 2**).

Table 1: Distribution of healthcare workers according to their vaccination status and COVID-19 PCR (+) status before and after vaccination

Parameter	Pre-Vaccination Period (14.12.2020-13.1.2021)	The period in which the 1st dose of vaccine was administered (14.1.2021-10.2.2021)	The period in which the 2nd dose of vaccine was administered (11.2.2021-13.3.2021)	Period After two doses of Vaccination (14.3.2021-15.4.2021)
Total PCR (+) Cases*	8641 (21,68%)	3028 (7,59%)	6057 (15,19%)	22138 (55,54%)
Total PCR (+) Healthcare Worker*	515 (38,60%)	101 (7,57%)	132 (9,90%)	586 (43,93%)
Total PCR (+) Healthcare Professional/ Total PCR (+) Case (%)	5,96	3,34	2,18	2,53
Number of Healthcare Workers Vaccinated**	0	17253 (70,65%)	16588 (67,93%)	17531 (71,79%)
Number of Non-vaccinated Healthcare Workers**	0	7168 (29,35%)	7833 (32,07%)	6890 (28,21%)
PCR (+) Healthcare Workers/Total Healthcare Workers (%)	2,11	0,41	0,54	1,33
Vaccinated Healthcare Workers/ Total Healthcare Workers (%)	0	70,65	67,93	71,79
Vaccinated PCR (+) Healthcare Workers/Vaccinated Healthcare Workers (%)	0	0,32	0,43	1,02
Non-Vaccinated PCR (+) Healthcare Workers/Non-Vaccinated Healthcare Workers (%)	0	0,64	0,70	2,13

PCR: Polymerase Chain Reaction
* : Row percentages are given
**: Their percentages in total healthcare workers (n=24,421) are given.

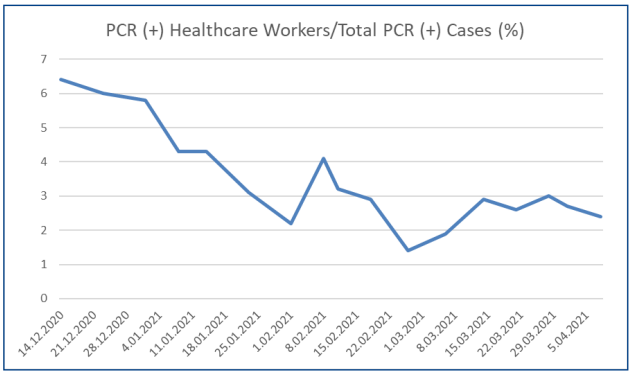

Figure 1: The rate of the change of PCR (+) healthcare workers to total PCR (+) cases (%) according to time

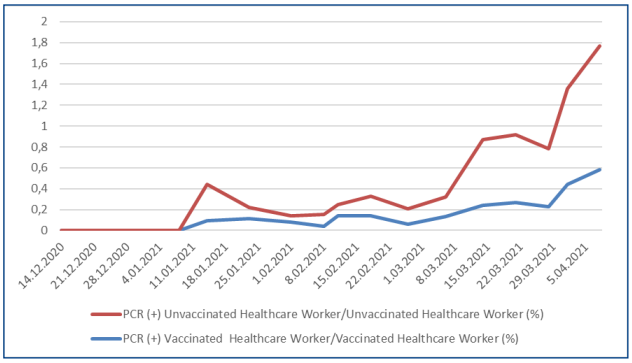

Figure 2: The ratio of vaccinated PCR (+) healthcare workers to vaccinated healthcare workers (%) and the ratio of unvaccinated PCR (+) healthcare workers to unvaccinated healthcare workers (%) according to time

Table 2: Comparison of the PCR (+) rate in unvaccinated healthcare workers with the PCR (+) rate in vaccinated healthcare workers

	COVID RT-PCR*				
	Positive	Negative	Total	RR (%95 GA)	p value
Unvaccinated	326 (5,14%)	6011 (94,86%)	6337 (100,00%)	2,52 (2,18-2,92)	<0,0001
Vaccinated	356 (2,04%)	17180 (97,96%)	17457 (100,00%)		
Total	682 (2,87%)	23112 (97,13%)	23794 (100,00%)		

