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On behalf of the Medical Faculty of Gaziantep Islam Science and Technology University
Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi adına

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Chief Editor/Baş Editör

İbrahim Halil Türkbeyler, Prof.

Clerk of Editorial Office/Sorumlu Yazı İşleri Müdürü

Mehmet Göl, Asst. Prof.

Aim

Experimental and Applied Medical Science aims at being a current and easily accessible academic publication in which striking research results that will improve the quality of life and are unique from every field of medical sciences.

Amaç

Experimental and Applied Medical Science, yaşam kalitesini arttıracak çarpıcı araştırma sonuçlarının sunulduğu, tıp bilimlerinin her alanında benzersiz, güncel ve kolay erişilebilir bir akademik yayın olmayı hedeflemektedir.

Scope

Experimental and Applied Medical Science is an open-access, internationally double-blind peer reviewed academic medical journal which is published in English four times a year, under the auspices of Medical Faculty of Gaziantep Islam Science and Technology University. The journal receives manuscripts for consideration to be publishing in the form of research articles, reviews, letter to editor, brief notification, summary notification etc. which could have been presented from within the country or abroad and including experimental animal studies related to the pathogenesis of diseases, pharmacological, clinical, epidemiological and deontological studies, also studies in the fields of improving public health, health services or health insurance.

During evaluation or publication no charge is demanded from authors. The journal is published every 3 months (March, July, September and December) with 4 issues per year. The literary language of the journal is English. Abstract part of the manuscript only should also be submitted in Turkish.

Kapsam

Experimental and Applied Medical Science, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi himayesinde yılda dört kez İngilizce olarak yayınlanan açık erişimli, uluslararası çift kör hakemli bir akademik tıp dergisidir. Dergi, yurt içinden veya yurt dışından, hastalık patogenezleri ile ilişkili deneysel hayvan çalışmaları, klinik, farmakolojik, epidemiyolojik, deontolojik çalışmalar ile beraber halk sağlığının geliştirilmesi amacı taşıyan ve sağlık hizmetleri veya sağlık sigortaları konularında araştırma makaleleri, derlemeler, vaka sunumları, kısa bildirimleri, özet bildirimleri vs. yayınlamak için değerlendirmeye kabul etmektedir. Değerlendirme veya yayın sırasında yazarlardan herhangi bir ücret talep edilmez.

Dergi 3 ayda bir (Mart, Temmuz, Eylül ve Aralık) yılda 4 sayı olarak yayımlanır. Derginin yazı dili İngilizcedir. Makalenin sadece özet kısmı Türkçe olarak da gönderilmelidir.

Ethical Principles and Publication Policy

Manuscripts are only considered for publication provided that they are original, not under consideration simultaneously by another journal, or have not been previously published. Direct quotations, tables, or illustrations that have extracted from any copyrighted material must be accompanied by written authority for their use from the copyright owners. All manuscripts are subject to review by the editors and referees. Deserving to be publishing is based on significance, and originality of the material. If any manuscript is considered to deserve publishing, it may be subject to editorial revisions to aid clarity and understanding without changing the data presented.

Experimental and Applied Medical Science strictly adheres to the principles set forth by "Helsinki Declaration" whose web address is below.

https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210525133548_b192cec0.pdf

Editorial Board declares that all reported or submitted studies conducted with "human beings" should be in accordance with those principles.

Manuscripts presenting data obtained from a study design conducted with human participants must contain affirmation statements in the *Material and Methods* section indicating approval of the study by the institutional ethical review committee and "informed consent" was obtained from each participant. Also all manuscripts reporting experiments in which laboratory animals have been used should include an affirmation statement in the *Material and*

Etik İlkeler ve Yayın Politikası

Makaleler, orijinal/özgün olmaları, eş zamanlı olarak başka bir dergi tarafından incelenmemeleri veya daha önce yayınlanmamış olmaları koşuluyla yayına kabul edilir. Telif hakkıyla korunan herhangi bir materyalden alınan doğrudan alıntılar, tablolar veya resimler, kullanımları için telif hakkı sahiplerinden alınan yazılı izinle birlikte sunulmalıdır. Tüm yazılar editörler ve hakemler tarafından incelemeye tabidir. Yayınlanmaya hak kazanılması, materyalin önemine ve özgünlüğüne bağlıdır. Herhangi bir makalenin yayınlanmayı hak ettiği düşünülürse, sunulan veriler değiştirilmeden netlik ve anlayışa yardımcı olmak için editör revizyonlarına tabi tutulabilir.

Experimental and Applied Medical Science, internet adresi aşağıda yer alan "Helsinki Deklarasyonu" ile belirlenen ilkelere sıkı sıkıya bağlıdır.

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Editör Kurulu, "insan" ile yapılan tüm raporlanan veya sunulan çalışmaların bu ilkelere uygun olması gerektiğini beyan eder. İnsan katılımcılarla yürütülen bir çalışma tasarımından elde edilen verileri sunan makaleler, *Gereç ve Yöntemler* bölümünde çalışmanın kurumsal etik inceleme komitesi tarafından onaylandığını ve her katılımcıdan "bilgilendirilmiş onam" alındığını belirten onay ifadeleri kullanmalıdır. Ayrıca laboratuvar hayvanlarının kullanıldığı deneyleri bildiren tüm yazılar, *Gereç ve Yöntemler* bölümünde, internet adresi aşağıda

Methods section validating that all animals have received human care in compliance with the "Guide for the Care and Use of Laboratory Animals" whose web address is below and reveal approval by the institutional ethical review board. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818130308_dca61056.pdf

If there is a commercial relation that contributes to the study process or there is an institution that provides financial support for the study; the authors must declare that they have no commercial relationship with the commercial product, drug, company used, or what kind of relationship (consultant or any other agreement) they have, if any.

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

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belirtilmiş olan "Laboratuvar Hayvanlarının Bakımı ve Kullanımı Kılavuzu"na uygun olarak tüm hayvanların insanî bir bakım aldığını doğrulayan bir beyan ile kurumsal etik inceleme kurulunun onayını içermelidir. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818130308_dca61056.pdf

Çalışma sürecine katkı sağlayan ticari bir ilişki veya çalışmaya maddi destek sağlayan bir kurum varsa; yazarlar ticari ürün, ilaç, aracılık eden şirket ile ticari bir ilişkilerinin olmadığını veya varsa ne tür bir ilişkisi (danışmanlık veya başka bir anlaşma) olduğunu beyan etmelidir.

Değerlendirme ve yayınlama süreçleri ücretsizdir. Değerlendirme ve yayın sürecinin hiçbir aşamasında yazarlardan ücret talep edilmez. Tüm yazılar https://dergipark.org.tr/tr/pub/eams adresinde bulunan çevrimiçi başvuru sistemi üzerinden gönderilmelidir. Dergi ile ilgili kullanım kılavuzları, teknik bilgiler ve gerekli formlar derginin internet sayfasında yer almaktadır.

Derginin tüm masrafları Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi tarafından karşılanmaktadır. Reklam vermeyi düşüne kişi veya kurumlar yayın ofisi ile iletişime geçmelidir. Reklam görselleri sadece Baş Editör'ün onayı ile yayınlanabilir.

Tüm araştırmacılar, makaleye doğrudan akademik veya bilimsel olarak katkıda bulunmuş olmalıdır. Yazarlar, makalenin planlanması, uygulanması, yazılması veya gözden geçirilmesi aşamalarından birine veya birkaçına katkıda bulunmuş olmalıdır. Tüm yazarlar nihai versiyonu onaylamalıdır. Bilimsel kriterlere uygun bir makale hazırlamak yazarların sorumluluğundadır.

the final version. It is the authors' responsibility to prepare a manuscript that meets scientific criterias.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Medical Faculty of Gaziantep Islam Science and Technology University, editors, editorial board, and/or publisher; the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

All manuscripts involving a research study must be evaluated in terms of biostatistics and it must be presented altogether with appropriate study design, analysis and results. ***p*** values must be given clearly in the manuscripts. Other than research articles, reviews, case reports, letters to the editor, etc. should also be original and up to date, and the references and, if any, their biostatistical parts should be clear, understandable and satisfactory.

The publication language of the journal is English. In addition, the abstract part of the article must be uploaded in both Turkish and English. Manuscripts should be evaluated by a linguist before being sent to the journal.

All manuscripts and editorial correspondence must be submitted online to the editorial office, https://dergipark.org.tr/tr/pub/eams.

According to the Law on Intellectual and Artistic Works, which was first published in the Official Gazette with the law number 5846 on 13/12/1951, whose web address is below, and on which subsequently various changes have been made or novel parts have been added in time, all kinds of publication rights of the articles accepted

Dergide yayınlanan yazılarda ifade edilenler veya görüşler, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi, editörler, yayın kurulu ve/veya yayıncının görüşlerini değil, yazar(lar)ın görüşlerini yansıtır; editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez.

Araştırma çalışması içeren tüm yazılar biyoistatistiksel açıdan değerlendirilmeli ve uygun çalışma düzeni, verilerin analizi ve sonuçları ile birlikte sunulmalıdır. ***p*** değerleri yazılarda açık olarak verilmelidir. Araştırma makaleleri dışında derlemeler, olgu sunumları, editöre mektuplar vb. de orijinal/özgün ve güncel olmalı, kaynaklar ve varsa biyoistatistiksel kısımlar açık, anlaşılır ve tatmin edici olmalıdır.

Derginin yayın dili İngilizce'dir. Ayrıca makalenin özet kısmı hem Türkçe hem de İngilizce olarak yüklenmelidir. Yazılar dergiye gönderilmeden önce bir dilbilimci/konunun uzmanı tarafından değerlendirilmelidir.

Bütün çalışmalar ve editör kurulu ile yazışmalar çevrimiçi olarak, https://dergipark.org.tr/tr/pub/eams adresi üzerinde yayın ofisine gönderilmelidir.

İnternet adresi aşağıda belirtilmiş olan, ilk olarak 13/12/1951 tarih ve 5846 sayılı Kanun ile Resmi Gazete'de yayımlanan, sonraları üzerinde değişiklikler yapılmış veya yeni kısımlar eklenmiş olan Fikir ve Sanat Eserleri Kanunu'na göre; yayına kabul edilen makalelerin her türlü yayın hakkı dergiyi yayınlayan kuruma aittir. Ancak makalelerdeki düşünce ve öneriler tamamen yazarların sorumluluğundadır. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818145630_406d24df.pdf

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Author Guidelines

Submission of a paper will be taken to imply that it has not previously been published and that it is not being considered for publication elsewhere. Decision as to publication of papers submitted to the Experimental and Applied Medical Science will be based on the opinion of the Editorial Board as to the significance and originality of the work.

Manuscripts should be prepared electronically using an appropriate “office word” compatible text-processing package, formatted for A4 size, double-spaced throughout, and using a “Times New Roman” 12 point font. Articles must be written in English. Abstracts must be written in both Turkish and English. Text should flush left, and not be justified. Words should not be hyphenated. Pages should be numbered sequentially.

There should be a separate title page with:

a) The title

b) The authors' names

c) The laboratory of origin, with complete address of each author

d) A running title

e) Corresponding author and e-mail

f) Conflict of interest

g) Acknowledgements

The main body of full-length paper should be divided into:

1. Abstract

2. Introduction

3. Material and Methods

4. Results

5. Discussion

Yazım Kuralları

Bir çalışmanın dergimize gönderilmesi için bu çalışmanın daha önce yayınlanmamış veya başka bir akademik dergide şu anda yayınlanmak üzere değerlendirilmiyor olması koşulu ile mümkündür. Experimental and Applied Medical Science’a gönderilen her türlü çalışmanın yayınlanmasına ilişkin karar, Yayın Kurulu'nun çalışmanın önemi ve özgünlüğü konusundaki görüşüne dayanacaktır.

Çalışmalar, ya “office word” programı ile ya da bu program ile uyumlu uygun bir metin işleme programı kullanılarak, A4 boyutunda hazırlanmalı, baştan sona çift aralıklı ve “Times New Roman” tarzında 12 punto yazı tipi kullanılarak elektronik ortamda yazılmalıdır. Makaleler İngilizce yazılmalıdır. Özetler hem Türkçe hem de İngilizce olarak yazılmalıdır. Metin iki yana yaslandırılmamalı, sadece sola yaslanmamalıdır. Kelimeler kısa çizgi ile hecelenmemelidir. Sayfalar sırayla numaralandırılmalıdır.

Aşağıdakileri içeren ayrı bir başlık sayfası olmalıdır:

a) Başlık

b) Yazarların isimleri

c) Her yazarın tam adresi ile birlikte çalıştıkları laboratuarlar

d) Kısa başlık

e) İletişimdeki yazar ve iletişim bilgileri

f) Çıkar çatışması beyanı

g) Teşekkür, bilgilendirme

Tam uzunluktaki kağıdın ana gövdesi şu bölümlere ayrılmalıdır:

1. Özet

2. Giriş

6. Conclusion
7. Conflict of interest
8. Acknowledgement
9. References

In general, there are no specific word lengths for any manuscript. The general principle is that a manuscript can be as long as necessary to communicate clearly and most effectively the scientific message, but should be as short as possible to achieve a complete presentation of the information without undue repetition or redundancy.

