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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

Aliye Bulut, Assoc. 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.

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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.

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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.

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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.

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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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iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.
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.

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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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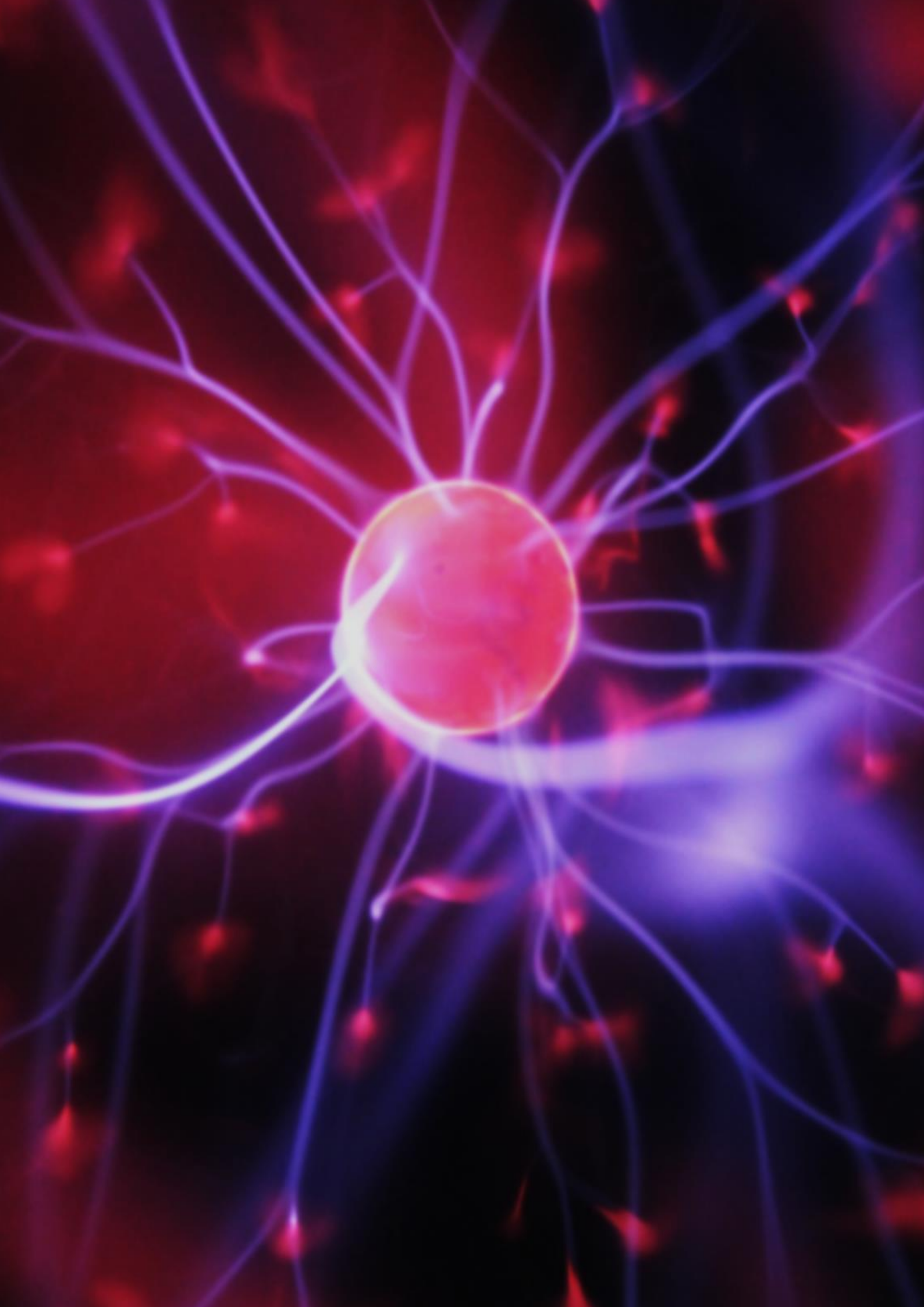

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Letter to Editor

The Role of Artificial Intelligence in the Ethical Relationship of Virtual Cadavers

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Dear Editors,

The advancement of technology has led to a transformation in medical education. At this stage, the ethical considerations surrounding the use of cadavers in medical education are particularly intriguing. Nowadays, it is possible to digitally recreate real cadavers with virtual content. Such materials are referred to as virtual cadavers in the literature. Just like with real cadavers, the use of images of donors in virtual cadavers is subject to ethical permissions. At this point, the use of artificial intelligence tools comes to the forefront.

The use of cadavers in medical education has been a traditional method for many years. The use of cadavers in medical education is a critical component for students to develop their understanding of human anatomy and clinical skills. Cadaver dissection provides medical students with the opportunity to learn the structure of the human body in detail, allowing them to translate theoretical knowledge into practical application. Additionally, it provides students with the opportunity for clinical experience. The use of cadavers in medical education helps students develop professional skills by providing them with practical experience on a real body (1).

Cadavers are obtained from human donors. In Türkiye, there are various problems regarding cadaver donation rates. Cadaver donation is extremely low in our country, making it difficult for medical faculty students to access cadavers (2). On average, there is only one cadaver for every 20 students studying at medical faculties in our country. It is even challenging to find 1-2 cadavers in departments of anatomy (3). Additionally, there are issues arising from the irreversible nature of procedures performed on cadavers.

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Due to such reasons, studies related to virtual cadavers in digital environments have become increasingly important. Virtual cadavers represent an important solution brought about by technology in the field of medicine and generally in health education. Through the use of virtual cadavers, procedures that are difficult or even impossible to perform repeatedly on real cadavers can be achieved. Additionally, virtual cadaver modeling eliminates the possibility of tissue degradation. Desired tissues, systems, and structures can be modeled in a manner closely resembling reality. In addition to providing unlimited repetition capabilities, virtual cadavers revolutionize the use of cadavers by offering access at any desired time (4).

The development of virtual cadavers poses certain challenges. For instance, the use of programs like Unity and Blender is necessary in the process of developing organs and structures. Besides the requirement of knowing how to use such programs, extensive hours are needed to create a model (5, 6). Additionally, if virtual cadaver images are intended to be realistic, there are also some issues to address. The usage and dissemination of virtual cadaver contents obtained from real cadaver images on the internet are subject to ethical considerations. Just like with real cadavers, obtaining permission from the legal heirs of the donor is necessary when using images of donors in virtual cadavers (7, 8).

The term artificial intelligence was first introduced by John McCarthy in 1956, and its foundation lies in discussions on the ability of machines to think (9). AI has become increasingly popular in recent times, both as natural language processing models and in the field of image processing. With the use of AI tools, it is possible to generate visual and textual content without the need for detailed software and programming knowledge. It is even possible to create videos consisting of unreal images but resembling real ones. At this stage, the use of AI tools is considered important for virtual cadavers. By using AI visual generation tools, content that can be used in virtual cadavers can be easily created. Thus, virtual cadaver examples that are indistinguishable from real cadaver images but do not belong to a real person can be obtained. At this point, it is important for medical education and healthcare professionals to ethically examine this situation.