*: The data are according to the records between 25.2.2021-15.4.2021. PCR:Polymerase Chain Reaction

In the second phase of the study, 493 PCR (+) healthcare workers were reached by phone. 309 (62.7%) of the participants were female, and 184 (37.3%) were male. The mean age was 34.88±9.3 years. The number of vaccinated healthcare workers is 247 (50.1%), while 246 (49.9%) healthcare workers are not vaccinated. When the source case is questioned, the source case of 397 (80.5) people is uncertain, and the source case of 98 (19.4) people is the home or workplace environment. Also, PCR (+) status after two vaccination doses was similar in gender (p:0.156). In addition, PCR (+) status was similar to groups younger than 40 and older (p:0.654).

Table 3: Comparison of the PCR (+) status of the healthcare professionals called after two doses of vaccination, according to age and gender characteristics

Characteristics	Rate of PCR (+) After 2 Doses of Vaccination *		Total	X2	p value
	Yes	No			
Under 40 years	121 (35,3%)	222 (64,7%)	343 (100%)	2,016	0,156
40 years and older	63 (42,0%)	87 (58,0%)	150 (100%)		
Total	184 (37,3%)	309 (62,7%)	493 (100%)		
	Yes	No	Total	X2	p value
Female	113 (36,6%)	196 (63,4%)	309 (100%)	0,201	0,654
Male	71 (38,6%)	113 (61,4%)	184 (100%)		
Total	184 (37,3%)	309 (62,7%)	493 (100%)		

*: Row percentages are given. PCR: Polymerase Chain Reaction

DISCUSSION

In our study, while the ratio of total PCR (+) healthcare workers to total PCR (+) cases was 5.96% before vaccination, this rate decreased to 2.81% after the second dose of vaccination. Therefore, the infection protection rate of the inactivated vaccine administered to healthcare workers was found to be 52.86% in the field.

COVID-19 vaccine studies continue in many centers at preclinical and clinical stages. The results of the studies conducted in different centers for the inactivated COVID -19 vaccine (CoronaVac) vary, and the results are as follows: In the Phase 3 results of the inactivated COVID-19 vaccine, it has been reported that the vaccine protects 50.65% from infection, 83.70% from medical intervention, and 100% from death and severe illness (8). In Phase 3 studies by Hacettepe University, the vaccine's effectiveness was determined as 83.5% and the rate of preventing hospitalization as 100% (9). A study conducted in Brazil showed that the effectiveness in preventing infection was 50.70% in Phase 3 studies (10).

In field studies conducted in Chile, it is known that the rate of protection against infection is 67%, and the rate of preventing hospitalization is 85% (11). In our study, when the rate of PCR (+) health care workers to total PCR (+) case numbers (%) changes according to time, the decrease in the number of cases in vaccinated healthcare workers suggests that the vaccine's protection is effective and overlaps with the literature.

In the Phase 3 studies of the inactivated COVID-19 vaccine, 25,000 participants in Brazil (8) and 10,216 participants in Turkey took part (9). Twelve thousand four hundred healthcare workers participated in the Phase

3 studies conducted by the Butantan Institute in Brazil (10). Furthermore, in studies conducted on 10.5 million people in the field in Chile, the vaccine's effectiveness was measured by comparing those who were vaccinated and those who did not (11). Our study determined that 17,253 of 24,421 healthcare workers serving in our province were administered inactive COVID-19 vaccine, and the number of evaluated patients was similar to the studies conducted.