In the *Materials and Methods* section, the source of all compounds, equipment or software should be identified by the full name of the supplier, city, state/country. The chemical names of any drug should precede the trade name.

Papers describing animal experiments must define species, strain, sex, age, supplier and number of animals used. An ethical statement concerning the use of animals, or the details of ethical approvals, consent and recruitment of human subjects should be clearly stated. *Results* and *Discussion* can be broken down into subsections for improving the comprehensibility. The Results should not repeat methodological details and should avoid the discussion of the data.

The results of statistical tests should be incorporated in the body of the text, typically in the *Results* section, rather than in figure legends. Adequate description of statistical analysis should be provided. Statistical measures of variation in the text, illustrations and tables, should be identified. All dimensions and measurements must be

3. Gereç ve Yöntemler
4. Sonuçlar
5. Tartışma
6. Bağlam
7. Çıkar çatışması
8. Teşekkür, bilgilendirme
9. Kaynaklar

Genel olarak, herhangi çalışma için şart koşulan belirli bir kelime sayısı/metin uzunluğu yoktur. Genel ilke; bir makalenin bilimsel mesajı açık ve etkili bir şekilde iletmek için gerektiği kadar uzun olabileceği, ancak gereksiz tekrar veya fazlalık olmadan bilgilerin eksiksiz bir sunumunu elde etmek için mümkün olduğunca kısa olması gerektiğidir.

Gereçler ve Yöntemler bölümünde, tüm bileşiklerin, malzemelerin veya yazılımların kaynağı, tedarikçinin tam adı, şehir, eyalet/ülke ile tanımlanmalıdır. Herhangi bir ilacın kimyasal isimleri ticari isminden önce gelmelidir.

Hayvan deneylerini açıklayan makaleler, tür, soy, cinsiyet, yaş, tedarikçi ve kullanılan hayvan sayısını açıkça tanımlamalıdır. Hayvanların kullanımına ilişkin bir etik beyan veya insan deneklerin etik kurul onayları, bilgilendirilmiş onamları ve çalışmaya dâhil edilmelerine ilişkin ayrıntılar açıkça belirtilmelidir. *Sonuçlar ve Tartışma* bölümleri, anlaşılırlığı artırmak için alt bölümlere ayrılabilir. Sonuçlar, metodolojik ayrıntıları tekrarlamamalı ve verilerin tartışılmasından kaçınmalıdır.

İstatistiksel testlerin sonuçları, şekillerin altındaki açıklama kısımlarından ziyade metnin gövdesine, tipik olarak Sonuçlar bölümüne dâhil edilmelidir. İstatistiksel analizin yeterli bir şekilde açıklaması sağlanmalıdır. Metinde, resimlerde ve

specified in the metric system.

All subscripts, superscripts, Greek letters and unusual characters must be clearly identified.

In the text, abbreviations should be used consistently. Abbreviations should be defined on first use.

References should be designed in “Vancouver” style. While writing references, “Times New Roman” 10 point font should be used. Multiple authors should be separated by a comma. If there are more than three authors, after the 3rd author, "et al." should be inserted without a comma for both article and book references. If reference is made from a chapter in a book and there are many authors belonging only to this chapter, the title and chapter of the book are indicated, the first three of the chapter authors are written, and "et al." statement is added for subsequent authors.

Example:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.

2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.

3. Çekmen MB, Turgut M, Türköz Y, et al. Nitrik Oksit (NO) ve Nitrik Oksit Sentaz (NOS)'ın Fizyolojik ve Patolojik Özellikleri. Türkiye Klinikleri Journal of Pediatrics. 2001;10(4):226-35.

4. Parlakpınar H, Örüm MH, Acet A. Kafeik asit fenetil ester (KAFE) ve miyokardiyal

tablolarda istatistiksel varyasyon ölçütleri tanımlanmalıdır.

Tüm boyutlar ve ölçüler metrik sistemde belirtilmelidir.

Tüm alt simgeler, üst simgeler, Yunan harfleri ve olağandışı karakterler açıkça tanımlanmalıdır.

Metinde kısaltmalar tutarlı bir şekilde kullanılmalıdır. Kısaltmalar ilk kullanımda tanımlanmalıdır.

Kaynaklar “Vancouver” tarzında yazılmalıdır. Kaynaklar yazılırken, “Times New Roman” 10 punto kullanılmalıdır. Birden çok yazar virgülle ayrılmalıdır. Hem makale hem de kitap referanslarında, eğer üçten çok yazar varsa, 3. Yazardan sonra virgül ve “et al.” ifadesi kullanılmalıdır. Kitapta bir bölümden referans yapılıyorsa ve sadece bu bölüme ait çok sayıda yazar varsa, kitabın başlığı ve bölümü belirtilip, bölüm yazarlarının ilk üçü yazılıp ve ardından sonraki yazarlar için “et al.” ifadesi eklenmelidir.

Örnek:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.

2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.

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5. Yıldırım AB. The effects of maternal hypothyroidism on the immunoreactivity of cytochrome p450 aromatase in the postnatal rat testes. 2015; Doctoral thesis.
6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).
7. Kuran O, İstanbul, Filiz Kitabevi. Sistematik Anatomi. 1983 p. 76-9.
8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.
Submit illustrations as separate files, only as TIFF or EPS files, with a minimum resolution of 300dpi.
Tables of numerical data should each be typed with double spacing on separate pages numbered in sequence in numerals, provided with a heading, and referred to in the text, as Table 1, Table 2, etc. Each table should have a brief but descriptive heading. Explanatory matter should be included in footnotes to the table.
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4. Parlakpınar H, Örüm MH, Acet A. Kafeik asit fenetil ester (KAFE) ve miyokardiyal iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.
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6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).
7. Kuran O, İstanbul, Filiz Kitabevi. Sistematik Anatomi. 1983 p. 76-9.
8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.
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Bilimsel araştırmalarınızı desteklemek ve geliştirmek için elektronik ek materyaller kabul edilmektedir. Ek dosyalar, yazara, destekleyici uygulamaları, filmleri, animasyon dizilerini, yüksek çözünürlüklü

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görüntüleri, arka plan veri kümelerini, ses kayıtlarını ve daha fazlasını yayınlamak için ek olanaklar sunmaktadır.

Başvuru sırasında çıkar çatışmasının ve mali destek konularının açıklanması elzemdir. Yazarlar, makalelerinin yayımlanma tarihinden önce ortaya çıkabilecek ek çıkar çatışmalarını veya bulunan mali destekleri dergiye bildirmekle yükümlüdür. Tüm yazarlar, makalelerinin konusuyla doğrudan ilgili olsun ya da olmasın, tüm olası çıkar çatışmalarını ve mali desteği bireysel olarak açıklamalıdır.

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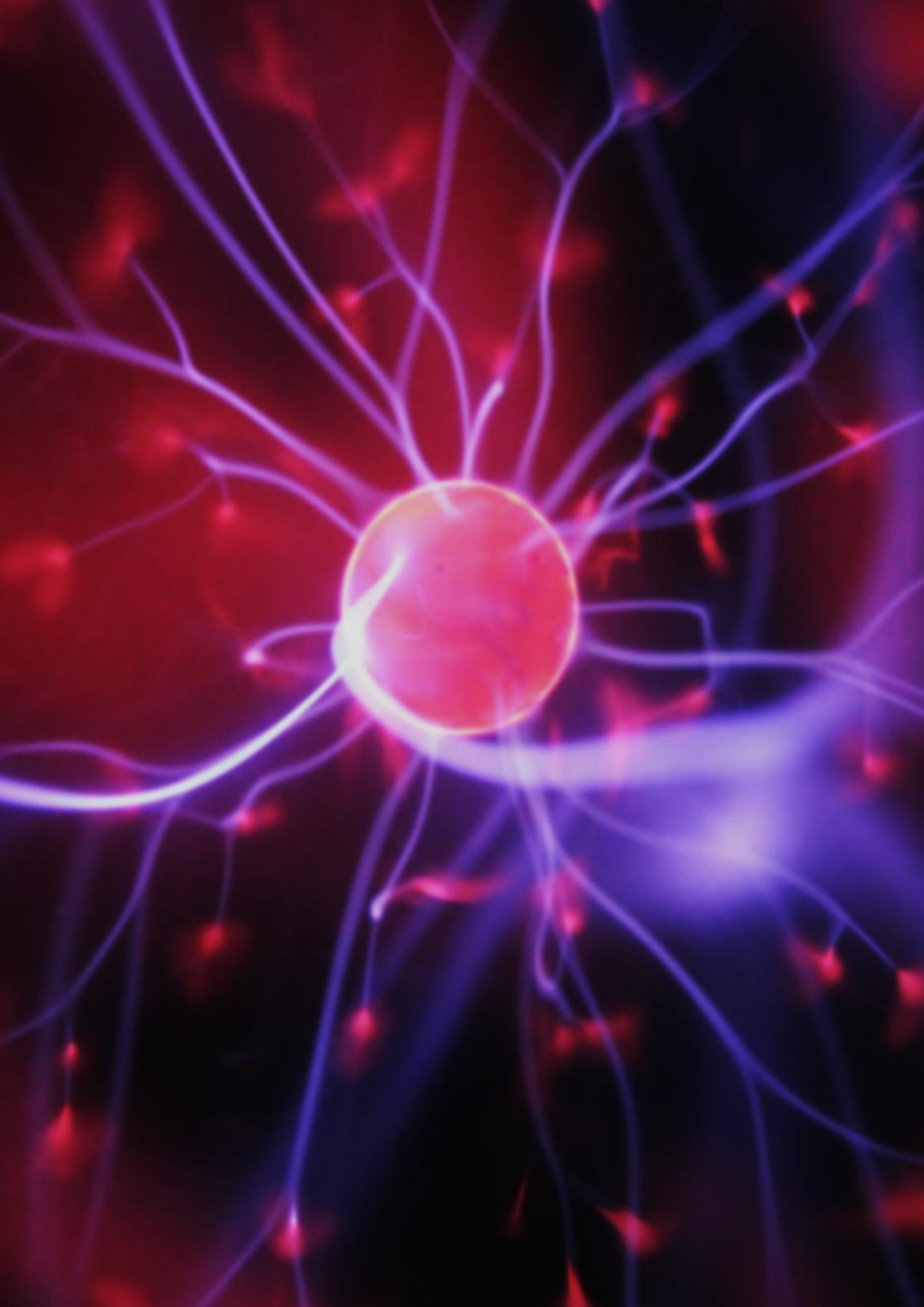

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Review Article

Exploring the Potential of Artificial Intelligence in Infectious Disease

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Abstract

Artificial intelligence (AI) is effectively addressing numerous challenges in the detection and treatment of infectious diseases, leveraging its inherent capabilities. Our research's primary focus was on the key obstacles associated with AI in the context of infectious diseases. This review recommends using AI in both clinical practice and infectious disease research. AI assists academics in saving time by efficiently arranging the various components of a paper, including the title, abstract, introduction, methodology, findings, and discussion. As a result, the pace of academic writing increases and improves. Certain assumptions in the field of AI can be misleading or incorrect, compromising the study's validity. Contemporary AI systems offer precise and dependable outcomes, although they frequently lack profound understanding. The lack of self-diagnostic technology in AI results in incorrect object or situation identification and poses potential safety risks. Effective medical technology utilization requires regulatory scrutiny and monitoring. Several institutions have halted their research activities because of AI inefficiency. AI can aid researchers in gathering medical data and conducting patient surveys.

Key words: *Infectious disease, Medical data, Artificial intelligence*

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Introduction

Artificial intelligence (AI) is the emulation of human cognitive processes by computers, especially computer systems. The processes include learning (acquiring material and rules for its application), reasoning (using rules to draw approximate or definite conclusions), and self-correction (1). AI is often classified into two categories: Narrow AI, often known as weak AI, is specifically created and educated to do a single job. It is focused on efficiently carrying out a certain activity, such as face recognition, language translation, or playing chess. The majority of current AI systems belong to this group (2). Strong AI, also known as general AI, has human-like capabilities and can comprehend, acquire, and use knowledge in several fields. AI is mostly theoretical and continues to be the focus of current research. AI approaches include machine learning for computers to learn from data and make predictions or judgements, and natural language processing for computers to comprehend and produce human language (3). Additional methods include computer vision, robotics, expert systems, and neural networks. AI is used in many sectors, such as healthcare, finance, education, transportation, entertainment, and beyond. It has the capacity to transform industries, enhance efficiency, and address intricate issues (4). Nevertheless, technology also gives rise to ethical and cultural difficulties, including employment displacement, algorithmic prejudice, privacy concerns, and the risk of abuse. It is crucial to tackle these difficulties and guarantee that the development and use of AI contribute positively to society (5).

AI has great promise in the areas of infectious disease research, prevention, and control. Here are some applications of AI:

AI algorithms can examine extensive datasets of clinical symptoms, test findings, and demographic information to detect patterns that suggest infectious illnesses. AI models may aid in the early identification of epidemics by assessing social media postings, internet search patterns, and news stories to identify signals of increasing sickness activity. AI algorithms can evaluate molecular structures to predict the efficacy of new medication molecules in fighting infectious illnesses, aiding in drug discovery and development. This may greatly speed up the drug development process by cutting down on the time and money needed for laboratory testing (6).