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Original Article

Relationship Between Clinical and Laboratory Parameters at Admission and Pregnancy Outcomes in Cases of Preterm Premature Rupture of Membranes

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Abstract

Background*:Preterm premature rupture of membranes (PPROM) is a significant complication in pregnancy, often associated with adverse maternal and fetal outcomes. Understanding the relationship between clinical and laboratory parameters at admission and pregnancy outcomes in PPROM cases is essential for effective management and intervention.*
Methods: *The study was conducted retrospectively to examine the relationship between clinical and laboratory parameters at the time of admission and the latent period in pregnant women with PPROM. Records of pregnant women diagnosed with PPROM between 2015-2017 in the obstetrics department of a university hospital were reviewed. The patients were grouped according to gestational weeks, clinical parameters at admission were recorded, and their relationships with the latent period were analyzed.*
Results: *When the data obtained in the study were analyzed, it was shown that cervical length ($p = 0.008$) and the gestational week at the time of admission had an effect on the latent period ($p < 0.001$). However, the other parameters examined, such as amniotic fluid index (AFI), C-reactive protein (CRP), white blood cells (WBC), and Hemoglobin (HGB), were not found to have a statistically significant relationship with the latent period.*
Conclusions: *In cases of PPROM that do not require urgent medical intervention, a multidisciplinary approach should be used. In this way, the latent period can be extended and fetal outcomes can be improved. In this direction, clinical and laboratory parameters at the time of presentation should be carefully considered, and detailed evaluations with ultrasonographic examination and vaginal examination should be continued.*

Keywords*: Early membrane rupture, Cervical length, Preterm premature membrane rupture, Prematurity*

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Introduction

Premature Rupture of Membranes (PROM) is the rupture of fetal membranes before the onset of labor contractions. Preterm Premature Rupture of Membranes (PPROM) is defined as the rupture of membranes before 37 weeks of gestation (1). PPROM holds a significant place among the causes of prematurity, and gestational age and birth weight are important determinants of mortality and morbidity in premature infants (2). PPROM occurs in approximately 0.3%-0.4% of all pregnancies (3). In these cases, the rates of preterm birth reach 20%-50% (4). Other significant issues that may be observed besides prematurity include maternal and fetal infections, hypoxia, asphyxia, lung hypoplasia, respiratory distress syndrome, or fetal deformity (5).

Management of PPROM cases, which pose a risk to maternal and fetal health, is highly important. In this context, the main goal in PPROM is to prolong the "latent period" — the time from the rupture of membranes to delivery — and to reduce the rates of preterm birth (6). The latent period is the duration that starts with the leakage of amniotic fluid and continues until the birth of the fetus (7). Prolonging the latent period positively contributes to improving fetal outcomes (8).

The latent period in PPROM is influenced by factors such as the gestational age at the time of presentation, cervical length, and the presence of pregnancy complications. One of these factors is the clinical laboratory parameters at the time of presentation (8).

In light of all this information, assessments such as "cervical length measurement" and "gestational age" in PPROM cases can be beneficial for determining the duration of labor and the treatment approach, as well as for reducing potential complications. In addition to these, this study aims to evaluate parameters such as "Amniotic Fluid Index" and laboratory analyses including "White Blood Cell (WBC), Hemoglobin (HGB), and C-reactive protein (CRP)" to see if there is any relationship with the latent period.

Material and Method

The study was conducted retrospectively to examine the relationship between clinical and laboratory parameters at the time of admission and the latent period in pregnant women with PPROM. Records of pregnant women diagnosed with PPROM between 2015-2017 in the obstetrics department of a university hospital were reviewed. Initially,

data from 205 pregnant women were accessed, but 61 women with an additional medical history (diabetes mellitus, gestational diabetes, hypertensive disorders, placental abruption, placenta previa, thyroid dysfunctions, maternal cardiovascular diseases, chronic infectious diseases, rheumatologic diseases, severe anemia, fetal growth restriction, fetal anomalies, intrauterine fetal demise) were excluded from the study. The study was completed with data from 144 pregnant women. The patients were divided into five groups according to their gestational weeks (<24, 24-28, 28-32, 32-34, >34 weeks).

The socio-demographic data (age, education level), obstetric data (gestational age, fetal biometric measurements, cervical length, amniotic fluid volume, mode of delivery, gestational week at delivery, birth weight, obstetric complications), medical treatment protocol, and laboratory findings of the pregnant women were obtained and evaluated from hospital records. A diagnostic and management protocol for PPROM cases is implemented at the specified hospital.

In the clinic where the research was conducted, the diagnostic and management protocol for preterm premature rupture of membranes (PPROM) includes physical examination, ultrasound (USG), laboratory tests, detection of placental alpha microglobulin-1 (PAMG-1) (AmniSure® test), and Non-Stress Test (NST). The diagnosis of membrane rupture is confirmed by detecting PAMG-1 in vaginal fluid. To monitor for the development of chorioamnionitis in patients, daily tracking of fever, abdominal pain, abdominal tenderness, and fetal tachycardia is initiated, along with Hemogram and CRP monitoring. To ensure fetal lung maturation, patients for whom labor is planned receive intramuscular injections of betamethasone ampoules at a dose of 2x2 every 24 hours (9). All patients are started on intravenous Ampicillin-Sulbactam 1 g, 4x1 dose for 10 days (9). For pregnant women over 32 weeks, daily NST evaluation is performed, and all patients undergo daily ultrasound assessments of the placenta, amniotic fluid evaluation, and fetal movement examination.

According to the protocol, pregnant women diagnosed with PPROM who are less than 23 weeks pregnant are offered the option of termination. Women who wish to continue the pregnancy are admitted to the hospital for monitoring and treatment.

Statistical Analysis

The data were analyzed using IBM SPSS 22 software. Descriptive statistics, including mean, standard deviation, frequency, percentage, and arithmetic mean, were used

for evaluation. The Shapiro-Wilk test was employed to determine the normal distribution of the data. One-way analysis of variance (ANOVA) was chosen for data with a normal distribution, while the Kruskal-Wallis H test and Mann-Whitney U test were selected for data that did not show normal distribution. Tukey and Tamhane T2 tests were chosen as post-hoc tests. Categorical variables were analyzed using the Chi-square test and Exact test. Pearson correlation and Spearman correlation tests were utilized to determine the relationship between the data. In test results, $p<0.05$ was considered statistically significant.

Results

It was determined that the mean age of the pregnant women was 29.04±6.1, with 46.3% being primigravida, 51.9% being nulliparous, and 69.8% having never had a miscarriage. The mean gestational age at the initial presentation of patients was determined to be 29.8±7 weeks (Table 1).

Table 1. Distribution of pregnant women according to age and obstetric history.

Gravida	**n**	**(%)**
1	25	46,3
2	7	13,0
3	7	13,0
4	8	14,8
5	3	5,6
6	3	5,6
12	1	1,9
Para	**n**	**(%)**
0	28	51,9
1	8	14,8
2	12	22,2
3	4	7,4
4	2	3,7
Abortus	**n**	**(%)**
0	37	69,8
1	10	18,9
2	4	7,5
3	1	1,9
10	1	1,9

In the grouping based on gestational weeks at the time of presentation, it was found that 36 patients (25.4%) were less than 24 weeks, 16 patients (11.3%) were between 24-28 weeks, 20 patients (14.1%) were between 28-32 weeks, 16 patients (11.3%) were between 32-34 weeks, and 54 patients (38%) were over 34 weeks. The average gestational age at birth was determined to be 30.8±6.7 weeks, and the average birth weight was 2049±973.7 grams in the study. It was observed that 93.7% of patients received antibiotic therapy, 55.3% had cesarean delivery, 57.5% developed chorioamnionitis, and 21.9% had placental abruption (Table 2).

Table 2. Distribution of Pregnant Women According to Clinical and Obstetric Characteristics.

Pregnancy groups	**n(%)**
< 24 weeks	36 (% 25,4)
24- 28 weeks	16 (% 11,3)
28- 32 weeks	20 (% 14,1)
32- 34 weeks	16 (% 11,3)
> 34 weeks	54 (% 38)
Antibiotherapy status	134 (% 93,7)
Caesarean section	68 (% 55,3)
Chorioamnionitis	42 (% 57,5)
Abruptio plasenta	16 (% 21,9)
Birth week (Mean± SD)	30,8±6,7
Birth Weight (Mean (±SD)	2049±973,7 gram

When examining the relationship between parity and the latent period, although the latent period was shorter in multiparous women compared to nulliparous women, it was not statistically significant (0.07 vs. 0.28 days) (p = 0.153) (Table 3).

Table 3. Parity - Latent Period Relationship.

	Nullipar	**Multipar**	**p**
Latent Period, med (min- max)*	0,28 (0,14- 8,8)	0,07 (0- 0,3)	0,153

Mann-Whitney U test Med: Medyan, min: Minumum, max: Maksimum *day

The analysis results of the gestational weeks and the latent period in patients were found to be as follows: for those <24 weeks, it was 0.28 (0.00-9.28), for 24-28 weeks it was

0.85 (0.00-2.71), for 28-32 weeks it was 0.71 (0.00-3.72), for 32-34 weeks it was 0.29 (0.00-2.44), and for >34 weeks it was 0.14 (0.00-1.30). It was observed that as gestational weeks decreased, the latent period increased, and there was a significant relationship (p<0.001) (Table 4).