The effect of the number of doses and the duration of administration between doses of the inactivated COVID-19 vaccine on protection is unclear. In the study of Palacios et al., the vaccination of the inactivated COVID-19 vaccine was administered to the participants with an interval of 14 days in the phase 3 studies, with an interval of 1 month in the study of Akova et al.. In another study involving only healthcare professionals, the vaccine was administered to the participants in two doses with an interval of 21 days (8–10). Although a 14-day interval between two doses of vaccine has been adopted in clinical studies, it is known that a 1-month interval between two doses in field applications increases the protection (12). Some authors also reported that the interval between two doses of more than 21 days increased the vaccine's efficacy rate to 62.3% (10). In the study, which included the results of vaccination studies carried out on 10.5 million people in the field in Chile, it was stated that the risk of contracting the disease was much higher in those who received a single dose of vaccine than those who received two doses (11). In our study, vaccination, which was done in 2 doses with one-month intervals, was evaluated following the calendar established by the Ministry of Health. While the ratio of PCR (+) healthcare workers to PCR (+) cases in the community was 5.6% in the pre-vaccination period, this rate decreased to 2.53% in the post-vaccination period. It is 3.34% at the time of the first dose and 2.31% at the time of the second dose, and it is similar to the studies done. It is thought that the increase in the PCR (+) case rate in the period after the administration of two doses of vaccine, compared to the period in which the second dose was administered, is due to a new peak of the COVID-19 epidemic in Turkey. In the study conducted by Bueno et al., it was emphasized that the low level of protection compared to the vaccine's effectiveness against mortal cases in clinical trials might be related to the severe second wave of the epidemic (11).

In the vaccination program carried out by Palacios on 12,396 registered health workers, 253 (2%) PCR (+) cases were detected at the end of the observation period (8). In our study, 586 (2.3%) PCR (+) cases were found out of 24,421 registered health workers at the end of the observation period, which is similar to our study (8).

57.8% of the study participants in Hacettepe on a healthy population were male, 42.2% were female, and the median age was 45 years (9). In the second independent phase of our study, 62.7% of the healthcare professionals who were contacted by phone and whose PCR (+) was detected after the vaccination process started were female and 37.3% male. Katılımcıların ortalama yaşı 34,88±9,3'tür. We obtained different data from the literature, and this may be the questioning of health workers, who are a special group and have PCR (+).

While evaluating the effectiveness of the vaccine in vaccinated and unvaccinated groups, the continuation of the current vaccination process and the periodical changes in the policies to combat the epidemic are the limitations of our study. However, although it is a limitation that the first phase of our study was scanned through the records, the inclusion of 24,421 health workers is one of its strengths. Another strength of our study is that our study consists of two phases and that the information in the 2nd phase is obtained directly from the individuals.

CONCLUSION

In the fight against the COVID-19 virus, which has been in our lives since December 2019, it is clear that vaccination has an indispensable importance in addition to basic measures such as hygiene and maintaining social distance. In this context, it is important to evaluate the vaccines that have passed the clinical stages and are still in use. Our study, in which we evaluated a Turkey experience with inactive CoronaVac vaccine; It is revealed that positive results occur in the period of inactive COVID-19 vaccine in healthcare workers and it reduces the spread of the disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karabuk University Non-Interventional Clinical Trials Ethics Committee (Date: 02/06/2021, Decision No: 2021/584).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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CASE REPORT
OLGU SUNUMU

Oral Isotretinoin Intake and Thyroiditis: Exploring the Association of a Rare Side Effect

Oral İzotretinoin Alımı ve Tiroidit: Nadir Bir Yan Etki İlişkisini Araştırmak

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ABSTRACT

Isotretinoin has been widely used to treat severe and resistant acne. While it has many beneficial effects, it is not without undesirable consequences. Most commonly, hypothyroidism has been reported as an adverse effect on the thyroid hormone pathway, which is an infrequent presentation of isotretinoin intake. In this report, we present the case of a 21-year-old woman who had taken oral isotretinoin for severe acne vulgaris for one month and subsequently complained of palpitations. On physical examination, tachycardia was noted. Laboratory tests and imaging results were consistent with thyroiditis. After discontinuing isotretinoin treatment, all symptoms and laboratory test results improved within one month. Hyperthyroidism is a rare adverse effect associated with isotretinoin treatment. Therefore, it is recommended to closely monitor thyroid function tests at more frequent intervals during the course of isotretinoin treatment.