Epidemiological Modelling: AI-driven models may mimic the transmission of infectious illnesses across populations and forecast upcoming epidemics. These models include elements including

population density, travel patterns, and environmental conditions to provide significant insights for public health planning and response operations (7).

Customised Treatment: AI algorithms may examine patient data to create treatment regimens that are specific to individual risk factors, genetic predispositions, and reactions to therapy. Enhancing patient outcomes by refining treatment approaches and minimising the likelihood of problems (8).

AI systems can analyse real-time data from many sources including electronic health records, wearable devices, and environmental sensors to track disease spread and detect emergent hazards. This allows public health officials to promptly carry out interventions and containment measures. AI algorithms may aid in developing and refining vaccines by forecasting antigen structures, pinpointing new vaccination options, and enhancing vaccine compositions. This may expedite the process of creating vaccines for newly developing infectious illnesses. AI algorithms can assess healthcare resource utilisation trends to anticipate future demand for medical supplies, hospital beds, and healthcare professionals during infectious disease epidemics. This aids healthcare companies in optimising resource allocation and guaranteeing prompt patient access to services (9, 10).

How can AI be Applied in Infectious Disease?

AI may be used in several ways to tackle issues of infectious illnesses. AI algorithms may evaluate various datasets, such as patient symptoms, test findings, and environmental variables, to identify patterns that suggest infectious illnesses. Machine learning models may assist healthcare practitioners in diagnosing infections more precisely and rapidly, which can aid in prompt treatment and containment efforts. AI-powered models in epidemiological modelling may mimic disease transmission dynamics in communities by considering demographics, movement patterns, and environmental circumstances (11, 12).

These models allow academics and public health officials to forecast the transmission of infectious illnesses, evaluate the efficacy of intervention efforts, and distribute resources effectively. AI approaches like deep learning and molecular modelling help accelerate drug research by forecasting the effectiveness and safety of possible medication candidates. AI algorithms examine extensive databases of chemical compounds and biological targets to identify potential candidates for future testing, expediting the development of novel antiviral medicines and vaccines (13, 14).

AI systems may assess current data from many sources, such as social media, news stories, and healthcare databases, to track disease outbreaks and identify new risks. AI-powered surveillance systems detect clusters of cases and unique sickness patterns, allowing for early warning and swift response to infectious disease epidemics. Personalised therapy and care include using AI algorithms to assess individual patient data, including genetic information, medical history, and treatment outcomes, in order to customise treatment plans and actions. AI facilitates personalised medicine by forecasting specific patient outcomes and treatment responses, leading to optimised patient care and enhanced treatment results (15, 16).

AI methods may expedite vaccine development by forecasting antigen structures, refining vaccine compositions, and pinpointing possible vaccination options. AI-driven vaccine design platforms expedite the development and testing of vaccines for new infectious illnesses, thereby decreasing the time and expenses involved in vaccine creation. AI algorithms can assess healthcare resource utilisation trends to anticipate future demand for medical supplies, hospital beds, and healthcare professionals during infectious disease epidemics (17).

AI assists healthcare systems in efficiently allocating resources and planning capacity to properly handle increases in demand and provide sufficient treatment for patients. AI has promising prospects to improve the prevention, diagnosis, treatment, and management of infectious illnesses. AI utilises sophisticated algorithms and computational methods to enhance proactive and efficient strategies for managing infectious illnesses, leading to better public health results and decreased global infectious disease impact (18).

AI in Clinical Practice of Infectious Disease

AI is being more often used in the therapeutic field of infectious illnesses, providing many advantages in diagnosis, treatment, and care. Here are some of the primary applications of AI:

AI algorithms may aid physicians in detecting infectious illnesses by evaluating medical pictures like X-rays, CT scans, and MRIs to discover patterns that suggest certain infections. AI-driven image analysis technologies can identify distinct characteristics of pneumonia, TB, and other infectious illnesses, aiding physicians in making precise and prompt diagnoses. Antimicrobial stewardship involves using AI systems to examine electronic health records (EHRs) and microbiological data. AI algorithms assist doctors in optimising antibiotic prescription practices, reducing needless antibiotic administration, and preventing the spread of antimicrobial-

resistant illnesses by recognising patterns of antimicrobial use and resistance (4, 19).

AI-driven predictive analytics models can anticipate the likelihood of healthcare-associated infections (HAIs) and other infectious problems in hospitalised patients. By examining patient data, including vital signs, test findings, and clinical notes, these models allow for the early detection of high-risk patients and support specific treatments to avoid infections and enhance patient outcomes (20).

AI algorithms may assist physicians in optimising treatment plans for infectious illnesses by assessing patient-specific data such as microbiological test results, comorbidities, and medication history. AI-supported therapy suggestions allow for tailored and successful treatment methods by taking into account specific patient features and pathogen characteristics (21).

AI-powered surveillance systems can monitor real-time data streams, such as electronic health records, laboratory results, and syndromic surveillance data, to identify outbreaks of infectious illnesses. By examining the timing and location of illnesses, these systems provide advance notice of developing dangers and enable rapid public health response actions. Genomic analysis may be conducted using AI methods like machine learning and deep learning to examine pathogen genomic data and identify genetic changes linked to virulence, antibiotic resistance, and transmission dynamics. AI-supported genomic analysis clarifies the genetic epidemiology of infectious illnesses, improving our comprehension of disease transmission routes and guiding specific management strategies (22, 23).

AI-driven telemedicine technologies provide remote consultations and monitoring of patients with infectious illnesses, especially in underserved or rural regions. Telemedicine improves access to infectious disease care and maintains continuity of care for patients by using AI algorithms for triage, symptom evaluation, and remote monitoring of vital signs. AI has the potential to revolutionise the clinical practice of infectious illnesses by boosting diagnosis accuracy, optimising treatment choices, improving surveillance capacities, and allowing more customised and proactive ways to manage infectious diseases. AI technologies are anticipated to have a growing impact on fighting infectious illnesses and enhancing patient outcomes as they progress (24, 25).

ChatGPT in Scientifc Writing of Infectious Disease

Title

Many publishing requirements state that a research report's title is the most essential portion since it summarises the study's results. ChatGPT lists infectious disease

research paper names. ChatGPT answers natural language inquiries using machine learning from a large text corpus. With relevant keywords and proper writing, this programme may produce numerous suitable research paper titles. Knowing ChatGPT cannot replace human judgement and aptitude is crucial. The tool may propose titles, but researchers must verify that they match the article's content and context. When naming a research article, researchers should consider readership, publication requirements, and ethics (8).

Abstract

An abstract should be short, concentrate on important concepts, follow an organised framework, include relevant keywords, verify for accuracy and clarity, and consider the audience. Summarising primary results, methods, and conclusions using ChatGPT may assist in producing an infectious disease study abstract (8).

Introduction

ChatGPT helps academics write infectious disease research papers. ChatGPT may discuss the epidemiology and clinical features of the infectious illness in the study paper. ChatGPT proposes ways the article might cover research topic-related gaps. ChatGPT may suggest discussing infectious disease research to contextualise the study question and article. ChatGPT may suggest presenting the research question, aims, and a brief summary of the study methods and results to form a logical framework (26-29).

Method

ChatGPT may also provide comments on infectious disease research methodologies. Provide a checklist or directions for structuring the methods section to incorporate all necessary information. Advise on study design, participant selection, data collection, and statistical analysis. These concepts might be tailored to the study. Verify the methods section for clarity and consistency. It recommends alternative words or phrases to simplify the sentence. Find missing or contradictory data in the technique. Examples of well-written infectious disease methods sections to help with formatting and style (26-30).

Results

ChatGPT offers infectious disease research report results authoring. Summarise results via tables, graphs, or diagrams. Clearly explain the results, including statistical analysis and trends. Include any study design or data collection biases in your interpretation. This software can check that the findings are accurate and include all important information (8).

Discussion

ChatGPT may aid in the infectious illness research report debate. Summary of research results, including data patterns and trends. Explain the study results and any design or data collection biases. Discuss

how the results of infectious disease research relate to past and future research. Give answers to study limitations and suggest further research. Develop a concise conclusion that outlines the discussion section's important points (8).

Can AI substitute for an infectious disease doctor?

Although AI has advanced in healthcare and may aid infectious disease physicians in many activities, it is improbable that AI will entirely replace infectious disease doctors in the near future. Here are several reasons:

Sophisticated Decision-Making: Diagnosing and treating infectious diseases involves complex decision-making based on patient history, test findings, epidemiological considerations, and clinical expertise. AI may assist in data analysis and provide suggestions, but human physicians have the skills and experience required to evaluate complex clinical situations and make knowledgeable judgements (31).

Infectious disease specialists not only diagnose and treat diseases but also provide emotional support and direction to patients and their families, enhancing patient interaction and empathy. AI lacks the capacity for empathy and good communication with patients, which are crucial elements of medical treatment. Infectious illness specialists take into account several aspects of patients' lives, such as socioeconomic issues, cultural views, and psychological concerns, while creating treatment programmes. AI may find it challenging to successfully integrate these environmental aspects into therapeutic decision-making (32).

Medical decision-making often entails ethical difficulties and concerns about patient autonomy, beneficence, and non-maleficence. Infectious disease specialists are skilled in handling intricate ethical dilemmas, but AI lacks moral judgement and may not consistently follow ethical standards (33).

Continuous learning and adaptation: contagious illness Doctors participate in continuous learning and professional advancement to be informed about the most recent research, guidelines, and best practices in infectious diseases. AI systems may be proficient in learning from extensive datasets but may not be as adept as human physicians in adapting to new knowledge and changing therapeutic recommendations (34).

Collaborative healthcare approach: Infectious disease specialists work with diverse teams, such as nurses, chemists, laboratory scientists, and public health experts, to provide thorough treatment to patients with infectious disorders. AI may aid in data integration and communication in healthcare, but it cannot substitute for the collaborative aspect of healthcare teams. AI may enhance the skills of infectious disease

physicians and enhance patient outcomes, but human knowledge and judgement are still essential in medicine. AI is unlikely to completely replace infectious disease physicians. Instead, it will likely be used as a beneficial tool to assist their clinical decision-making and improve patient care (35, 36).

What Problems will AI Bring in the Field of Infectious Disease?

AI has several advantages in the realm of infectious illness, but it also brings out multiple obstacles and issues. For training and validation, AI algorithms rely on sizable datasets that might contain biases or errors. Biases in training data, including the lack of representation of certain demographics or locations, may result in algorithmic biases and discrepancies in diagnosis, treatment, and results. Incomplete or noisy data might hinder the effectiveness and dependability of AI models in predicting and managing infectious diseases (37).

Interpretability and Transparency: AI models, especially deep learning algorithms, are often opaque systems with decision-making processes that are challenging to comprehend or explain. Insufficient openness in AI algorithms may erode confidence among professionals, patients, and policymakers, especially in crucial areas like infectious disease diagnosis and treatment. It is crucial to guarantee the interpretability and transparency of AI models for their acceptance and use in clinical practice (38). Utilising AI in infectious illnesses presents ethical dilemmas regarding patient privacy, permission, autonomy, and fairness. Data privacy, informed consent for AI-driven diagnoses and treatments, and the risk of algorithmic discrimination need thorough examination and regulation. It is crucial to ensure that AI technologies comply with ethical norms and regulatory requirements to reduce possible damages and provide fair access to healthcare services (39).

Collaboration between humans and AI: AI may aid physicians in diagnosing, treating, and controlling infectious illnesses, but human supervision and discretion in clinical decision-making must be maintained. Relying too much on AI algorithms without thorough evaluation and confirmation by human specialists might result in mistakes, incorrect diagnoses, and negative consequences. Facilitating successful cooperation between people and AI systems, referred to as human-centred AI, is essential for maximising the capabilities of both and enhancing patient care (40).

Allocation of resources and accessibility: Implementing AI technology in infectious illnesses might worsen current gaps in healthcare access and resource distribution. The high expenses of AI adoption, inadequate infrastructure, and differences in

digital literacy and technology access might exacerbate the divide between affluent and underprivileged areas. To achieve fair access to AI-powered healthcare solutions, it is essential to tackle socioeconomic obstacles and provide resources to enhance healthcare infrastructure and capacity-building programmes (41).

AI-driven infectious disease monitoring systems and healthcare platforms face security and privacy risks, including susceptibility to cybersecurity threats such as data breaches, malware attacks, and unauthorised access. Ensuring patient data security, confidentiality, and protection against harmful activity are crucial factors in creating and implementing AI-powered healthcare technology. Enforcing strong cybersecurity protocols and complying with data protection laws are crucial for maintaining patient confidence and confidentiality (42).

To tackle these difficulties, multidisciplinary cooperation among doctors, academics, policymakers, ethicists, and technologists is needed to create responsible AI solutions that focus on patient safety, equality, and ethical concerns. Proactively tackling these obstacles, AI has the potential to change infectious disease management and effectively enhance public health results (43). The main topic points of recent studies are shown in Tables 1, 2, and 3.