Table 4. Distribution According to Weeks of Gestation and Latent Period.

Gestation Week	Latent Period, med (min- max)	p
<24	0,28 (0,00- 9,28)	
24- 28	0,85 (0,00- 2,71)	
28-32	0,71 (0,00-3,72)	p<0,001
32-34	0,29 (0,00-2,44)	
>34	0,14 (0,00-1,30)	

Kruskal Wallis H test; a;0,05; Med: Medyan, min: Minimum, max: Maksimum

Correlation analysis was performed between the latent period and variables such as cervical length, amniotic fluid index, HGB, WBC, and CRP. Only cervical length showed a significant difference (p=0.008) (Table 5).

Table 5. Latent Period - Cervical Length, HGB, WBC, CRP, AFI Relationship.

	Latent period	
	r	p
Cervical Length[a]	0,420	0,008
Hemoglobin[a]	-0,061	0,483
White Blood Cell[a]	0,101	0,282
C-Reaktiv Protein[a]	-0,058	0,570
Amniotic Fluid Index[b]	0,142	0,098

a:Pearson Correlation test; b:Spearmann Correlation test

Table 6 presents the relationship between gestational weeks and complications such as mode of delivery, chorioamnionitis, and placental abruption. It was found that as gestational weeks decreased, the rate of cesarean section increased, but in the group with gestational age less than 24 weeks, the rate of vaginal delivery was higher. The rates of chorioamnionitis increased as gestational weeks decreased, and

significantly decreased after 34 weeks. However, there was no significant difference observed among the groups regarding placental abruption (p=0.647) (Table 6).

Table 6. Distribution of Pregnant Women According to Mode of Delivery and Complications.

	<24 weeks	24-28 weeks	28-32 weeks	32-34 weeks	>34 weeks	X^2	p
Caesarean section, n (%)	6 (% 19,4)	11 (% 84,6)	15 (% 93,8)	12 (% 80)	23(% 48,9)	34,7	0,001
Chorioamnionitis, n (%)	14 (% 87,5)	7 (% 77,8)	9 (% 75)	8 (% 88,9)	4 (% 14,8)	32,6	0,001
Abruptio Plasenta, n (%)	5 (% 31,3)	3 (% 33,3)	2 (% 16,7)	2 (% 22,2)	4 (% 14,8)	2,4	**0,**647

X^2: Chi-Square test. Exact test.

Discussion

Although our medical knowledge and experiences are growing day by day, uncertainties persist in the field of preterm premature rupture of membranes (PPROM), and visible success has not been achieved. Mortality and morbidity rates associated with PPROM remain high, and PPROM continues to be a significant clinical problem. Therefore, a critical aspect in deciding whether to pursue a monitoring approach or make a delivery decision in patients diagnosed with PPROM is to make a reasonable decision by considering the advantages and disadvantages between the risk of developing intrauterine infection and the risk of developing complications. While the gestational weeks of 32-34 are suggested by many as appropriate for delivery, there is no consensus on issues such as reducing complications, improving prognosis, or determining the duration of antibiotic therapy, so much more work needs to be done in this regard (10). Therefore, patients diagnosed with PPROM should be monitored for vital signs in a fully equipped center, carefully monitored for symptoms such as fever, abdominal pain, and abdominal tenderness, monitored for laboratory parameters, and should be monitored by a ready team for urgent intervention when necessary. In patients under observation, steroid administration should be considered with regard to fetal lung maturation, and prophylactic antibiotic therapy should be initiated to prevent the development of intrauterine infections, particularly chorioamnionitis.

Although the etiology of preterm labor is not fully understood, "chorioamnionitis" holds a significant place among risk factors. This risk is further increased in PPROM patients. Therefore, Group B Streptococcus positivity should be investigated in PPROM patients. Additionally, pathogens such as Neisseria Gonorrhoeae, Trichomonas vaginalis, species of Bacteroides, Chlamydia trachomatis, and Mycoplasmas can also be involved, albeit less frequently. These pathogens can cause defects in membrane integrity through certain enzymes they secrete. The presence of pathogens can be investigated through vaginal culture examination (11). When an infection develops with any of these pathogens, chorioamnionitis occurs. Since there is no definitive marker for chorioamnionitis, the diagnosis is confirmed based on clinical findings such as abdominal pain, fever, and abdominal tenderness following PPROM.

One of the acute phase reactants, CRP, increases in conditions such as infection, stress, and trauma. Hvilsom et al. suggested a relationship between elevated CRP levels in the later stages of pregnancy and preterm birth in their study (12). In another study, it was suggested that CRP could be considered a moderately significant marker for chorioamnionitis and related preterm delivery (13). However, contrary to these findings, our study did not observe a significant increase in CRP levels in cases of PPROM.

In daily practice, some inflammatory markers such as CRP, WBC, IL-6 are used for the follow-up and diagnosis of PPROM and chorioamnionitis; however, their clinical value is debatable due to the lack of specific markers and the physiological elevation of values such as WBC during pregnancy. Pandey et al. claimed that they could predict clinical outcomes with 85.7% sensitivity and 87.6% specificity by recording WBC values at admission in cases of PPROM, with a leukocyte count of 15,850 /mm3 (14). In contrast, Musilova et al. observed in their study that maternal WBC values at admission did not contribute to the prediction of PPROM and chorioamnionitis diagnosis (15). Turhan et al. stated that IL-6 had a more valuable predictive value than WBC and CRP in cases of PPROM (16). In our study, IL-6 value was not examined and the WBC value at admission was not found to be a significant finding in terms of influencing the latent period and predicting the development of chorioamnionitis.

It is believed that cervical length, which is measured by transvaginal ultrasound starting in the second trimester and is shorter than 25-26 mm, plays an important role in the etiology of preterm labor. Sweed

et al. observed in their study that the measured cervical length in PPROM patients had a significant relationship with the latent period, and as the cervical length increased, the latent period also increased (17). Hassan et al. suggested that a short cervix is a clinical reflection secondary to infections originating from fetal membranes (18). However, Carlan et al. compared women with a short cervix to those with normal cervical length and claimed that there was no significant difference between them in terms of the latent period (19). In our study, similarly to the general consensus, a linear relationship was found between cervical length and the latent period, and it was observed that the shorter the cervix, the shorter the latent period.

According to the information in the literature, the larger the gestational age, the shorter the latent period, and in term pregnancies, this period falls below twenty-four hours (20). Consistent with this information, in our study, it was observed that the latent period was longer in pregnancies with a smaller gestational age.

Amniotic fluid has the potential to protect the fetus against bacteria. Additionally, there are views suggesting that the amount of amniotic fluid also plays a protective role against potential infections (21, 22). In their study, Ekin et al. suggested that if oligohydramnios accompanies PPROM, there is a higher risk of both chorioamnionitis and preterm labor and other complications (21). Although Piazze et al. also suggested a linear relationship between the amount of amniotic fluid and the latent period to support this idea, our study did not find a relationship between the amount of amniotic fluid and the latent period (23).

As a result, in cases of PPROM where there is no indication for urgent medical intervention, the first choice should be a follow-up option with a multidisciplinary team. Because in this patient group, extending the latent period contributes to reducing fetal mortality and morbidity. While doing this, practices such as initiating antibiotic therapy and administering corticosteroids for fetal lung development should be considered. Vaginal culture examinations should be performed to investigate conditions predisposing to infection. Considering the data from our study, it should be kept in mind that a low gestational age at admission and cervical length measurement within normal limits according to gestational age may have a positive contribution to the latent period.

Although the contribution of other parameters examined in our study was not observed, cervical length measurement becomes important during the follow-up process in this patient group. Conducting

studies with larger patient groups is important for further development or confirmation of these ideas.