Keywords: Isotretinoin, thyrotoxicosis, thyroiditis

ÖZ

İzotretinoin şiddetli ve dirençli akne tedavisi için yaygın olarak kullanılmaktadır. Birçok faydalı etkisi olmasına rağmen, istenmeyen sonuçlar olabilmektedir. İzotretinoin kullanımına bağlı tiroid hormon aksı üzerinde en sık hipotiroidizm advers etki olarak rapor edilmiştir. Bu vaka bildiriminde, şiddetli akne vulgaris için bir ay boyunca oral izotretinoin alan 21 yaşındaki çarpıntı şikayeti olan bir kadın hasta sunulmaktadır. Fizik muayenede taşikardi saptanmıştır. Laboratuvar testleri ve görüntüleme sonuçları tiroidit ile uyumludur. İzotretinoin tedavisi kesildikten sonra, tüm semptomlar ve laboratuvar test sonuçları bir ay içinde düzelmiştir. Hipertiroidizm, izotretinoin tedavisi ile ilişkili nadir bir advers etkidir. Bu nedenle, izotretinoin tedavisi sürecinde tiroid fonksiyon testlerinin daha sık aralıklarla yakından izlenmesi önerilir.

Anahtar Kelimeler: İzotretinoin, tirotoksikozis, tiroidit

INTRODUCTION

Isotretinoin is a curative treatment for moderate acne. Nevertheless, despite the established efficacy of isotretinoin in the treatment of acne, there exists a multitude of unforeseen adverse effects, including but not limited to allergic reactions, tinnitus, gastrointestinal disturbances, impaired nocturnal visual perception, photosensitivity, exacerbation of acne, and instances of palpitations, as reported in the literature (1,2). Fatigue, headache, mouth and eye dryness, and skin exfoliation are some of the frequent but disturbing adverse effects. Patients often tolerate these side effects in pursuit of improved skin health. However, some biological adverse effects have been reported, which can disrupt the functionality of the human body (3,4). Many of these effects have been observed during isotretinoin treatment (5).

As isotretinoin is fat-soluble and distributes to various tissues, numerous side effects can arise depending on the organs affected (6). Among these, the thyroid gland has been identified as a potential target. Hypothyroidism is a common occurrence in the reported cases (3), while thyrotoxicosis, a condition where there are elevated levels of thyroid hormones in the blood due to damaged thyroid cells, is a rare but serious complication.

While many groups of medications have been associated with thyrotoxicosis, there are not enough case reports linking it to isotretinoin use. Therefore, this case report provides valuable insights beyond current expectations.

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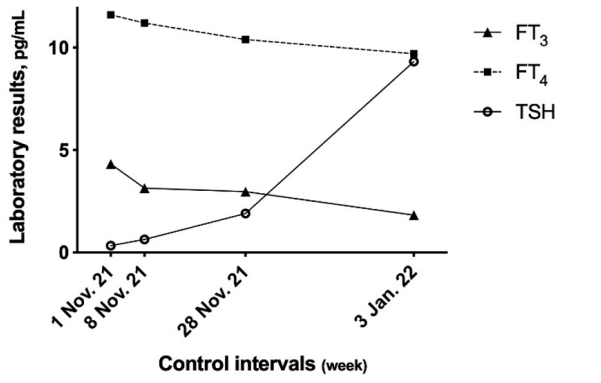
CASE REPORT

A 21-year-old female patient presented with severe acne vulgaris that had been refractory to treatment since 2018. She had previously received tetracycline and azithromycin therapies without success. In October 2021, the patient began taking oral isotretinoin, a dermatologist prescribed. Prior to initiating the treatment, the patient underwent a series of laboratory tests, including assessments of liver and kidney function, thyroid function, and a complete blood count, all of which yielded normal results. Isotretinoin was initiated by the dermatologist at an initial dosage of 10 mg once daily (below the recommended dose for acne treatment) and was increased to twice daily after one week.