Table 1. The main topic points of recent studies

Reference no.	Authors	Subjects	Main theme
Ref [1]	Brownstein et al.	Infectious-Disease	Artificial intelligence (AI) is the emulation of human cognitive processes by computers, especially computer systems. The processes include learning (acquiring material and rules for its application), reasoning (using rules to draw approximate or definite conclusions), and self-correction.
Ref [2]	Smith et al.	Infectious-Disease	Narrow AI, often known as weak AI, is specifically created and educated to do a single job. It is focused on efficiently carrying out a certain activity, such as face recognition, language translation, or playing chess.
Ref [3]	Wong et al.	Infectious-Disease	AI approaches include machine learning for computers to learn from data and make predictions or judgements, and natural language processing for computers to comprehend and produce human language.

Ref [4]	Chu et al.	Infectious-Disease	AI is used in many sectors, such as healthcare, finance, education, transportation, entertainment, and beyond. It has the capacity to transform industries, enhance efficiency, and address intricate issues.
Ref [5]	Schwalbe et al.	Review	It is crucial to tackle these difficulties and guarantee that the development and use of AI contribute positively to society.
Ref [6]	Shi et al.	Infectious-Disease	AI algorithms can examine extensive datasets of clinical symptoms, test findings, and demographic information to detect patterns that suggest infectious illnesses.
Ref [8]	Cheng et al.	Review	AI algorithms may examine patient data to create treatment regimens that are specific to individual risk factors, genetic predispositions, and reactions to therapy.
Ref [9]	Parums et al.	Infectious-Disease	AI systems can analyse real-time data from many sources including electronic health records, wearable devices, and environmental sensors to track disease spread and detect emergent hazards.
Ref [10]	Relf et al.	Review	AI algorithms can assess healthcare resource utilisation trends to anticipate future demand for medical supplies, hospital beds, and healthcare professionals during infectious disease epidemics.
Ref [12]	Peiffer-Smadja et al.	Review	AI algorithms may evaluate various datasets, such as patient symptoms, test findings, and environmental variables, to identify patterns that suggest infectious illnesses.
Ref [13]	Tran et al.	Infectious-Disease	AI approaches like deep learning and molecular modelling help accelerate drug research by forecasting the effectiveness and safety of possible medication candidates.
Ref [15]	Bess et al.	Infectious-Disease	AI systems may assess current data from many sources, such as social media, news stories, and healthcare databases, to track disease outbreaks and identify new risks.

Table 2. The main topic points of recent studies

Reference no.	**Authors**	**Subjects**	**Main theme**
Ref [17]	Park et al.	Review	AI methods may expedite vaccine development by forecasting antigen structures, refining vaccine compositions, and pinpointing possible vaccination options.

Ref [18]	Tran et al.	Infectious-Disease	AI assists healthcare systems in efficiently allocating resources and planning capacity to properly handle increases in demand and provide sufficient treatment for patients.
Ref [19]	Kulkarni et al.	Review	AI-driven image analysis technologies can identify distinct characteristics of pneumonia, TB, and other infectious illnesses, aiding physicians in making precise and prompt diagnoses.
Ref [20]	Babcock et al.	COVID-19	AI-driven predictive analytics models can anticipate the likelihood of healthcare-associated infections (HAIs) and other infectious problems in hospitalised patients.
Ref [21]	Mali et al.	COVID-19	AI-supported therapy suggestions allow for tailored and successful treatment methods by taking into account specific patient features and pathogen characteristics.
Ref [22]	Edeh et al.	Hepatitis C Disease	AI-powered surveillance systems can monitor real-time data streams, such as electronic health records, laboratory results, and syndromic surveillance data, to identify outbreaks of infectious illnesses.
Ref [23]	Kaur et al.	COVID-19	AI-supported genomic analysis clarifies the genetic epidemiology of infectious illnesses, improving our comprehension of disease transmission routes and guiding specific management strategies.
Ref [24]	Karimzadeh et al.	COVID-19	AI-driven telemedicine technologies provide remote consultations and monitoring of patients with infectious illnesses, especially in underserved or rural regions.
Ref [27]	Howard et al.	Review	ChatGPT may discuss the epidemiology and clinical features of the infectious illness in the study paper.
Ref [29]	Wang et al.	Review	ChatGPT may suggest presenting the research question, aims, and a brief summary of the study methods and results to form a logical framework
Ref [30]	Brainard et al.	Review	ChatGPT may also provide comments on infectious disease research methodologies. Provide a checklist or directions for structuring the methods section to incorporate all necessary information. Advise on study design, participant selection, data collection, and statistical analysis.
Ref [32]	Lee et al.	Infectious diseases	AI may find it challenging to successfully integrate these environmental aspects into therapeutic decision-making

Table 3. The main topic points of recent studies

Reference no.	Authors	Subjects	Main theme
Ref [33]	Tran et al.	COVID-19	Medical decision-making often entails ethical difficulties and concerns about patient autonomy, beneficence, and non-maleficence. Infectious disease specialists are skilled in handling intricate ethical dilemmas, but artificial intelligence lacks moral judgement and may not consistently follow ethical standards.
Ref [34]	Parvatikar et al.	Review	Continuous learning and adaptation: contagious illness Doctors participate in continuous learning and professional advancement to be informed about the most recent research, guidelines, and best practices in infectious diseases. AI systems may be proficient in learning from extensive datasets but may not be as adept as human physicians in adapting to new knowledge and changing therapeutic recommendations.
Ref [35]	Giacobbe et al.	Infectious diseases	Collaborative healthcare approach: Infectious disease specialists work with diverse teams, such as nurses, chemists, laboratory scientists, and public health experts, to provide thorough treatment to patients with infectious disorders.
Ref [37]	Malani et al.	Review	For training and validation, AI algorithms rely on sizable datasets that might contain biases or errors. Biases in training data, including the lack of representation of certain demographics or locations, may result in algorithmic biases and discrepancies in diagnosis, treatment, and results. Incomplete or noisy data might hinder the effectiveness and dependability of AI models in predicting and managing infectious diseases.
Ref [38]	Equbal et al.	COVID-19	AI models, especially deep learning algorithms, are often opaque systems with decision-making processes that are challenging to comprehend or explain.
Ref [40]	Kim et al.	Infectious diseases	AI may aid physicians in diagnosing, treating, and controlling infectious illnesses, but human supervision and discretion in clinical decision-making must be maintained.
Ref [41]	Marcus et al.	HIV Prevention	Implementing AI technology in infectious illnesses might worsen current gaps in healthcare access and resource distribution. The high expenses of AI adoption, inadequate infrastructure, and differences in digital literacy and technology access might exacerbate the divide between affluent and underprivileged areas.
Ref [42]	Barbieri et al.	COVID-19	AI-driven infectious disease monitoring systems and healthcare platforms face security and privacy risks, including susceptibility to cybersecurity threats such as data breaches, malware attacks, and unauthorised access.

Conclusion and Outlook

AI answered most infectious illness issues connected to its capabilities and restrictions, with some changes and explanations. The research answered infectious disease AI issues of prime importance. This review suggests AI for infectious disease clinical practice and research. Article title, abstract, introduction, technique, findings, and debates are organised via AI, saving

researchers time. This speeds up and improves scientific writing. According to the responses, some may be misleading or inaccurate, compromising study accuracy. Existing AI answers inquiries correctly, securely, and superficially but lacks information and references. The absence of diagnostic technologies in AI causes misidentification and safety issues. The moral use of medical technology requires direction and control. Several institutes have barred AI from scientific investigation due to its ineffectiveness. However, AI infectious disease research is promising. By gathering medical information and patient case studies, AI may help practitioners. Emerging technologies must be recognised and rigorously controlled. ChatGPT and other medical AI models require additional data to learn.

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Review Article

Pituitary Diseases and Midwifery Care in Pregnancy

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Abstract

The pituitary gland causes very serious effects on the body thanks to the hormones it secretes. These effects are also reflected in the pregnancy process and can cause some changes. The main effects of pituitary diseases are prolactinoma, acromegaly, lymphocytic hypophysitis, pituitary insufficiency (hypopituitarism), Cushing's Syndrome and Sheehan's Syndrome. Since pregnancy is rare in these diseases, diagnosis is usually made in the pre-pregnancy period. A definitive diagnosis is made thanks to the disease-specific diagnostic tests accompanied by the signs and symptoms seen in the pre-pregnancy period. The anatomical and physiological changes that occur in the pituitary gland during pregnancy cause difficulties in diagnosing pituitary diseases. Therefore, midwifery care to be given in pituitary diseases should be carried out effectively from the pre-pregnancy period. These diseases cause serious complications for both the mother and the fetus and require a multidisciplinary care approach. Midwives, who have a major role in the multidisciplinary team providing care, should be familiar with the symptoms, diagnosis and treatment methods of pituitary diseases and should be managed with individualized midwifery care specific to the disease.

Key words: *Midwifery, Midwifery care, Pituitary dıseases, Pregnancy, Postpartum*

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Introduction

The pituitary gland is located in the sella turcica at the skull base and is a small endocrine organ weighing 0.5-1 g. Although it is a very small endocrine gland, it has an important role in the regulation of the hormonal system of the whole body and is also defined as the 'master gland' (1). The pituitary gland also has important functions in the formation and maintenance of pregnancy. The pituitary gland consists of two different parts: adenohypophysis (anterior part) and neurohypophysis (posterior part) (2). The anterior part, called adenohypophysis, constitutes 80% of the gland and is connected to the hypothalamus via the bloodstream. The posterior part, called the neurohypophysis, is directly connected to the hypothalamus through the pituitary stalk (3). There are 5 cell groups secreted under the control of the hypothalamus in the adenohypophysis. These are somatotrope cells: GH which is growth hormone, gonadotrope cells: FSH and LH which are gonadotropins, lactotrope cells: prolactin (PRL), thyrotrope cells: TSH which is thyroid stimulating hormone and corticotrope cells: ACTH which is adrenocorticotropin (4). Both anatomical and functional changes occur in the pituitary gland during pregnancy. During pregnancy, the pituitary gland grows by approximately 136%, reaches its highest level on postpartum day 3 and returns to its prenatal size within 6 months (5). This growth in the pituitary is due to hypertrophy and hyperplasia of PRL-secreting lactotrope cells with the effect of increasing oestrogen hormone during pregnancy. Lactotroph cells constitute 60% of the anterior pituitary cells in pregnancy and 20% in non-pregnant individuals (6). There is an increase in serum PRL level during pregnancy, and it returns to normal levels around postpartum day 7 in non-breastfeeding women. While there is a decrease in the number of gonadotrope cells in the pituitary during pregnancy, there is no change in the number of corticotrope and thyrotrope cells (7). Serum gonadotropin levels decrease during pregnancy due to the negative feed-back effects of increasing estrogen and progesterone. In addition, pituitary cells do not respond adequately to placenta-derived gonadotropin releasing hormone (GnRH) (8). At the beginning of pregnancy, serum TSH levels decrease slightly due to increased placenta-induced hCG levels. There is activation in the hypothalamo-pituitary-adrenal axis during pregnancy. Placenta-derived corticotrope releasing hormone (CRH) stimulates ACTH release from the pituitary (6). Serum free and total

cortisol and cortisol binding globulin levels increase in pregnancy. Somatotropes are suppressed by the effect of insulin like growth factor-1 (IGF-1) which increases during pregnancy and they may function similar to lactotropes. The amount of pituitary-derived GH decreases during pregnancy and the amount of GH produced by the placenta increases instead (9).

Pituitary Diseases in Pregnancy

Prolactinoma

Prolactinoma is one of the most common causes of persistent hyperprolactinaemia in pregnancy and accounts for approximately 50% of pituitary tumours. Anovulation and infertility are frequently seen in a woman diagnosed with prolactinoma (10).

Diagnosis: The chance of pregnancy increases in women who respond rapidly to treatment and have regular ovulatory cycles. Therefore, it is very important for women diagnosed with prolactinoma to receive counselling in the pre-pregnancy period to prevent or reduce the side effects of the drugs used on the pregnancy process and the fetus (11).

Treatment: In prolactinoma, treatment with the dopamine agonist cabergoline provides a more rapid response and is generally used as the first-line treatment (11). Because of the fetal risks in terms of pregnancy, it is generally recommended to use a contraceptive method during this period. Although there is insufficient evidence for the use of both dopamine agonists in pregnancy, there are studies showing that treatment with bromocriptines is safe in pregnancy or when pregnancy is considered (12).

In pregnancy, there is a physiological increase in pituitary size and prolactin level. Since this increase is considered normal, prolactinoma is usually ignored. Cases in which the increase in prolactin level is significantly above normal values and accompanying symptoms are observed are also examined in terms of prolactinoma (13). Prolactinoma affects pregnancy and pregnancy is also affected by increased prolactin levels. Prolactinomas diagnosed and treated before pregnancy have a very low risk of growth during pregnancy (14). In pregnant women with microprolactinoma (<1cm), dopamine agonists are generally not used in the first trimester. In case of macroprolactinoma, medical treatment is continued during pregnancy and bromocriptine dopamine antagonist is usually used. In pregnant women diagnosed with prolactinoma, the size of the tumour is monitored every trimester with magnetic resonance imaging (MRI) and treatment is regulated. In cases where there is no response to medical

treatment, termination of pregnancy or surgical intervention is planned (15).