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Clinical Study

Evaluation of the Correlation Between Brucella Serum Agglutination Titre and Liver Involvement

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Abstract

Objective: *Brucellosis is a zoonotic infectious disease transmitted to humans. Typical symptoms of brucellosis are undulant fever, malaise and night sweats. It can lead to complications with involvement of many organs. Early and effective treatment strategies can be effective in preventing these complications. However, different complications can be seen in some cases. Liver involvement is one of these complications.*

Methods: *In this retrospective study, we aimed to investigate the relationship between serum agglutination titre and liver involvement in patients with brucellosis in a city in Turkey. Liver involvement was considered absent if ALT and AST <35 U/L and present if ALT and/or AST ≥35 U/L and patients were divided into two groups.*

Results: *A total of 970 patients with a standard tube agglutination test ≥1/20 were included in the study. 658 (67.8%) of the patients were female. Alanine aminotransferase (ALT) median 20 U/L (6-903) and aspartate aminotransferase (AST) median 21 U/L (9-716) were detected in pretreatment tests. The rate of liver involvement was 25.9% among all patients. A positive correlation was found between serum agglutination titres and serum transaminase levels in our study (AST, $r = 0.269$, $p < 0.001$; ALT, $r = 0.249$, $p < 0.001$).*

Conclusion: *The results of our study indicate that a positive correlation between high serum agglutination titre and liver involvement. In this study, we aimed to contribute to the literature on this subject.*

Key words: *Liver, Serum agglutination titre, Brucella*

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Introduction

Brucellosis is a zoonotic infectious disease transmitted from infected animals (sheep, goats, cattle, camels, pigs, or other animals) to humans. It is also known as undulant fever, Mediterranean fever, or Maltese fever. It is the most common zoonosis worldwide (1). The endemic areas of brucellosis include the Mediterranean basin countries, Central Asia, China, the Middle East, the Indian subcontinent, sub-Saharan Africa, Mexico, and parts of Central and South America. Approximately 500,000 cases are reported worldwide annually (2). Brucellosis is an endemic disease in Turkey. It is especially more common in the Southeastern and Eastern Anatolia regions of the country (3).

Typical symptoms in patients with brucellosis are insidious onset of undulant fever, malaise, and nocturnal sweating. Accompanying symptoms include arthralgia, chills, anorexia, weight loss, depression, headache, low back pain, myalgia, fatigue, and concomitant localised infection-related symptoms. Asymptomatic course may be observed in some patients. One or more focal involvement complications of brucellosis are observed in approximately 30% of cases with a range of 6-92% according to literature data (4, 5). Osteoarticular involvement (spondylitis, sacroiliitis and peripheral arthritis) is the most common form of involvement in focal brucellosis and is observed around 40-50 % (1). Genitourinary involvement is the second most common form of focal involvement due to brucellosis. It may lead to orchitis, epididymitis, prostatitis and testicular involvement in males and tubo-ovarian abscess in females. It is observed in approximately 10 % of cases. Neurological involvement (encephalitis, brain abscess, neuritis, myelitis, etc.), pulmonary involvement (interstitial pneumonia, bronchitis, lobar pneumonia, etc.), intra-abdominal involvement (hepatic or splenic abscess, cholecystitis, pancreatitis, etc.), ocular involvement (keratoconjunctivitis, corneal ulcer, iridocyclitis, etc.), cardiovascular involvement (endocarditis, myocariditis, pericarditis, thrombophilebitis, etc.), dermatological involvement (maculopapular, papulonodular or erythema nodosum-like rashes, granulomatous vasculitis, etc.) are complications caused by brucellosis. Brucellosis may affect any organ system (6).

Brucellosis can be transmitted to humans by consumption of unpasteurised infected milk and meat products, contact of skin or mucous membranes with infected animal tissue (placenta, etc.), contact with infected animal fluids (milk, blood, urine, etc.),

inhalation of infected aerosols or inoculation into the eye. Consumption of unpasteurised dairy products (raw milk, butter, cheese and ice cream) is the most common route of transmission (7).

The definitive diagnosis of brucellosis can be made,

1) by culture of the bacteria from blood, body fluids (cerebrospinal fluid, synovial fluid, urine, pleural fluid, etc.) or tissue (bone marrow or liver biopsy) or

2) in the presence of a quadrupling or more in *Brucella* antibody titre between serum samples taken ≥2 weeks apart during the acute and convalescent phase. Possible diagnosis of brucellosis can be made by standard tube agglutination test ≥1:160 in a serum sample taken after the onset of symptoms or by detection of *Brucella* DNA in a clinical sample by polymerase chain reaction test (8).

In the literature, there are some studies investigating the relationship between serum agglutination titre and brucellosis complications. The study included not only cases with brucella serum agglutination titre >1/160 but also those with <1/160 according to the diagnostic criteria because our aim was to evaluate the relationship between serum agglutination titre and liver involvement.

Materials and Methods

Study design and sample size: In our study, the data of patients who were asked for brucella test (Rose-Bengal, standard tube agglutination, Coombs standard tube agglutination) between 01.01.2013 and 10.04.2023 in a tertiary education and research hospital in Turkey were scanned. Those with negative results of all three tests and only those with positive Rose-Bengal test were excluded from the study. The data of those with positive Rose-Bengal test, standard tube agglutination and Coombs standard tube agglutination tests were analysed. Patients with incomplete data, patients with previous brucellosis, patients who were started brucellosis treatment, hepatitis B surface antigen positive, hepatitis C antibody positive, patients with known chronic liver disease, alcohol users, drug users for any reason and patients with comorbid diseases were not included in the study. In this retrospective study, a total of 970 individuals with brucella standard tube agglutination titre ≥1/20 were included.

Statistical analysis: Median, minimum, and maximum values were given for the quantitative variables used in the study. Liver involvement was considered absent if alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <35 U/L and present if ALT and/or AST ≥35 U/L and the patients were divided into two

groups. The conformity of serum agglutination titre measurement of patients with brucellosis to normal distribution was analysed by Kolmogorov-Smirnov test and it was found that it did not conform to normal distribution ($p > 0.05$). Mann-Whitney U test was used to compare the variables according to liver involvement. Logistic regression analysis was performed to determine whether gender, age and serum agglutination titre variables affected liver involvement, and the reference value was taken as male (first).Spearman correlation analysis was used to determine the correlation between ALT and AST quantitative values and serum agglutination titre measurement. Statistical analyses were performed using IBM SPSS v25 (IBM SPSS, Inc., Chicago, IL, USA) and statistical significance level $p < 0.05$ was accepted.

Ethical approval: This study complied with the standards of medical ethics as so endorsed by decision 300.30.09, dated 21.09.2023, of the Ethics Committee of Gaziantep Islam Science and Technology University.

Results

Brucella tests were performed in 151335 patients. 147622 patients had negative results of all three tests. Among the remaining 3713 patients, patients with positive Rose-Bengal test but negative standard tube agglutination test were excluded from the study and the data of 1644 patients were analysed. Patients with incomplete data, hepatitis B surface antigen positive, hepatitis C antibody positive, previously known chronic liver disease, alcohol users, drug users for any reason and patients with comorbid diseases were excluded. A total of 970 patients with standard tube agglutination test ≥1/20 were included in the study .

658 (67.8%) of the patients were female and 312 (32.2%) were male.AST median 21 U/L (9-716), ALT median 20 U/L (6-903) were found. Liver involvement was not detected in 719 patients (74.1%), while liver involvement was present in 251 patients (25.9%). No statistically significant difference was found in terms of age of the patients according to liver involvement status ($p = 0.070$). When serum agglutination titre values are compared according to the liver involvement status of the patients, there is a statistically significant difference ($p<0.05$) (Table 1).

Table 1. Mann-Whitney U results by liver involvement.

	Liver involvement (n=251)	No-liver involvement (n=719)	p-value
Age	41 (7-79)	44 (4-93)	0.070
Serum agglutination titre	320 (20-5120)	80 (20-2560)	**<0.001**

It is observed that serum agglutination titre value is high in patients with liver involvement. A positive correlation was found between serum agglutination titres and ALT levels, r = 0.249, p < 0.001) (Figure 1).