However, during the third week of treatment, the patient experienced severe palpitations, fatigue, hair loss, and headaches. A physical examination revealed a pulse rate of 116 bpm and sweaty skin but no objective hair loss. On November 1, 2021, thyroid function tests were conducted, which revealed low levels of thyroid-stimulating hormone (TSH) = 0.07 mIU/L, (normal range 0,35-4,94), slightly elevated levels of free thyroxine (FT4) = 1.16 ng/dL, (normal range 0,61-1,12), and elevated levels of free triiodothyronine (FT3) = 4.32 pg/mL, (normal range 1,71-3,71), indicating a diagnosis of T3-T4-thyrotoxicosis. A radioactive iodine uptake study was also performed, which showed no nodules but revealed suppressed parenchyma. No nodules or volume enlargement were reported in the thyroid ultrasonography. Regrettably, the patient did not experience any significant improvement in her acne formation.

Subsequent to the discontinuation of isotretinoin treatment, thyroid function tests were repeated on November 8, 2021. The patient's complaints had resolved, and the TSH level had increased to 0.13 mIU/L, while the FT4 level had slightly decreased to 1.12 ng/dL. At the last control on November 28, 2020, the patient's thyroid function tests showed normal euthyroid status with a TSH level of 0.39 mIU/L and an FT4 level of 1.04 ng/dL. The patient's thyroid function was normal in the last control test in January 2021, with a TSH level of 1.91 mIU/L. The effect of thyroid cell damage on laboratory results over time is detailed in **Figure 1**.



FT$_3$, free triiodothyronine; **FT$_4$**, free thyroxine; **TSH**, thyroid-stimulating hormone

Figure 1. Variations in thyroid function test results during the presentation of the side effect and discontinuation of isotretinoin therapy.

DISCUSSION

The focus of this discussion is to consider the potential adverse effects of isotretinoin when prescribed. There have been many reports of side effects related to isotretinoin use, and the relationship between isotretinoin and autoimmune disorders is well known. In particular, gastrointestinal system problems are the most common unwanted presentations of isotretinoin intake (7). Popescu (2011) demonstrated that irritable bowel syndrome (IBS) is the leading complaint caused by isotretinoin (7). Conversely, the risk of IBS is dose-dependent, and discontinuation of treatment can lead to patient recovery. Gursoy (2012) drew our attention to several synchronous side effects of isotretinoin use (8), including autoimmune thyroiditis and ocular myasthenia gravis, which developed in the third week of isotretinoin use. Moreover, further medication was needed to recover from both complications, such as botulinum toxin A, prednisolone, and anti-thyroid treatment. In a case report, a higher level of TSH was noticed, as expected, in a young patient with complaints of menorrhagia and weight gain after isotretinoin use for 6 months (3). In another case reported by Minuk et al. (4), thyrotoxicosis was revealed in a young man who complained of fatigue and heat intolerance and had taken isotretinoin treatment for a month.

The common point in all these cases is that patients received drug treatments for at least one month, and the side effects occurred indirectly. Sometimes isotretinoin directly damages tissues, and local adverse effects may happen at that time. In their review, Brezezinski et al. (2017) identified the local and systemic adverse effects of using isotretinoin. Dermal complaints were numerically higher than the other systems (9). A housewife with serious hoarseness during isotretinoin treatment recovered three weeks after discontinuing isotretinoin (10). In most cases, the side effect disappears after the treatment is stopped. Some of them require further medication.

Like these uncommon reports, our case report is a result of the destruction of the thyroid gland by isotretinoin. Our patient had complaints within three weeks after starting the treatment. Although the laboratory tests were compatible with the early stages of thyrotoxicosis, she was symptomatic and had to perform the tests. If the tests were done later, an obvious thyrotoxicosis could be detected. Our case was presented with hyperthyroidism rather than hypothyroidism, which is not a common side effect. All of the cases had been taking isotretinoin for at least three weeks, so there should be an accumulation time for triggering the clinical or biochemical damages.