Midwifery Care Management

- Women with symptoms of high prolactin levels should be referred to an endocrinologist.

- Women diagnosed with prolactinoma and receiving treatment should be given appropriate family planning counselling for contraception.

- Prenatal follow-up of pregnant women diagnosed with prolactinoma should be performed regularly and they should be evaluated in terms of obstetric risks at each follow-up.

- Pregnant women receiving dopamine agonist treatment during pregnancy should be monitored in terms of fetal and maternal risks.

- In the case of prolactinoma and pregnancy, a multidisciplinary approach is important and the cooperation of gynaecologist, endocrinologist, neonatologist, midwives and nurses is very important for follow-up and treatment (14,16).

Acromegaly

Acromegaly is a clinical condition resulting from increased hepatic insulin-like growth factor 1 (IGF-1) levels due to uncontrolled release of growth hormone (GH). The etiology of acromegaly is 95% isolated pituitary tumours that secrete growth hormone. In cases of acromegaly, prolactin level is usually found to be high, however, the metabolic effect caused by excessive secretion of growth hormone and the effect of pituitary adenoma increase the mortality and morbidity rate (17). Symptoms generally include growth in hands, feet and extremities, coarsening of the face, gonadal dysfunctions, excessive sweating, headache, sleep apnoea syndrome and fatigue. In pregnancy, the diagnosis of the disease becomes difficult because the symptoms and signs that occur as a result of physiological changes are similar to acromegaly. Elevated serum IGF-1 level is an important value for the diagnosis and the diagnosis of acromegaly should be made together with both clinical and biochemical results (18).

Diagnosis: Oral glucose tolerance test (OGTT) is the most specific test for the diagnosis of acromegaly. It is recommended that GH response should be examined in patients with clinically elevated IGF-1 value and patients with acromegaly considered to have oral glucose tolerance test (19). GH suppression during glucose tolerance test strengthens the diagnosis of acromegaly. Since a method that separates GH secreted

from the placenta from pituitary GH has not yet been developed, it is very difficult to diagnose acromegaly in pregnancy, in this sense, all values should be considered (20).

Treatment: Treatment is planned according to the size of the tumour and compression symptoms. Generally, surgical treatment is the first option; if serum IGF-1 levels are high after surgical treatment, medical treatment with long-acting somatostatin analogues (SSA) is recommended. Medical treatment is planned when patients are not suitable for surgical treatment. Radiotherapy is recommended as the last option for treatment (21).

Although there is not enough data on acromegaly in pregnancy, pregnancy in women with acromegaly should be postponed, if possible, until GH, IGF-1 normalises and no residual tumour can be seen (19). In cases of acromegaly, the risk of pituitary tumour growth, gestational diabetes mellitus (GDM) and pre-eclampsia increases during pregnancy. Intrauterine growth retardation may be observed if octreotide treatment is continued during pregnancy. In case of increased headache and tumoural growth during pregnancy, SSA treatment is initiated according to clinical conditions (18). The use of pegvisomant (GH receptor antagonist) is not recommended during pregnancy. If macroadenoma is present, visual field should be evaluated in each trimester. Pituitary surgery is recommended to be performed after the first trimester in pregnant women. If GH suppressor treatment is not continued, breastfeeding should be encouraged after delivery (22).

Midwifery Care Management

-Appropriate family planning counselling should be provided for contraception in women diagnosed with acromegaly and receiving treatment.

- Women considering pregnancy should be referred to a physician for monitoring the course of the disease and organising the treatment.

- When suspicious signs and symptoms of acromegaly are detected during pregnancy, they should be referred to a physician (14).

- Pregnant women with acromegaly should be closely followed up in terms of GDM and pre-eclampsia risks.

- If medical treatment is continued, the pregnant woman and foetus should be monitored in terms of side effects of the drug; suspected risky conditions should be reported to the physician.

- Women who do not receive GH suppressive therapy after delivery should be encouraged to breastfeed.

- In pregnancy, labour and postnatal period, the course of the disease, treatment and obstetric risks should be worked in cooperation as a team (23).

Lymphocytic Hypophysitis

Hypophysitis is defined as a non-tumoural heterogeneous inflammatory disease of the pituitary gland (24). Symptoms and findings vary according to the acute, subacute and chronic stages of the disease. Headache, nausea, vomiting and visual field defects can be seen due to the compression of the edematous pituitary gland on the surrounding tissues (25).

Diagnosis: Gestational or postpartum pituitary insufficiency without haemorrhage or hypotension leads to the diagnosis of lymphocytic hypophysitis. Magnetic resonance imaging and the presence of other autoimmune diseases strengthen the diagnosis of lymphocytic hypophysitis. However, histopathological examination is required for definitive diagnosis (26).

Treatment: Steroid treatment is considered to reduce the size of the pituitary mass, and surgical treatment is considered in cases where there is no response and visual status is at risk. Patients are followed up for long-term hormone deficiencies and hormone replacement therapy is initiated when necessary.

Midwifery Care Management

- Pregnant and postpartum women with autoimmune disease should be carefully monitored in terms of symptoms of lymphocytic hypophysitis.

- Women with symptoms such as headache, nausea, vomiting and diplopia during pregnancy and postnatal period should definitely be referred to a physician (14).

- Postpartum women who are diagnosed and treated should be counselled about breastfeeding, and the side effects of the drug and its effect on breastfeeding should be discussed with the physician.

- Counselling should be provided for contraception in the postpartum period and during treatment (27).

Pituitary Insufficiency (Hypopituitarism)

Pituitary insufficiency (hypopituitarism) is a syndrome caused by inadequate production and release of one or more pituitary hormones. Pituitary insufficiency can develop due to hereditary and acquired

disorders. The most common causes of pituitary insufficiency are pituitary adenoma surgery, traumatic brain injury and Sheehan syndrome (28).

Diagnosis: It is only possible to determine that the symptoms are due to pituitary insufficiency by detecting pituitary hormone deficiencies (29).

Treatment: Treatment in pituitary insufficiency is planned according to the cause and hormonal deficiency. Gonadotropin therapy is applied in patients with fertility desire. In pituitary insufficiency, infertility is frequently seen due to the lack of gonodotropins, while pregnancy is possible in treated cases (29). When pituitary insufficiency is treated before pregnancy and adequate hormone replacement is provided, fetal and maternal outcomes are generally good. In cases of undiagnosed or untreated pituitary insufficiency, the risk of abortion and stillbirth increases (30).

Midwifery Care Management

- Obstetric history and lactation status of women should be questioned carefully.

- Precautions should be taken against the risk of haemorrhage during pregnancy, labour and postnatal period.

- Midwives and other caregivers should have sufficient knowledge and skills in the emergency management of obstetric haemorrhage (14).

- Women with excessive bleeding during pregnancy, labour and postnatal period should be carefully monitored.

- When hypotension, tachycardia, hypoglycaemia and signs of lactation failure are detected in the postnatal period, the physician should be informed.

- Cases with suspicious pituitary insufficiency findings in pre-pregnancy, pregnancy and postnatal follow-up should be referred to a physician (29,31).

Cushing's Syndrome

Cushing's syndrome (CS) causes hypercortisolemia due to pituitary ACTH hypersecretion. Hypercortisolemia usually leads to oligo/amenorrhoea and, more importantly, to hypogonadotropic hypogonadism, which is a risk factor for fertility (32). Pregnancy is rare in CS due to fertility-related problems such as oligo/amenorrhoea and hypogonadotropic hypogonadism. Maternal-fetal complications such as pre-eclampsia, eclampsia, hypertension, gestational diabetes, congestive heart disease, pulmonary oedema, preterm delivery, stillbirth and abortion are common in pregnant women with CS (33).

Diagnosis: The diagnosis of CS can be made during or before pregnancy. Since changes such as weight gain, glucose intolerance, hypertension, and striae observed during pregnancy are seen in common with CS symptoms, it is not easy to make a diagnosis. However, in normal pregnancies the striae are white in colour, whereas in CS they are often large and purple. In addition, muscle weakness, hypokalaemia and pathological fracture are also important symptoms for the diagnosis of CS (32).

Treatment and Midwifery Care Management: Treatment of CS in pregnancy is decided based on the state of hypercortisolemia and gestational week. If the diagnosis is made in the first trimester, medical treatment can be followed. If the diagnosis is made in the second trimester, removal of the tumour with surgical treatment depending on the level of hypercortisolemia is the recommended treatment approach (32). If the diagnosis is made in the third trimester, surgical treatment can be postponed until the postnatal period by applying medical treatment (33). Conditions such as diabetes, hypertension and pre-eclampsia in pregnant women diagnosed with CS may cause pregnancies to be more challenging. Prematurity, fetal mortality and intrauterine growth retardation increase in the babies of pregnant women diagnosed with CS. Due to these risks, it is very important to closely monitor pregnant women with maternal diagnosis (34).

Sheehan's Syndrome

Sheehan's Syndrome (SS) is a condition of anterior pituitary hormone deficiency caused by physiological enlargement and necrosis of the pituitary gland during pregnancy. It usually occurs after postpartum haemorrhage (PPH) (35).

Although this syndrome is rare in developed countries, it is common in developing countries. The growth of the pituitary during pregnancy causes compression of the upper pituitary artery, and any hypotension that may occur during labour leads to arterial spasm in smaller vessels, apoplexy and subsequent pituitary necrosis (36). Although the pathogenesis of SS is not clear, the effect of autoimmunity in its formation is quite large. It is thought that it may trigger pituitary autoimmunity and delayed hypopituitarism by releasing antigens spread to the developed tissue necrosis (36,37).

Diagnosis The diagnostic criteria for Sheehan's Syndrome are as follows:

a) History of severe postnatal haemorrhage

b) Severe hypertension or shock requiring blood or fluid replacement

c) Failure in breastfeeding in the postnatal period (14).

d) Failure of the menstrual cycle to resume

e) Anterior pituitary insufficiency and panhypopituitarism

f) Sellada gap in imaging in MRI (38).

Treatment and Midwifery Care Management: Treatment of SS consists of fulfilment of deficient hormone requirements. Glucocorticoids are replaced without the need for fludrocortisone and treatment should be started before thyroxine completion (14). Hypogonadism increases the likelihood of osteoporosis and leads to a decrease in secondary sex characteristics, so replacement therapy should be applied, especially in premenopausal women. GH replacement appears to improve quality of life in these patients (38).

Conclusion

Changes in the pituitary gland during pregnancy cause difficulties in diagnosing pituitary diseases. Although pituitary diseases occurring during pregnancy are rare, scientific data for care management in these diseases are quite limited. For this reason, a multidisciplinary approach should be taken as the basis for care management of pituitary diseases occurring during pregnancy, prevention of complications and optimization of treatment. Midwives in the multidisciplinary team have a key role in detecting abnormal conditions during pregnancy, delivery and postpartum periods from the preconception period throughout all stages of the woman's life and in planning midwifery care for these conditions, if any. In midwifery care, midwives should know the symptoms of pituitary diseases well and provide individualized holistic care specific to the disease to pregnant women diagnosed with pituitary disease or suspected of having the disease. It can be recommended that guidelines and guides specific to midwifery care of pituitary diseases be prepared in clinics, new studies be conducted on pituitary diseases seen during pregnancy and educational plans and various activities be organized to raise public awareness on this issue.

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Original Article

Characteristics and Outcomes of Patients Admitted to a Tertiary Pediatric Intensive Care Unit in Western Black Sea Region of Turkey

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Abstract

Objective*: To evaluate the demographic and clinical characteristics of patients admitted to a tertiary pediatric intensive care unit (PICU) in Karabuk, Western Black Sea Region of Turkey.*

Methods*: Patients admitted to the PICU between June 2023 and June 2024 were analysed retrospectively. It were evaluated age, gender, presence of chronic disease, reason for admission to the PICU, length of stay in both the intensive care unit and hospital stay, need and duration of high-flow nasal cannula (HFNC), need and duration of invasive mechanical ventilation, type of nutrition, need for inotropic drugs, the glasgow coma scale (GCS), nutrition, pretransport pediatric risk of mortality (PRISM) score and mortality rates.*

Results*: Forty-three (48.9%) of these patients were female. The median age of the patients was 4.5 years [1.0-12.75]. According to the intensive care unit hospitalisation diagnoses, 37 (42.0%) of the patients had respiratory distress at the highest rate. It was observed that 24 (27.3%) of the patients had a chronic disease. Mechanical ventilation support was required in 19.3% of patients admitted to PICU, and the mean duration of mechanical ventilation was 10.0 [1.5-50.0] days. GCS score was found to be significantly lower in the group with mortality (p= 0.004). PRISM scores of patients with mortality were found to be statistically significantly higher (p<0.001).*

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***Conclusion**: The study revealed that prolonged hospital and intensive care unit stay, higher PRISM score, lower GCS score and the requirement for more inotropic agents might be associated with higher mortality. In addition, the presence of underlying chronic disease contributes to the mortality process and might be associated with mortality.*

***Key words**: Mortality, Children, Pediatric intensive care unit, Comorbidities*

Introduction

Patients with high risk requiring close monitoring should be followed up in pediatric intensive care units and their treatment should be arranged by a pediatric intensive care specialist. The first pediatric ICU was established at Children's Hospital of Goteburg in Sweden (1). Over the following years, pediatric ICUs will be established in many academic institutions and children's hospitals (2). PICUs were established much later in Turkey and there was a lack of proper organization until the mid-1990s (3).