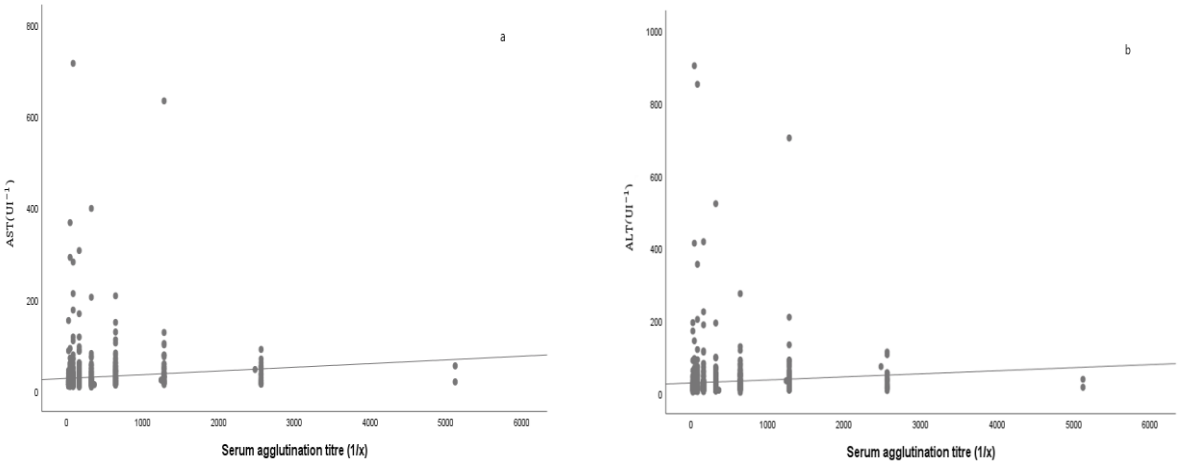

Figure 1. A positive correlation was found between serum agglutination titres and serum transaminase levels. (a) AST, r = 0.269, p < 0.001. (b) ALT, r = 0.249, p < 0.001.

According to the results of logistic regression analysis, the effects of age, serum agglutination titre and gender variables on liver involvement were found to be statistically significant (p < 0.05). A one-year increase in age reduces the risk of liver involvement by 2%. A one time increase in serum agglutination titre variable increases the risk of liver involvement by 1.001 times (95% CI 1.000-1.0001). The risk of liver involvement in males was 2.087 times higher than in females, in other words, the risk of liver involvement in females was 0.521 times lower than in males (Table 2).

Table 2. Logistic regression analysis of factors affecting liver involvement.

	B	S.E.	Wald	p-value	Exp(B)	95% CI
Age	-0.020	0.003	52.463	**<0.001**	0.980	0.975-0.985
Serum agglutination titre	0.001	0,000	44.905	**<0.001**	1.001	1.001-1.001
Gender	-0.736	0.146	25.449	**<0.001**	0.479	0.360-0.637

S.E: Standard error, **CI:** confidence interval, **Exp (B):** Odds ratio.

Discussion

The liver is the most commonly affected organ in patients with active brucellosis. Approximately 50% of patients have clinical and biochemical data related to liver involvement. The most common clinical presentation of liver involvement is hepatomegaly. Liver biopsies from patients with brucellosis showed necrosis of liver cells, parenchymal lesions and granuloma in liver tissue caused by inflammation. In brucella-related hepatitis, an increase in serum aminotransferase levels is observed in 5-40% of patients (9, 10).

There are studies showing that the increase in serum aminotransferase levels in brucellosis patients is related with age. In the pediatric age group, the increase in serum aminotransferase levels has been observed at 60% and even higher rates in older adults, while in the young adult group it has been observed at a rate of 25% (11-13). In the study by Sahinturk et al. no effect of age and gender on liver involvement was demonstrated (p = 0.46) (14).

Various serological methods are used in the diagnosis of brucellosis that enable the detection of antibodies against lipopolysaccharide or other antigens. The most commonly used serological methods are serum agglutination titre and enzyme-linked immunosorbent assays (ELISAs). The risk of clinical progression and complications can be predicted with symptoms and signs such as myalgia, low back pain, weakness/fatigue, weight loss, splenomegaly, and easily accessible laboratory parameters such as serum agglutination titre (15).

The correlation between serum agglutination titre and complications has been researched for years. There are mostly related case reports in the literature. In a meta-analysis of *Brucella* spp. endocarditis cases, it was determined that a Wright agglutination titre above 1/1280 at the time

of diagnosis significantly increased the risk of mortality (16). Brucellosis-related complications have been reported in patients even at low titre standard tube agglutination values. In the case report by Khorvash et al., a 26-year-old male patient had a standard tube agglutination test result of 1/80 and liver involvement was observed (17). Kayaaslan et al. analysed long-term osteoarticular, neurobrucellosis, epididymo-orchitis and hepatic complications in 700 brucellosis patients. Patients were divided into two groups as those with and without complications, and the standard tube agglutination titre was ≥1/160 in 97.1% of patients with complications and 97.8% of those without complications ($p = 0.584$) (18). In a study of 195 patients, it was found that high standard tube agglutination titre was an independent risk factor for liver involvement. In the study, the mean standard tube agglutination titre was found to be higher in patients with liver involvement compared to those without (1/485 and 1/306, respectively) ($p = 0.001$). A positive correlation was found between serum transaminase levels and serum agglutination titres (AST, $r = 0.164$, $p = 0.022$; ALT, $r = 0.138$, $p = 0.054$) (14). Similarly, a positive correlation was found between serum agglutination titres and serum transaminase levels in our study (AST, $r = 0.269$, $p < 0.001$; ALT, $r = 0.249$, $p < 0.001$).

In the study of Akritidis et al. no effect of gender and age on liver involvement was observed in 14 patients with brucellosis, 9 of whom were isolated from blood culture and 5 of whom were serologically diagnosed (9). In our study, liver involvement was found to be more common in males than females.

Limitations

The limitation of the study was the lack of physical examination and ultrasonographic hepatomegaly and splenomegaly data. We did not have radiologic and histopathologic data of our patients.

Conclusion

In conclusion, brucellosis is a zoonotic disease that should be followed closely in terms of diagnosis, treatment, and complications especially in endemic regions. Brucellosis is a public health problem that can be prevented with effective strategies. In this study, a positive correlation between high serum agglutination titre and liver involvement was shown. In the literature, there is a need for multicentre studies in which more patients are evaluated to examine the correlation between serum agglutination titre and complications.

Conflict of interest: The authors declare that they have no relevant conflict of interest.

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Case Report

Colonoscopy-Related Nephropathy

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Abstract

Acute phosphate nephropathy (APhN) is a clinical entity which causes acute and subsequent chronic renal failure after exposure to oral sodium phosphate (OSP) bowel purgatives. Generally, patients who will undergo colonoscopy are given 45 ml of OSP twice, starting 12-24 hours before the procedure. After intestinal absorption, elevated urea and creatinine, transient hyperphosphatemia, hypocalcemia, hypernatremia, hyponatremia, hypokalemia and high anion gap metabolic acidosis may also be observed. The case presented in this article is that of a 60-year-old patient diagnosed with type 2 diabetes, hypertension and dyslipidemia. A colonoscopy was performed to investigate the aetiology of her iron deficiency anaemia. The patient was prepared for the colonoscopy with OSP, and following the procedure, an acute kidney injury developed that was clinically compatible with APhN.