These clinics may also consider the possibility that the increased prevalence of hypothyroidism in isotretinoin treatment could be attributed to chronic destruction of the thyroid gland, leading to its impairment. Furthermore, during the process of destruction, some patients might manifest evident hyperthyroidism, while others may present with subacute clinical features.

We may have rushed to do the initial tests after starting the isotretinoin treatment, but the presence of the patient's hyperthyroid clinic made us perform the tests earlier. In conclusion, isotretinoin still maintains its reputation for having beautiful skin without a knife. However, humanity can exacerbate the immune system for the sake of beauty. Both clinicians prescribing isotretinoin and patients should be alert for this potential risk. Therefore, it would be appropriate to repeat laboratory tests monthly.

ETHICAL DECLARATIONS

Informed Consent: The patient signed the informed consent form.

Review Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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LETTER TO THE EDITOR
EDİTÖRE MEKTUP

Bebeklerde Serum γ-Glutamil Transferaz Düzeyleri

Reference Values of Serum γ-Glutamil Transferase Levels in Infants

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Sayın Editör,

Chronicles of Precision Medical Researchers Dergisi'nin son sayısında (1) yayımlanan Menekşe E tarafından yazılan "Preterm ve Term Bebeklerde Serum γ-Glutamil Transferaz Düzeylerinin Referans Değerlerinin Belirlenmesi" başlıklı makaleyi ilgi ile okuduk. Makale ile ilgili olarak dikkatimizi çeken bazı eleştirilerimizi aşağıda özetlemeyi uygun bulduk;

1. "Giriş" bölümünde yenidoğanlarda gama-glutamiltransferaz (GGT) düzeyi referans aralığının nispeten düşük hasta sayısı ile yapılmış eski çalışmalar ile hesaplandığı gerekçesiyle yenidoğan bebeklerin ilk bir ayı için referans GGT değerlerinin belirlenmesinin amaçlandığı bildirilmektedir. Ancak CALIPER veritabanı ve mobil uygulaması ile GGT için yaşa ve cinsiyete özel referans değerleri sağlanabilmektedir (www.sickkids.ca/Caliperproject/index.html) (2).

2. "Gereç ve Yöntem" bölümünde çalışma grubunun "Yenidoğan Yoğun Bakım Ünitesi" hastalarından oluştuğu anlaşılmaktadır. Herhangi bir metabolik veya karaciğer hastalığı, kolestazı, kültürle kanıtlanmış enfeksiyonu, serum aminotranferaz enzim düzeyleri yüksek olan hastaların çalışmaya alınmadığı belirtilmiştir. Bu durumda herhangi bir ilaç alan bebeklerin çalışma dışı bırakılmadığı anlaşılmaktadır. Bazı antikonvülzan ilaçlar (fenobarbital, fenitoin) tarafından indüklenmesi sonucu GGT aktivitesinin etkilenebildiği ve bazı ilaçların hepatotoksik etkisine bağlı olarak GGT düzeylerinin yükselebildiği bilinmektedir (3). Ayrıca, bebeğin entübe olup olmaması, hipoksi durumu, kardiyovasküler hastalık, kalp yetmezliği veya böbrek yetersizliği gibi durumlar da GGT düzeyini etkileyebilmektedir (4). "Yenidoğan Yoğun Bakım Ünitesi" hastalarında ilaç tedavilerinin kullanılması gerekliliği dikkate alındığında bu hastaların GGT değerlerinin referans olarak kullanılmasının yanıltıcı olacağı unutulmamalıdır.