The challenges related to pediatric critical care in developing countries are the low number of beds, limited resources and difficulty in acquiring equipment. Lack of training programs as well as qualified personnel and inadequate commitment by those responsible for planning health services leads to increased mortality and morbidity. While the mortality rate is as low as 2.39 in developed countries, the rates reported in developing countries are much higher (4,5).

Pediatric intensive care services are estimated to contribute significantly to child health in developed countries; without pediatric intensive care services, child mortality would doubling. In countries like Turkey, where child mortality rates are approaching those of developed countries, providing intensive care services to children with a chance of recovery is expected to reduce child mortality (6,7).

This study aimed to assess the demographic and clinical characteristics of the patients who had been admitted to our unit in the last year and to identify the patients who were served as well as to evaluate the outcomes of the patients.

Methods

Study design and patient selection

The study was a retrospective research performed in the Pediatric Intensive Care Unit of Karabük Training and Research Hospital. The study was initiated after the approval of the ethics committee of Karabük University.

Patients who younger than 1 month and older than 18 years, with missing data and without PICU admission were not included in the study.

Data collection

Demographic parameters of children between the ages of 1 month and 18 years who were hospitalized in the PICU of Karabük Training and Research Hospital in the last 1 year were evaluated. The records of 88 patients admitted PICU within one years were retrospectively analyzed. Age, gender, presence of chronic disease, reason for intensive care unit admission, duration of intensive care unit stay, duration of hospitalization, need and duration of HFNC, need and duration of invasive mechanical ventilation, type of nutrition, need for inotropes, service of admission, GCS, nutrition, PRISM (pediatric risk of mortality) score, reason for hospitalization, mortality rates were evaluated. PRISM score includes; systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, PaO2/ FiO2 value, INR, total bilirubin, calcium, potassium, glucose, bicarbonate values and pupil reaction parameters.

Statistical analysis

IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses. Ordinal and non-normally distributed data were expressed as median and first and third quartiles (Q1 and Q3). Categorical variables were presented as frequency distributions and percentages (%). The normality of the data was tested using the Shapiro-Wilk and Kolmogorov–Smirnov test. Mann Whitney U test was used in the assess-ment of independent groups that did not comply with the normality test. Spearman correla-tion test was used to evaluate the relationship between ordinal data that were not normally distributed. A p-value of <0.05 was considered statistically significant in all analyses.

Results

88 patients were enrolled to the study. Among these patients, 43 (48.9%) were female. The median age of the patients were 4.5 years [1.0-12.75]. When the diagnoses of the patients admitted to the pediatric intensive care unit were evaluated, it was seen that 37 of the patients (42.0%) were due to upper and lower airway infections such as pneumonia, bronchiolitis and croup, which caused respiratory distress at the highest rate.

The second most common cause was drug intoxication with 16 (18.2%). It was observed that 24 (27.3%) of the patients had a chronic disease. Moreover, 75 (85.2%) of the patients were admitted to

the intensive care unit from the emergency department, while the rest were admitted from the pediatric service, pediatric surgery service and neurosurgery service (Table 1).

Table 1: Sociodemographic features of patients

Parameters		n (%)/n[Q1-Q3]
Age		4.5[1.0-12.75]
Sex	Female	43 (48.9%)
	Male	45(51.1%)
Causes	Drug intoxication	16 (18.2%)
	Pesticide intoxication	2 (2,3%)
	Traumatic brain injury (SAH, subdural hemorrhage, epidural hemorrhage, contusion, etc.)	5 (5,7%)
	Respiratory distress (pneumonia, bronchiolitis, croup etc.)	37 (42.0%)
	Multitrauma	4 (4.5%)
	Postoperative surgical patient	5 (5.7%)
	Status epilepticus	4(4.5%)
	Anaphylaxis	2(2.3%)
	Foreign body in the airway	2(2.3%)
	Acute kidney insufficiency	3(3.4%)
	Sepsis	5(5.7%)
	CO intoxication	1(1.1%)
	Cardiogenic shock	1(1.1%)
	Penetrating-Sharp object injury	1(1.1%)
The underlying chronic conditions		24 (27.3%)
Origin of the patient	Emergency Department	75(85.2%)
	Pediatrics ward	5(5.7%)
	Pediatric surgical ward	5(5.7%)
	Neurosurgery ward	1(1.1%)
	Neonatal Intensive Care Unit	2(2.3%)

While 19.3% of the patients admitted to PICU needed mechanical ventilation support, the median duration of mechanical ventilation was 10.0 [1.5-50.0] days. Also 38.6% of the patients needed high flow nasal cannula oxygen treatment. The median length of stay in the intensive care unit was 4.0 [2.0-6.0] days and the median length of hospitalization was 7.0 [4.0-13.0] days for patients hospitalized in PICU. Most of the patients 80 (90.9%) were fed with enteral nutrition. Furthermore, 10.2% of patients needed inotropic support (Table 2).

Table 2: PICU patients' special requirements and length of stay

		N %
Mechanical ventilation requirement		17 (%19.3)
Days on mechanical ventilation		10.0[1.5-50.0]
High flow nasal cannula requirement		34(%38.6)
Number of days on a high-flow nasal cannula		4.0[3.0-6.0]
Length of stay in pediatric intensive care unit		4.0[2.0-6.0]
Length of hospitalization		7.0[4.0-13.0]
Nutrition pattern	Enteral nutrition	80(%90.9)
	Parenteral nutrition	8(%9.1)
Mortality rate		6(%6.8)
Inotrope requirement		9(%10.2)
PRISM		4[2.0-10.25]
GCS		15[13.0-15.0]

When patients with and without chronic disease admitted to the PICU were evaluated, GCS was significantly lower in patients with underlying chronic diseases ($p<0.001$). PRISM scores of patients with known chronic disease were higher than those of patients without chronic disease ($p= 0.036$). Compared with those who did not die, patients who died in the intensive care unit had a significantly lower GCS score in the group with mortality ($p= 0.004$). PRISM scores of patients with increased mortality were found to be statistically significantly higher ($p<0.001$) (Table 3).

Table 3: Factors affecting mortality as well as their underlying chronic conditions in PICU patients

	The underlying chronic conditions			Mortality		
	Existence	Nonexistence	p	Existence	Nonexistence	p
GCS	12.00[10.25-14.00]	15.00[15.00-15.00]	<0.001	12.00[9.75-13.50]	15.00[14.00-15.00]	0.004
PRISM	6.50[2.25-14.75]	4.00[1.25-6.75]	0.036	17.50[10.50-31.00]	4.00[2.00-7.00]	<0.001
Length of stay in pediatric intensive care unit	6.00[2.00-14.00]	3.00[2.00-5.00]	0.074	26.00[1.00-91.75]	4.00[2.00-6.00]	0.789
Length of hospitalization	13.50[3.00-37.00]	6.5[5.00-10.00]	0.122	32.00[1.00-90.75]	7.00[4.75-12.25]	0.973
Days on mechanical ventilation	1.00[0.00-27.00]	0.00[0.00-0.00]	<0.001	6.50[1.00-90.75]	0.00[0.00-0.00]	<0.001
The count of inotropes	0.00[0.00-2.00]	0.00[0.00-0.00]	<0.001	2.50[1.75-3.00]	0.00[0.00-0.00]	<0.001

As for the correlation of PRISM score with the duration of intensive care unit stay, hospitalization, time on mechanical ventilation and number of inotropic agents

in patients hospitalized in PICU were found a statistically significant positive correlation as r: 0.362 p<0.001, r: 0.347 p<0.001, r: 0.362 p<0.001, r: 0.435 p<0.001 respectively.

In addition, there was a positive correlation between the length of stay on mechanical ventilation support and the parameters including the count of inotropic agents, length of hospital stay, and length of intensive care unit stay (r: 0.706 p<0.001, r: 0.348 p<0.001, r: 0.369 p<0.001 respectively) (Table 4).

Table 4: Correlation test

	Correlation coenfficient (rho)	p
PRISM/ Length of stay in pediatric intensive care unit	0.362	<0.001
PRISM/ Length of hospitalization	0.347	<0.001
PRISM / Days on mechanical ventilation	0.362	<0.001
PRISM/ The number of inotropes	0.435	<0.001
Days on mechanical ventilation/ The number of inotropes	0.706	<0.001
Days on mechanical ventilation/ Length of hospitalization	0.348	<0.001
Days on mechanical ventilation/ Length of stay in pediatric intensive care unit	0.369	<0.001
Length of hospitalization/ The number of inotropes	0.159	0.139
Length of stay in pediatric intensive care unit/ The number of inotropes	0.206	0.054

Discussion

Our study revealed that pediatric patients with underlying chronic conditions had lower GCS scores and higher PRISM scores than patients without comorbidities, and demonstraded that there was no effect on the length of hospital stay and intensive care unit stay. By comparing patients who resulted in mortality with those who could be discharged from the PICU, it was observed that children discharged from the PICU had better initial GCS scores, lower PRISM scores and less requirement for inotropes.

A similar study by Botan et al. observed that the majority of the admissions to the PICU were respiratory problems, which was similar to present study. Likewise, the group with mortality was found to have worse neurologic status at admission. Moreover, the length of hospitalization in the mortality group in our study was longer than in the study by Botan et al. (8). We assume that the difference between the survival times of the patients might have been due to the fact that the patients were followed up in a more compact area and with a steadier team, which could have led to an increase in the survival time.

Unlike both the present study and Botan's study, another study by Kanthimathinathan et al. reported that the most common reason for admission to the PICU was cardiovascular diseases (8,9). In addition, a comparison of mortality rates shows that mortality rates vary between 17% and 31%. The annual mortality rate in our PICU was found to be 6.8%. Although cardiovascular diseases may have an altered effect on mortality, there are many variables that may alter intensive care mortality. We assume that the difference in mortality between Kanthimathinathan's study and this study might be due to the fact that their center was a large quarterry service and they followed up patients with multiple organ failure including cardiac and liver transplantation (9). Because their PICU's are a regional referral centre and also support large quarternary services.

In the study conducted by Tripathi et al, they divided their patients into two groups: those transferred from the emergency department to the PICU and those transferred throughout the hospital, and the proportion of patients transferred from other clinics was relatively higher (10). Respiratory distress ranked first in the distributions of the diagnoses in our clinic. Both studies are similar to each other in terms of patient distribution. According to the present study, 85.2% of the patients were admitted directly from the emergency department to the PICU and the rest were transferred from other clinics. However, the length of stay in the intensive care unit was found to be longer in the study. Six patients who enrolled in the study resulted in death and this represents 6.8% of PICU hospitalizations. According to a study by Volakli et al. comparing early and late mortality rates, the overall mortality rate was found to be 9.7% (11). Also, the mortality rate was found to be 12.9% in the study by Kılıç et al. (12). Also, similar to our study, high values in PRISM score, presence of comorbid diseases and number of days on mechanical ventilation were found to be associated with mortality. In the study by Musick et al. as well as in our study, the risk of mortality increased as the PRISM scores and inotropic requirement of the patients increased (13).

Limitations

Our study was performed with limited data and a small number of cases due to being a recently opened clinic. The retrospective design of the study lead to inadequate access to additional data.

Conclusion

Prolonged hospital and intensive care unit stay, higher PRISM score, lower GCS score, and increased requirement for inotropic agents may be associated with

higher mortality, however, the presence of an underlying chronic disease contributes to the mortality process and associated with mortality.

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Case Report

A Novel Homozygote EpCAM Gene Mutation in Turkish Neonate with Tufting Enteropathy

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Abstract

Congenital tufting enteropathy is characterized by intractable watery diarrhea, weight loss, malnutrition and growth retardation in newborn. It is a rare autosomal recessive disorder which is caused by mutations in the gene encoding human epithelial cell adhesion molecule (EpCAM). The diagnosis is based on a combination of clinical signs, histological findings and genetic tests that identify a mutation in the EPCAM gene. We report a Turkish neonate with congenital tufting enteropathy presenting to the emergency department with severe watery diarrhea and weight loss. He was diagnosed as having congenital tufting enteropathy based on his clinical signs and genetic analysis. He was fed by total parenteral nutrition and carbohydrate-poor formula. Despite fact that it is often difficult to find the etiology of conditions that cause congenital diarrhea, clinical suspicion and genetic analysis might be helpful in making the diagnosis of congenital tufting enteropathy.