Keywords: *Oral sodium phosphate therapy, Kidney injury, Acute*

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Introduction

Colonoscopy is a widely utilised diagnostic and therapeutic tool for the management of colonic disease. (1). It is the gold standart to visualize the large bowel (2). Acute phosphate nephropathy (APhN) is a clinical condition that results in acute and subsequent chronic renal failure following exposure to oral sodium phosphate (OSP) intestine purgatives. APhN is seen as a result of oral sodium phosphate use in patients undergoing bowel cleansing before colonoscopy (3). Generally, patients who will undergo colonoscopy are given 45 ml of OSP twice, starting 12-24 hours before the procedure. After intestinal absorption, elevated urea and creatinine, transient hyperphosphatemia, hypocalcemia, hypernatremia, hyponatremia, hypokalemia and high anion gap metabolic acidosis may also be observed (4). Advanced age, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) use, acute or chronic kidney disease or the presence of a kidney transplant, retention of oral sodium phosphate (OSP) resulting from poor bowel motility or colitis, female gender, volume depletion, hypertension, diabetes, and diuretic, lithium, or nonsteroidal anti-inflammatory drug use are considered risk factors. (5). This case report describes a patient who developed nephropathy and required urgent observation and treatment after phosphate administration before colonoscopy.

Case

60-year-old female patient, who had diabetes, hypertension and dyslipidemia, was continuing her follow-up due to polypectomy performed after a previously detected tubulovillous adenoma in the rectum. For preparation, two oral purgatives containing sodium phosphate were used 6 hours apart, starting 16 hours before the colonoscopy. The patient, who had fatigue, applied to the internal medicine clinic and was hospitalized after being diagnosed with acute renal failure.

Vital signs: Blood pressure: 90/60 mm Hg, fever: 36.5 degrees, pulse: 113/min. Physical examination findings were normal. In laboratory tests, creatinine: 2.03 mg/dL (0.79 mg/dL 1 week ago), urea: 52 mg/dL, sodium: 137 mmol/L, potassium: 4.16 mmol/L, phosphorus: 4.98 mg/dL, calcium: 9.86 mg/dL was detected. There was no proteinuria and urine sediment was within normal limits. The current history and laboratory findings suggested that acute renal failure might be due to acute phosphate nephropathy. All other etiological causes of acute kidney injury were excluded. Necessary parenteral hydration was provided. After the creatinine

value decreased to 0.88 mg/dL, the patient was called for a check-up and discharged.

In the literature, patients developing acute kidney injury after the use of OSP preparations have been reported. In the study conducted by Markowitz et al. (6), 21 patients who underwent colonoscopy preparation with oral phosphate solution were evaluated. As a result of the data obtained in the study, risk factors such as advanced age, hypertension, inadequate hydration and medication use were found to be associated with the risk of developing acute phosphate nephropathy. We think that risk factors such as advanced age, hypertension and diabetes history may be effective in the development of acute phosphate nephropathy in our patient.

Discussion

Colonoscopy is a frequently used method for many indications. OSP is frequently used for process preparation. It should be kept in mind that these preparations may cause phosphate nephropathy. Advanced age, diuretic use, female gender, and chronic diseases such as diabetes and hypertension are risk factors for the development of acute phosphate nephropathy. In order to reduce complications in high-risk patients, different alternatives for colonoscopy preparation should be tried or adequate hydration should be provided and the patient should be carefully monitored for the development of acute renal failure.

When we look at other studies in the literatüre, Şahin et al. (7) conducted a retrospective study on 122 patients who used OSP solutions for colonoscopy preparation and whose creatinine levels were within normal limits, and noted the creatinine values after an average of one month to determine the effect of OSP solutions on renal functions. There were 60 women and 62 men, and their average age was 64±13 years. While the patients' creatinine (0.87±0.38 mg/dL and 0.8±0.31 mg/dL; $p<0.05$) and phosphate (6.22±3.02 mg/dL and 3.51±0.63 mg/dL; $p<0.05$) values increased after OSP solution use, their GFR (94.12 ± 28.70 and 84.99±26.67; $p<0.05$) values decreased. OSP solution preparation was associated with a decrease in GFR levels in elderly patients whose creatinine levels were within normal limits.

In the study conducted by Lieberman et al. (8), there were 32 patients scheduled for elective colonoscopy who had a serum creatinine level of less than 1.5 mg/dL. After use of OSP solutions, significant increases in serum phosphate and sodium and decreases in serum calcium and potassium were observed.

In the study conducted by Gumurdulu and colleagues (9), a total of 70 individuals were included, comprising 38 men and 32 women with a mean age of 47 ± 12 years

and a range of 25–80 years. After administration of OSP, a notable decline was observed in serum calcium and potassium levels ($P < 0.05$), while there was a marked increase in serum phosphate and sodium levels ($P <$ or $= 0.01$) compared to pre-treatment levels. There was a positive correlation found between the mean change in serum phosphate and age (Pearson's $r = 0.705$; $p < 0.001$).

Considering the studies in the literature and our patient, the indication of colonoscopy should be reconsidered in patients with high risk factors for acute phosphate nephropathy. The use of other effective agents other than phosphate solutions should be evaluated, or if the use of phosphate solution is necessary, the patient should be evaluated for adequate hydration and a break from the use of nephrotoxic drugs for a while.

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Case Report

Sustained Effect of Neurocreative Music Therapy on Upper Limb Abilities, Spasticity, Selective Control and Quality of Life in Cerebral Palsy: A Case Report

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Abstract

This case report, presents the sustained effect of Neurocreative Music Therapy (NCMT) which a unique music therapy approach on the upper limb in an individual with cerebral palsy (CP). Our case is a 19-year-old individual with hemiparetic CP and she was included in the 8-week NCMT application program. Before the application, a phenomenological interview was conducted in accordance with the principle of the NCMT approach, which prioritizes the needs and pleasures of the individual. Before and immediately after the 8-week NCMT application, the patient's spasticity was assessed with the Modified Ashwort Scale, selective motor control with the Selective Control of the Upper Extremity Scale, upper limb abilities in daily activities with the ABILHAND-Kids, and quality of life with the Pediatric Quality of Life Inventory CP Module 3.0. As a result of the assessments, an individual-specific music therapy program was planned and implemented. The outcome measurements made immediately after the NCMT application was repeated in the 4th and 8th weeks following the end of the application. According to the results of the scales, it was observed that spasticity decreased, selective motor control increased, upper limb abilities improved, and quality of life increased. The obtained improvements were generally maintained in the 4th week following the end of the therapy. It was observed that there was a decrease in the sustainability of the effect in the 8th week following the end of the therapy in other measurement parameters other than quality of life. As a result, we concluded that NCMT is an effective approach in the rehabilitation of individuals with CP and that its effects may be transferred to the post-rehabilitation period.

Key words: *Cerebral palsy, Music therapy, Upper extremity*

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Introduction

Cerebral palsy (CP) is a comprehensive term that refers to a group of non-progressive neurodevelopmental disorders that occur as a result of damage to the immature brain (1). One of the most important factors affecting daily living activities in individuals with CP, especially in the hemiparetic group, is upper extremity dysfunction (2). New technologies and interventions are constantly being developed to improve the quality of life of individuals with CP and to increase the efficacy and safety of existing treatments (3). Music therapy has also been a preferred and effective practice in the rehabilitation process of individuals with CP (4-6). In this study; Neurocreative Music Therapy (NCMT) approach developed by Torun that is a holistic music therapy approach was applied (7). The aim of this case report is to investigate the sustained effect of the NCMT approach on upper limb abilities, spasticity, selective control and quality of life in Cerebral Palsy (CP).

Case

In this report, a 19-year-old case diagnosed with left side hemiparetic CP is presented. The clinical type of the case is spastic, according to the Gross Motor Function Classification System it is level 1; can gait without restriction. According to the Manual Ability Classification System it is level 2; can hold and use objects, there is a decrease in the speed and quality of success. Upper extremity spasticity measurement of the patient was made according to the Modified Ashworth Scale (MAS). Forearm flexors, forearm pronators, wrist flexors, finger flexors, thumb adductors and total spasticity values were calculated. According to MAS, she has a spasticity of 3 in the forearm pronators and wrist flexors. The spasticity severity, which is 3 according to MAS, is expressed as 4 in the scoring due to the value 1+ in MAS. Selective Control of the Upper Extremity Scale (SCUES) was used to evaluate the selective motor control of the upper extremity of the patient. According to SCUES, there was a decrease in selective control in the forearm, wrist and fingers on the hemiparetic side; there was additional movement of other joints and the trunk. To assess the upper extremity skills during daily activities, Abilhand Kids which is a valid and reliable scale for CP (8), was used and to assess the quality of life, Pediatric Quality of Life Inventory CP Module 3.0 (PedsQL) was used. The NCMT approach, which is a unique music therapy approach, was planned for the case. NCMT, developed by Torun, is defined as “a holistic music therapy approach that addresses music-brain interactions within the framework of functional brain network

organization, evaluates the individual's health needs from a neurophenomenological perspective, and eclectic approach, focusing on improving the individual's quality of life." (7). Within the framework of this approach, it was aimed to evaluate the individual's feelings and subjective perception while experiencing her current neurological problem, and a phenomenological interview was conducted before the music therapy application in order to see the individual not only from the "outside" but also from the "inside". The details of this interview are given in Table 1.

adopts the use of relational and/or behavioral active music therapy methods and techniques with a creative and

Table 1. Phenomenological interview content.