3. "Bulgular" kısmında;

   - Çalışmaya dahil edilen erkek/kız bebek sayısı, gruplar için bebeklerin doğum ağırlıkları ve doğum şekilleri **Tablo 1** ile uyumlu değildir.
   - **Tablo 1**'de p-değeri sütununda verilen değerlerin hangi karşılaştırmalara ait olduğu belli değildir.
   - Bulgular kısmında verilen 1-7 gün ve 7-28 günlük ve 3 grup için GGT1 ve GGT2 değerleri arasındaki fark değerlendirilirken, Tek Yönlü Varyans Analizi ile kullanıldı ise (verilen istatistiklere göre) p-değerleri sırasıyla GGT1 için p=0.0576 ve GGT2 için p=.02112 olması gerekir. Eğer Kruskal Wallis testi ile analiz edildi ise de uygun istatistikler verilmeliydi.
   - Erkek ve kız bebeklere ait GGT1 ve GGT2 kıyasında eğer kıyas Bağımsız örneklemler t testi ile yapıldıysa, bulgular kısmında verilen GGT1 için p-değerleri sırasıyla p=0.00 yerine, 98 erkek ve 102 kız için p=0.4344; 105 erkek ve 95 kız için p=0.4406; GGT2 için p=.00 yerine p değerleri p=0.1644 ve p=0.1732 bulunmalıydı. Eğer cinsiyete göre bu kıyas Mann-Whitney U testi ile yapıldıysa da uygun istatistikler verilmeliydi.
   - Bebeklerin doğum şekline göre yapılan kıyas da cinsiyete göre kıyas gibi eğer parametrik test kullanılarak yapıldı ise p değerleri sırasıyla GGT1 için 166 ve 45 hacimle p=0.9041 ve p=0.9328 olarak; GGT2 için aynı sıra ile p=0.1893 ve p=0.3615 olarak hesaplanmalıydı.

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- Çalışmanın başlığında verilen referans değerinin belirlenmesine ilişkin bulgular kısmında herhangi bir sonuç yoktur. Referans aralığı belirlerken uygun birçok istatistiksel metot söz konusu iken, gerekli varsayımlar incelenmeden referans aralığını belirlemek uygun olmayacaktır.

4. Makalenin "Sonuç" bölümünde ise makale yazarları tarafından çalışmada bulunan değerlerin herhangi bir hastalığı olmayan yenidoğanlar için uygun bir referans olmasa bile yoğun bakım ünitelerinde izlenen yenidoğan bebekler için uygun referans aralığı olarak kullanılabileceğinin düşünüldüğü bildirilmiştir. Ancak değerlendirmelerde normal sağlıklı bebeklerin referans aralıklarına göre kıyaslamak yerine hasta bebeklerin referans değerlerinin kullanılması da doğru bir yaklaşım olmayacaktır.

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Elif Menekşe
Amasya Üniversitesi Sabuncuoğlu Şerefeddin Eğitim ve Araştırma Hastanesi

Munevver Bas
Balıkesir Atatürk Şehir Hastanesi, Yenidoğan Kliniği, Balıkesir,

Sayın Editör,

Değerli eleştiriler ve katkılar için teşekkür ederiz.

1. Caliper veritabanı ve mobil uygulaması ile hesaplanan GGT referans aralığı çok geniş bir yaş aralığını içermektedir ve doğum sonrası ilk 15 gün için yeterli bilgi sağlamamaktadır. Bu çalışma ile amacımız özellikle yenidoğan döneminde problem olabilecek yorumlara açık GGT değerinin daha spesifik olarak belirlemektir.
2. Çalışmamıza alınan hastalarda karaciğer fonksiyon testlerini etkileyecek ilaç alan hastalar çalışmaya dahil edilmemiştir. Yazıda belirtmeyi unuttuğumuz bu duruma dikkat çektiğiniz için teşekkür ederiz. Bunun haricindeki durumlarda (entübasyon, kardiyovasküler hastalık…) destek alan bebeğin GGT değerlerinin belirlenmesi açısından da yararlı olacağını düşündüğümüz için bu hasta grubunu çıkarmadık. Ayrıca daha önceki çalışmalarda bu hasta grubu çalışmaya dahil edildiği için biz de dahil edilmelerini uygun gördük. (1)
3. Tablo 1'deki geç preterm doğum 6/67 ve term 10/85 (doğum şekli Normal/sezaryan satırı) olacak şekilde geçirilecekken hata yapılmış. Katkınız için teşekkür ederiz.

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