Key words*: congenital diarrhea, tufting enteropathy, epithelial cell adhesion molecule, infant*

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Introduction

Congenital tufting enteropathy (CTE), also called intestinal epithelial dysplasia, is characterized by severe and intractable diarrhea in newborn. Its incidence is estimated as 1/50,000–100,000 live births in western Europe, although the cases were reported higher in the Middle East due to the high degree of consanguinity (1). Histologically, CTE is characterized by abnormalities in the intestinal epithelium, including villous atrophy, crypt hyperplasia, and focal epithelial tufts (2). It is caused by a disease-related mutation in the gene encoding human epithelial cell adhesion molecule (EpCAM, MIM# 185535) (3). The gene defects in affected newborn usually presents with electrolyte imbalance, severe dehydration, impaired growth and weight loss (4). Most cases generally requires parenteral nutrition and in some severe cases small bowel transplantation can be required (5-6). It is important to manage parenteral nutrition and electrolyte supplements to acquire adequate caloric and fluid intake for normal growth and development (7).

Case

A term male neonate weighing 3210 g, 50 cm long, with a normal Apgar score was born by C/S (cesarean section) from a 31-year-old mother. In the family history, the parents were first consanguineous. Mother had FMF (familial mediterranean fever) (heterozygot, double gene) and lactose intolerance. In addition, the mother had no history of polyhydramnios in whom pregnancy follow-up was performed regularly.

The newborn was admitted to the emergency room 1 week after birth with complaints of diarrhea, severe dehydration and vomiting. Watery diarrhea was described after each feeding. He required admission to the neonatal intensive care unit due to dehydration and poor feeding with 20% weight loss. The patient could not tolerate breast milk or standard formula. Despite adequate hydration treatment, his diarrhea continued. On physical examination was remarkable for sunken fontanellea and distended abdomen. There was no dysmorphic findings. Blood analyses showed metabolic acidosis with pH 7.07 and base excess -20, sodium (Na+) 140 mmol/L, potassium (K+) 5.7 mmol/L, and chloride (Cl-) 121 mmol/L. The stool test was initially within normal limits. Both abdominal X-ray and ultrasound revealed moderate dilated intestinal loops and bowel distension. Watery diarrhea and metabolic acidosis led to a suspicion of congenital diarrheal disorders. Hence, additional laboratory studies including genetic test and endoscopic evaluation were carried out: His

stool electrolytes were as follows: Na+ of 43 (ref: 20–30) mmol/L, K+ of 45 (ref: 55–65) mmol/L and Cl- of 27 (ref: 5–20) mmol/L, (Increased osmotic gap: 110 mOsm/kg). Osmotic diarrhea was initially considered after the evaluation of electrolytes within normal limits and anyon gap. Upper gastrointestinal (GI) endoscopy and colonoscopy revealed no abnormality. However, duedonal biopsy revealed villous atrophy, focal clumping of surface epithelial cells, crypt hyperplasia, slight decrease in goblet cells, slight increase in intraepithelial lymphocytes. In genetic analysis, it was identified a homozygous mutation in the EPCAM gene: c.325C>T (p.Gln109Ter). The patient was treated with total parenteral nutrition (TPN). Diffrent types of formula were tried for the patient. He moderately tolerated low-carbohydrate formula. At three months of age, he is currently receiving TPN treatment and has diarrhea 4–5 times per day.

Discussion

Since the first case report of CTE was published by Reifen et al. in 1994 (2). More than 200 cases of CTE have been reported in the world. (4). The first case of tufting enteropathy in Turkey was reported by Kahvecioğlu D, et al. in 2014 (8).

Just like other congenital causes of diarrhea, CTE is a rare autosomal recessive disease that causes protracted watery diarrhea, abdominal distention, and repeated vomiting, leading to severe dehydration (3). Although the disease has a congenital onset, late presentation in adolescence has rarely been described (9). Our patient's complaints of severe watery diarrhea, abdominal bloating and recurrent vomiting occurred immediately after birth.

The etiology of congenital diarrhea is often difficult to establish, the diagnosis of CTE is based on clinical symptoms, histopathological findings and genetic analysis. It is characterized by recognition of villus atrophy and crypt hyperplasia of the intestinal epithelium. Focal epithelial tufts are typically found in the duodenum and jejunum (3-10). Lais Pegas et al. reported a newborn with CTE and they found the epithelial tufts in the terminal ileum and partial villous atrophy in duodenum (11). On the other hand, Bosaleh et al. found that duodenal and rectal biopsies of a patient diagnosed with CTE were normal (12). In our case, increased intraepithelial lymphocytes and villous atrophy were evident in the duodenum, while colon biopsies were within normal limits (Figure 1).

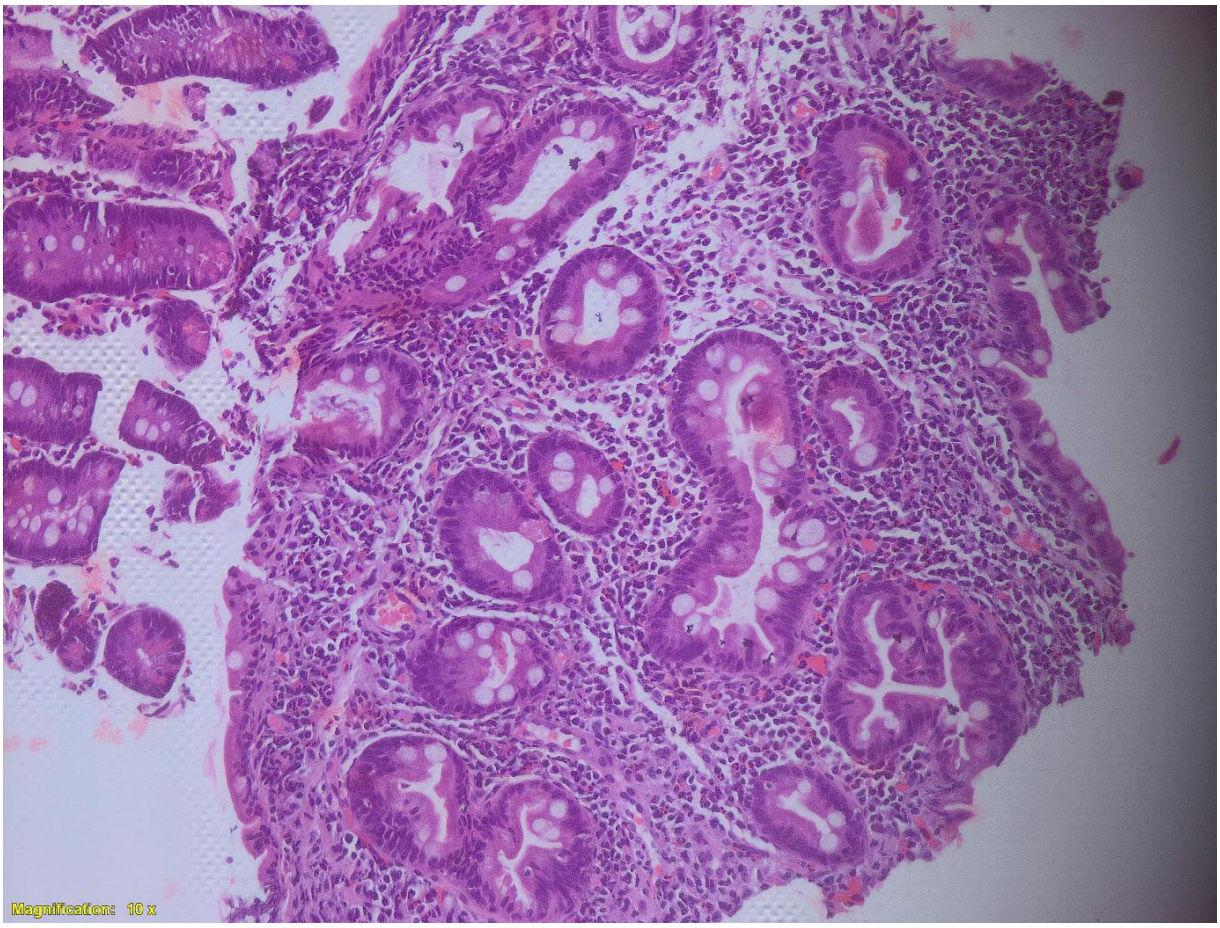

Figure 1. Severe villous atrophy and mixt inflammatory infiltrate in the lamia propria and epithelial tufts (H&E x 20)

Since the EpCAM gene was identified for tufting enteropathy, nearly 120 cases of tufting enteropathy with molecularly confirmed have been reported in the world (13). In 2008, Sivagnanam et al. (3) discovered EpCAM mutations in the epithelial cell cause CTE. Since then, more than 100 EpCAM variants have been identified (13). Furthermore, mutations in the serine peptidase inhibitor Kunitz type 2 (SPINT2, MIM# 605124) have been shown to be associated with syndromic CTE. Extraintestinal symptoms such as choanal atresia and ophthalmological findings represent syndromic forms of CTE (14-15). Moreover, mutations in the EPCAM gene have been shown to be associated with Lynch syndrome (16). We detected a homozygous c.325C>T (p.Gln109Ter) nonsense mutation in the EPCAM gene without phenotypic syndromic appearance in our patient. The variant was classified as "likely pathogenic" according to ACMG (American College of Medical Genetics and Genomics) guidelines. This variant has not been previously submitted to ClinVar (17). We found a novel point mutation in the EpCAM gene.

Prevention of malnutrition is the most important step in the management of CTE. There is no any specific formula for the disease. Furthermore, almost all patients require parenteral nutrition. Intestinal transplantation can be life-saving in cases where treatment fails. (5). We started treatment with parenteral nutrition and carbohydrate-poor formula. Our patient, who partially gained weight, is followed up by the pediatric gastroenterology clinic.

In conclusion, CTE is a rare inherited condition that can be difficult to diagnose and treat at any age. This is the first case report of novel homozygous mutation in EPCAM.

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Conflict of Interest

No conflict of interest was declared by the authors.

Author Contributions

Concept – E.S., S.N.N.; Design - E.S., K.A., S.N.N.; Supervision – K.A., E.S.; Funding – S.E., H.M.; Materials – S.E., H.M.; Data Collection and/or Processing - S.N.N., E.S.; Analysis and/or Interpretation – E.S., K.A., S.N.N; Literature Review – S.N.N., K.A.; Writing – S.N.N., E.S., K.A.; Critical Review – K.A., E.S. S.N.N.; Other – S.E., H.M.

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Original Article

Clinical Gestalt and TIMI Risk Score in Predicting Major Cardiac Event in Patients with Chest Pain at Emergency Department

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Abstract

Objective*: In this prospective observational study, the TIMI risk score and clinical gestalt were compared in terms of detecting a major adverse cardiac event (MACE) in patients presenting with chest pain at ED.*
Methods*: A total of 351 patients were evaluated by experienced clinicians in respect of the TIMI risk score (1-7 points) and clinical gestalt (in terms of low-, medium- and high-risk major adverse cardiac event). The primary outcome was a major adverse cardiac event within 14 days of presentation at ED.*
Results*: A major adverse cardiac event occurred within 14 days in 87 (24.7%) of 351 patients. The sensitivity of clinical gestalt was 93.10% (85.59%-97.43%), and the specificity of the TIMI risk score was 75.89% (71.33%-81.84%). The TIMI risk score and clinical gestalt were found to have similar results in detecting a major cardiac event (AUC: 0.75; AUC: 0.72).*
Conclusion: The results of the present study showed that TIMI scoring and clinical gestalt detect any major adverse cardiac event at similar rates in patients presenting with chest pain at ED.

Key words: *TIMI score, Clinical gestalt, Chest pain, Major adverse cardiac event*

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Introduction

Chest pain is a leading cause of Emergency Department (ED) admissions (1), with approximately 25% of all ED admissions due to acute coronary syndrome (ACS) (2). The use of specialized scoring methods (EDACS, TIMI, HEART, GRACE) is recommended for acute coronary syndrome (3).

The 2021 AHA Guideline recommends the use of HEART, TIMI and EDACS risk score (3). TIMI risk score is a practical, low-parameter, easy-to-use scoring method (4). A risk assessment is performed with TIMI risk score in terms of major adverse cardiac events (MACE) in a 14-day period, and a score of <3 is considered low-risk and > 5 as high-risk. Although many clinical scoring systems are used in the evaluation of patients presenting with chest pain, the clinician's clinical experience cannot be excluded in patient evaluation (3).

The scoring systems were created to help clinicians. However, many clinicians suppose that their clinical gestalt are superior. Clinical gestalt is defined as a clinician’s reasoning to find the appropriate diagnosis and make the most appropriate choice in a patient’s diagnosis/treatment process. As a brief definition, clinical gestalt is the opinion of a clinician (5).

Clinical gestalt is characterized by an intuitive approach to recognition and decision making. It has been reported in literature that the gestalts of experienced clinicians are more suitable (6,7). However, it should also be remembered that clinical gestalt is not faultless. Most clinicians make diagnostic mistakes when they encounter complex cases (8). In the literature, there are studies comparing clinical gestalts with HEART score and parameters, such as electrocardiography (ECG) and cardiac marker (1). However, there is no study in the literature which has compared clinical gestalt and TIMI risk score in terms of major adverse cardiac events.

In the study, clinical gestalt and TIMI risk score were compared in terms of a recent major adverse cardiac event in patients presenting with chest pain in ED.