Interview items for metaphorical perception	**X_1**	**X_2**
My left hand is like …X_1… to me; because …X_2…	cotton	it seems soft and tiny to me
Using my left hand is like …X_1… for me because …X_2…	success	my self-confidence increases
	X_1	
The most common thing I experience when using my left hand is that; …X_1…	cramping of my fingers	
The most interesting thing I have experienced with my left hand is that; …X_1…	when I try to use it, it stiffens and I cannot use it	
The thing I'm most curious about about my left hand is; …X_1…	what would be easier in my life if I could use my hands?	
The best thing I do with both hands is that; …X_1…	play volleyball	
The most difficult thing I do with my hands is that …X_1…	applying eyeliner	
I can describe the problem with my hand/arm as a "…X_1…"	disease	

NCMT sessions were applied for 30 minutes, 2 days a week for 8 weeks. During the application period and the follow-up period at the end of the application, she did not receive any additional treatment other than routine physiotherapy. In the NCMT sessions, a program specific to the individual, based on the needs and tastes of the individual, was created in the light of phenomenological interviews and other clinical measurements. The NCMT approach proceeded with the stages of getting acquainted-warming up (1), getting acquainted with the instruments-determining musical preferences (2), regulation-creating positive emotion (3), and creating an individualized eclectic music therapy practice (4). According to this program, techniques such as instrument playing exercises, sonification, musical motor imagery, and rhythmic auditory stimulation were used to develop creative motor behaviors. After 8 weeks of NCMT application, the patient's MAS, SCUES, ABILHAND Kids, and PedsQL measurements were made. To assess the sustained effect of NCMT, these measurements were repeated at 4th and 8th week after the end of NCMT application and the scores were recorded. According to these measurements, it was seen that the case's total upper extremity MAS score decreased from 12 to 9, thus the tone was regulated. Immediately after the 8-week NCMT application, forearm flexors, forearm pronators, wrist flexors MAS score decreased, and while these results in spasticity were maintained in the 4th week following the end of the application, only the effect in wrist flexors was preserved in the 8th week. The case's SCUES score increased from 7 to 10, thus improving upper extremity selective control. It was observed that the improvement in selective control was partially preserved in the 4th week and was better than pre-NCMT in the 8th week, but there was a decrease in selective control compared to the post-NCMT score-1. Her ABILHAND-Kids score improved from 33 to 38, thus her upper limb skills improved. According to ABILHAND-Kids scores, the development of upper limb skills was observed to follow a decreasing tend over time in the 4th and 8th weeks measurements after the end of NCMT application. Her PedsQL score dropped from 39 to 31, thus her quality of life improved. It was observed that the improvement in quality of life continued to increase following the NCMT approach (Table 2).

Table 2. Scale results of the case before and after the NCMT approach.

		Pre-NCMT score	**Post-NCMT score-1**	**Post-NCMT score-2** 4th week following NCMT	**Post-NCMT score-3** 8th week following NCMT
MAS score	forearm flexors	2	1	1	2
	forearm pronators	4	3	3	4
	wrist flexors	4	3	3	3
	finger flexors	1	1	1	1
	thumb adductors	1	1	1	1
	Total	12	9	9	11
SCUES score total		7	10	9	8
ABILHAND-Kids score		33	38	37	34
PedsQL CP 3.0 score		39	31	26	27

Discussion

It is stated that the effectiveness of rehabilitation for children with hemiparetic CP depends on the intensity and timing of the treatment, the extent to which the improvements are transferred to the patients' daily lives, and the child's ability to maintain attention during the session (9). Music therapy was included in a recent review examining current developments in intervention approaches for individuals with CP, and it was reported that neurological music therapy applied together with physiotherapy was effective in improving motor functions in CP rehabilitation (3). Consistent with this, it was observed that upper extremity spasticity was regulated, selective control increased, upper limb abilities improved, and quality of life increased in our patient at the completion of the 8-week NCMT intervention period. Moreover, these effects were still maintained at 1 month after the end of therapy, while there was a decrease in the sustainability of the effect in some parameters at 2 months. We relate the regulation result in spasticity after NCMT in our case to the systematic review by

Criekinge et al., which emphasized that music, which causes strong changes in brain activity, can cause differences in muscle tone because spasticity is the result of a lesion in the cortex or brainstem, and addresses the effect of music on hypertonus in neurological diseases (10). It has been shown that motor learning-based therapeutic approaches, which have variable and specific applications aimed at individual targets, are the most effective approaches in improving selective motor control (11). The improvement we achieved in selective control after NCMT in our case is consistent with the literature. We attribute the interesting fact that the improvement in quality of life after the NCMT approach continues to increase even after the therapy has ended to the fact that the NCMT approach sees the individual from the inside, as in the phenomenological interview, and has components that are compatible with the multidimensional structure of quality of life.

The long-term continuty of functionality gained from upper extremity therapies on CP is not often evaluated; however, some evidence suggests that gains in functionality may persist for at least 6–12 months after therapy in children with hemiparetic CP (12, 13). A study investigating the effects of neurologic music therapy on the functionality of children with CP observed significant improvements in motor function in the group receiving music therapy and revealed that all these improvements continued 4 months after the therapy. (6). Considering the results in our case, it is seen that similar developments were obtained with the literature during the 4-month follow-up period. This result motivates us to evaluate the long-term effects of our intervention more reliably in randomized controlled trials with a sufficient number of participants.

Conclusion

According to the results obtained in our case, we saw that NCMT meets the needs of the individual and is effective in achieving the goals. The NCMT approach can stand out as an effective approach in the rehabilitation of individuals with CP with its unique, individually structured and enriched content. Future studies should be planned with a large sample size and in a way that long-term effects can be observed specifically for CP, and the effectiveness of the NCMT approach should be investigated in other neurological diseases.

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Review Article

Use of Aromatherapy in the Perinatal Period

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Abstract

The entire process of pregnancy, birth and postpartum falls within the perinatal period. The perinatal period is a process that must be closely monitored in order to protect and ensure the continuity of the health of the woman and her baby. Many physiological, anatomical and emotional changes occur in the woman during pregnancy and birth. These changes can negatively affect the woman's health and reduce her quality of life. In order to cope with these changes and increase her quality of life, women may prefer non-pharmacological applications instead of pharmacological applications due to the thought of harming their baby and themselves. One of the non-pharmacological methods that can be used in the perinatal process is aromatherapy. Aromatherapy reduces the woman's fatigue and stress levels, allows her to relax and have a more positive experience. The purpose of this review is to examine the use of aromatherapy in the perinatal period and present it in line with the literature.

Keywords: *Aromatherapy, Perinatal period, Pregnancy, Birth, Postpartum*

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Introduction

Aromatherapy is a method among traditional and complementary medicine practices in which volatile, essential oils obtained from the roots, trunks, stems and leaves of plants and fruits are used (1). Aromatherapy is used to increase the physical and mental well-being of the individual, to provide spiritual balance, to prevent and treat diseases (1, 2). The history of aromatherapy dates back approximately 6000 years and it is known that it was first used in the ancient Egyptian Civilization for the production of mummies (3). The use of the therapeutic properties of aromatherapy was seen in ancient Greek civilizations (3). In the Middle Ages, it is known that Ibn-i Sina used rose oil, which he obtained by distilling aromatic oils from plants, in his treatments (3, 4). In 1936, French chemist Rene Maurice Gattefosse observed that when he was burned on his arm while performing the distillation process during a perfume production study with volatile essential oils, he poured a jar of lavender oil on the burned area, and that the pain decreased and that the wound healed faster when he applied it regularly to the wound (2). During World War II, Dr. Valnet used essential oils such as lemon, clove, thyme and chamomile to treat wounded and burnt soldiers (2, 3).