Materials and Methods

Study design and patient selection

The study was a prospective and observational study that was performed in the Emergency Department of XXXXX Hospital. The study was initiated after the approval of the ethics committee of Dokuz Eylül University. Patients aged 18 years and older from whom a participation consent form was received were included in the

study. Patients who were diagnosed in an external center, those with traumatic chest pain, who declined to participate in the study, and who could not complete the form in the ED were not included in the study. Patients with symptoms such as epigastric pain, known as the equivalent of chest pain, and dyspnea were not included in the study.

Data collection

The clinical gestalt evaluations of the patients were performed by physicians who had experience more than 24 months in emergency medicine. The patient's anamnesis, physical examination, and ECG results of the patient were used during these evaluations. During the evaluation, it was ensured that the evaluator was blinded to cardiac biomarker results and consultation opinions. Clinicians were requested to assess patients admitted to the hospital with chest pain as low, intermediate, and high risk for 14-day MACE. The TIMI risk score was carried out by the physicians who followed up with the patients. In the classification, 0-2 points were accepted as low risk, 3-4 points as moderate risk, and 5-7 points as high risk. The clinical gestalt and TIMI risk score were applied blinded by different physicians. The medical records of the patients included in the study were reviewed 14 days after ED admission and their presentations were re-evaluated or they were contacted and asked if they had experienced an MACE during this time.

Statistical Analysis

Absolute values were used for the descriptive statistics Groups were compared with Kruskal Wallis test. Afterwards, post-hoc analyses were performed with Mann-Whitney U test. During the evaluation of the analysis, the sensitivity, specificity, LR, LR, PPV, and NPV values were specified for each evaluation. Comparisons of paired evaluations were made using ROC analysis. The area under curve(AUC) values were calculated. The AUC value was also compared with the Long test. A confidence level of 95% was accepted for all tests. A value of $p<0.05$ was accepted as statistically significant. Statistical analyses of the data were made using Statistical Package for Social Sciences for Windows ver. 27.0 software

Results

The study initially included a total of 366 patients who presented with chest pain at ED. A total of 15 patients were excluded from the study; 10 because of unavailable medical records and they could not be contacted by telephone, and 5 because of incomplete data. Thus, evaluation was made of 351 patients.

131 (37.3%) of the patients were female. The median age of the patients was 53 (min-max 18-93). 165 (47%) of the patients had hypertension and 78 (22.2%) had diabetes mellitus. 125 (35.6%) were smokers. Cardiac marker elevation was present in 40 (11.4%) patients with chest pain. Of the patients with chest pain, 119 (33.9%) had previously been diagnosed coronary stenosis. 154 (43.9%) of the patients experienced chest pain 2 or more times within 24 hours. Other demographic data of the patients are summarized in Table 1.

Table 1. Demographic Information

Specifications		**Total population (n=351)**	**MACE (n=87)**	**Non-MACE (n= 264)**
Gender	**Female**	131 (37.3%)	31 (35.6%)	100 (37,95)
	Male	220 (62.7%)	56 (64.4%)	164 (62,1%)
Age	**Average**	53 (18-93)	60 (33-88)	52 (18-93)
	65 years and over	95 (27.1%)	33 (37.9%)	62 (23,5%)
The presence of CAD in the family		160 (45.6%)	49 (56.3%)	111 (42%)
HT		165 (47%)	53 (60.9%)	112 (42.4%)
DM		78 (22.2%)	27 (31%)	51 (19.3%)
Hyperlipidemia		85 (24.2%)	26 (29.9%)	59 (22.3%)
Smoking		125 (35.6%)	33 (37.9%)	92 (34.8%)
Aspirin use		108 (30.8%)	41 (47.1%)	67 (25.4%)
Cardiac marker elevation		40 (11.4%)	27 (31%)	13 (4.9%)
ST segment depression		26 (7.4%)	11 (12.6%)	15 (5.7%)
0.5mm elevation in ST segment		5 (1.4%)	3 (3.4%)	2 (0.8%)
≥1mm elevation in ST segment		18 (5.1%)	11 (12.6%)	4 (1.5%)
Presence of 50% excess coronary stenosis		119 (33.9%)	48 (55.2%)	71 (26.9%)
Recurrent chest pain (≥2 times in 24 hours)		154 (43.9%)	53 (60.9%)	101 (38.3%)

TIMI Risk Score and Clinical Gestalt Results

When the TIMI risk score of the patients was evaluated, it was seen that 233 (66.4%) patients were in the low-risk, 90 (25.6%) were in the moderate-risk and 28 (8.0%) patients were in the high-risk group. According to the clinical gestalt assessments, 111 (31.6%) patients were in the low-risk, 152 (43.3%) were in the moderate-risk and 88 (25.1%) patients were in the high-risk group.

Table 2. Possibility evaluation of TIMI risk score and clinical gestalt.

TIMI		**Low (n=233)**	**Moderete (n=90)**	**High (n=28)**	**p**		
MACE	**Yes n (%)**	30	40	17	<0.001	p^{1-2}	<0.001
	No n(%)	203	50	11		p^{1-3}	<0.001
						p^{2-3}	0.134
Clinical Gestalt		**Low(n=111)**	**Moderete(n=152)**	**High (n=88)**	**p**		
MACE	**Yes n(%)**	6	35	46	<0.001	p^{1-2}	<0.001
	No n(%)	105	117	42		p^{1-3}	<0.001
						p^{2-3}	<0.001

Patient Outcomes

It was determined that MACE developed within the first 14 days in 87 (24.7%) patients. Of these patients, 1 (1.1%) had patients received thrombolytic treatment and 3 (3.4%) patients died because of ACS. The first 2 of the death cases occurred within the first 24 hours. Coronary artery bypass graft (CABG) operation was performed on 8 (9.2%) patients because of multivessel disease. The sensitivity and specificity of TIMI scoring and clinical gestlt assessment were evaluated and patients were divided into two groups as AMI again within 14 days. Coronary angiography was applied to 81 (93.1%) patients during the same period and a stent was placed when needed. Only 1 of these

low risk and intermediate-high risk. The sensitivity and specificity values of the TIMI risk score in terms of predicting the development of MACE were determined as 65.52% (54.56%-75.39%) and 75.89% (71.33%-81.84%), respectively. According to the clinical gestalt, MACE was seen in 6(5.4%) patients in the low-risk patient group (n=111). The sensitivity and specificity values of the clinical gestalt were

determined as 93.10% (85.59%-97.43%) and 39.77% (33.82%-45.95%), respectively (Table 3).

In the ROC analysis of TIMI score and clinical gestalt, the area under the curve was 0.75 for clinical gestalt, and 0.72 for the TIMI score. When the AUCs of the groups were compared, no significant difference was found between the AUC areas (p=0.509) (Figure 1).

Table 3. Conformity comparison between the TIMI risk score and clinical gestalt risks.

	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR- (95% CI)	PPV (95% CI)	NPV (95% CI)
TIMI	65.52% (54.56%-75.39%)	75.89% (71.33%-81.84%)	2.84 (2.17-3.71)	0.45 (0.33-0.60)	48.31% (41.69%-54.98%)	87.12% (83.41%-90.11%)
Clinical gestalt	93.10% (85.59%-97.43%)	39.77% (33.82%-45.95%)	1.55 (1.38-1.73)	0.17 (0.08-0.38)	33.75% (31.26%-36.33%)	94.59% (88.85%-97.46%)

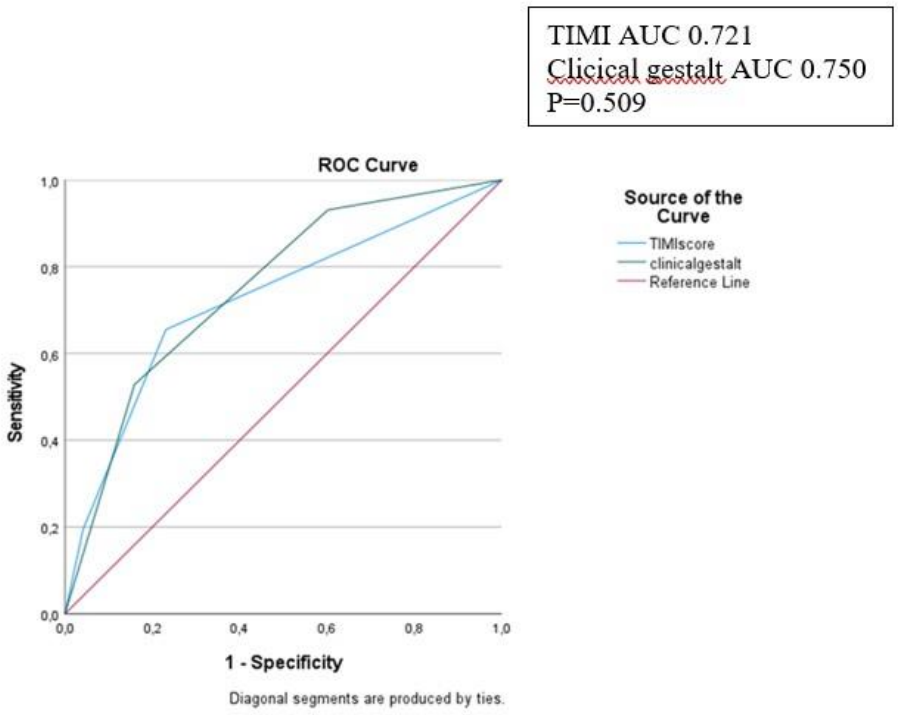

Figure 1. ROC analysis of TIMI risk score and clinical gestalt

Discussion

The results of the present study showed that the TIMI risk score and clinical gestalt methods have equal power in detecting a major cardiac event in patients with chest pain. This similarity in clinical detection supports the view that the clinical gestalt of a clinician is as valuable as at least one scoring system, because it is known that approximately 25% of patients who present at ED with chest pain experience a major cardiac event. In a previous study by Visser et al., it was shown that the clinical gestalt was able to detect acute coronary syndrome at similar rates to HEART scoring (1). However, no clear superiority was stated. Although there is the same similarity statistically in the present study, the fact that the 3 cases of mortality were in the low-risk group according to the TIMI risk score while they were in the moderate-risk group according to the clinicians shows the effect of the clinical gestalt. Even though scoring methods and clinical gestalt seem close to each other, they remain incapable in certain case groups. In these special cases, the joint use of these methods is more important in terms of patient safety. In a study by Wong CP et al., the risk scorings were compared in terms of detecting major cardiac events in patients by ignoring the clinical gestalt and the HEARTS method was the reported to be the first-, and the TIMI method the second-best scoring system for detecting MACE (9). The present study demonstrated that clinical gestalt is as good as TIMI risk score in detecting MACE. However, in the study by Visser et al., it was shown that clinical gestalt was as sensitive as HEARTS score in detecting MACE. Given this situation, the studies conducted have shown that clinical gestalt is as sensitive as these two scoring methods in detecting MACE.

Body et al. studied the effect of clinical gestalt on the recognition and exclusion of acute myocardium infarction in ED. In that study, it was emphasized that a recent MACE could not be detected with clinical gestalt alone without the ECG and biomarker values and it should not be used alone in making a diagnosis or exclusion (10). The ECG findings were added to the present study. The gestalt evaluation was made without seeing the cardiac biomarker values, then compared with the scoring method including the cardiac biomarkers and similar risk results were obtained.

Mokhtari et al. determined that clinic gestalt was superior to single parameters both in recognition and exclusion after comparing medical history, ECG and troponin with clinical gestalt in patients presenting at ED with chest pain (11). However, this is not a surprising result.

Clinical gestalt continues to be studied in many diseases, not only in the detection of acute coronary syndrome in patients with chest pain. In the study conducted by Soto-Mato et al. in which COVID-19 mortality scores and clinical gestalt were evaluated, no score evaluated was found to be significantly superior to clinical gestalt (11). In addition, in another study comparing pulmonary embolism prognostic scoring with clinical gestalt, it was reported that clinical gestalt did not outperform the prognostic score. In our study, although clinical gestalt was not inferior to the prognostic score, it was found to be functional in the detection of rare cases (12).

In the present study, the clinical gestalt evaluations and TIMI risk score evaluations cannot be compared because of statistical non-conformity between them. Considering the distribution, it is seen that physicians who perform a gestalt evaluation take a group with low-risk according to the TIMI risk score as a moderate-risk group, resulting in an inconsistent distribution. It can be seen that physicians were more clinically sensitive than any scoring and the specificity values were lower. This sensitivity includes all 3 cases in the present study which resulted in death. Although the scoring methods detect any MACE at similar rates to clinical gestalt, physicians should not remain limited by these methods but should listen to their inner voice and experience (clinical gestalt) in special cases.

Conclusion

In conclusion, clinical gestalt and TIMI risk score are similarly successful in detecting any major cardiac event in patients presenting with chest pain at ED. However, even if a patient seems to be at low risk, a re-evaluation must be carried out by the physician during the discharge period when there is any doubt.

Limitations

There were cases which could not be included in the study because of the workload in the ED.

Conflict of Interest

The financial support of our work was provided by the study team.

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