Aromatherapy Mechanism of Action

Aromatherapy is a very effective supportive treatment method when applied at the right time and in the right way (2). The use of volatile essential oils changes body chemistry, relieves pain, provides spiritual and emotional balance and relaxation of the body. Aromatherapy can be applied with methods such as inhalation, dermal; massage, bath and compress, oral; gargle. Aromatherapy application by inhalation is the most effective and oldest method and the scent of the volatile essential oil is converted into electrical impulses through the olfactory receptors in the nose. The resulting electrochemical message is transmitted to the limbic system. The message is activated by the hypothalamus and the resulting response is sent to other parts of the body (2, 3). As a result of the message, actions such as pleasure-giving, relaxation and sleepiness are created. It is known that the analgesic components found in some volatile oils are effective on the release of dopamine, endorphin, noradrenaline and serotonin in the brain (2, 5). As a result of aromatherapy application via dermal route, essential oils penetrate the skin barrier rapidly and reach the target area. Essential oils applied orally reach the target area and other parts of the body via

blood circulation and create biochemical and physical effects (2, 3, 5)

Aromatherapy During Pregnancy

Although pregnancy is a natural process, it causes anatomical, physiological, physical and psychological changes in women. As a result of the changes experienced, nausea, vomiting, fatigue, constipation, back pain, increased frequency of urination during the day and breast tenderness may occur (6, 7). The most common discomfort is nausea with a rate of 88%. It is reported that vomiting affects approximately 40% of women in the first trimester (7). These changes can negatively affect the health of the woman and reduce her quality of life (8, 9). Many women avoid pharmacological methods due to the thought that they will harm themselves and their babies and because of the ease of control, and they may resort to complementary therapy methods such as non-pharmacological herbal therapies, vitamin and mineral supplements, relaxation and relaxation exercises, music therapy and aromatherapy in order to cope with the changes experienced (7, 8). In a study conducted in our country, it was determined that 68.3% of pregnant women preferred vitamins, 45.1% massage and 3.6% aromatherapy applications as non-pharmacological methods. The lack of sufficient evidence about herbal and aromatherapy applications during pregnancy significantly affects the rate and reliability of application (9, 10).

During pregnancy, aromatherapy can be used for relaxation, relief, reducing stress, fatigue, stress and physical symptoms. There is little evidence regarding the use of essential oils during pregnancy. When essential oils are used during this process, it is recommended that they be diluted in small doses and that appropriate oils be used. Before application, essential oils can be diluted to 0.5-1% and applied by pouring 1-3 drops onto cotton when applied by inhalation. It is reported that the most commonly used oil during pregnancy is lavender. It is recommended that no essential oil be used during the first trimester, including in diluted form (11, 12). The oils that are suitable for use during pregnancy are cardamom, chamomile, frankincense, geranium, tangerine, lemon, melissa, lavender, ylang ylang, jasmine, sandalwood, rose, tea tree, rosemary, cedarwood, eucalyptus, bergamot, patchouli, bitter orange, cypress, and orange blossom oils (11, 12). Although the plants are completely natural, the oils that are not safe to use during pregnancy and for which there is insufficient evidence are anise seed, camphor, melon, sage, basil, buchu, cumin, cinnamon, juniper, cinnamon, sage, clove, cedarwood, cypress, bitter fennel, geranium, ginger, jasmine, sassafras, rue,

hyssop, mustard, marjoram, myrrh, nutmeg, and oregano (12, 13, 14).

Studies have shown that lemon and mint oils, when applied to women individually or in combination via inhalation, reduce the severity of nausea and vomiting, and that applying mint oil alone has no significant effect on anxiety (15, 16). Other studies have found that massage with rose oil reduces pain in low back and waist pain during pregnancy, orange flower aromatherapy applied in the last trimester of pregnancy increases the mood and endurance of the pregnant woman, Citrus aurantium essential oil aromatherapy reduces anxiety but has no effect on sleep quality, and massage with rosehip oil on the breast, hip and abdomen of pregnant women from the 12th week of pregnancy until birth reduces striae gravidarum (17, 18, 19, 20, 21).

Aromatherapy During Labor

Birth is a biological and physiological process in a woman's life, but it is also a normal, inevitable and multidimensional experience that includes feelings such as happiness, excitement and fear (13, 22). As the act of birth approaches, women experience pain in the lower back due to the descent of the fetus, nausea, diarrhea, regular/irregular uterine contractions, increased vaginal discharge and cervical plug expulsion (22, 23). In addition to these changes, becoming a parent, acquiring new roles and responsibilities, the unpredictability and uncertainty of birth, past birth experience, the meaning that the society in which they live attaches to birth, and the thought of experiencing pain suppress the feeling of reunion with the baby in the woman and cause feelings of fear, anxiety, restlessness and restlessness (24, 25). It has been determined that approximately 80% of women experience fear of birth, and it is reported that the fear of birth can negatively affect the pregnancy, birth and postpartum process (24).

Aromatherapy is used to reduce pain, anxiety and stress during the labor process (26, 27). One of the oldest non-pharmacological methods used to cope with labor pain is aromatherapy. Essential oils should not be used undiluted during the labor process, as they are during pregnancy. Studies examining the effect of aromatherapy on labor pain increased between 1996 and 2002 (27, 28). Today, data from aromatherapy studies are generally expressed as level III evidence (29, 30). It can be applied during labor by diluting it by 1-2% and pouring 1-3 drops onto cotton when applied by inhalation (13). The most commonly used aromatic oils during this process are lavender, mint, rose, sage and neroli oils and can be applied

by applying to the skin, massaging or inhaling (26).

In the study conducted by Tanvisut et al. (2018), women in the first stage of labor were applied one of the oils chosen by them, namely lavender, rose geranium, citrus, and jasmine, and the control group was not applied at all, and it was found that the pain levels of the latent and early active phases were significantly lower in the experimental group (28). In the study conducted by Tadokoro et al. (2023), it was determined that the sage and lavender aromatherapy foot bath applied to the women increased the oxytocin level but had no effect on uterine contractions and cortisol levels (31). In the study conducted by Sriasih et al. (2019) with frangipani oil, it was reported that aromatherapy massage reduced pain during labor (32). In meta-analysis study, it has been reported that aromatherapy reduces the level of pain, fatigue and stress felt during the birth process, reduces nausea and vomiting, positively affects the maternal mood, and facilitates episiotomy recovery (33).

Aromatherapy After Labor

The postpartum period is a transition period in which women experience intense physical, social and psychological changes as they begin to return to their pre-pregnancy state (34). As a result of the changes experienced, women may experience pain, fatigue, restlessness, sleep disorders and lack of energy, and 60% of women in this period may experience severe fatigue (35, 36).

The purpose of aromatherapy application after birth is to reduce pain, restlessness, fatigue, stress levels, accelerate episiotomy healing, and improve sleep quality (37). It can be applied in the postpartum period by diluting it by 1-2% and using methods such as massage, steam, and bath (12).

In the study conducted by Abedian et al. (2020), in an aromatherapy study conducted to improve the healing of postpartum episiotomy and reduce pain scores, it was determined that a sitz bath with lavender oil was effective in healing episiotomy and reducing pain scores (38). In a study conducted by Chen et al. (2022) to investigate the effect of aromatherapy on the psychology of women after birth, it was observed that bergamot oil had a positive effect on depressive mood in women, while it had no effect on sleep quality (39). In a systematic review, it was determined that aromatherapy applied after birth improved physiological and psychological health; It had a positive effect on anxiety, depression, stress, fatigue, weakness, pain, nausea, episiotomy healing and sleep quality, and in addition, it was reported that no serious side effects were observed during the intervention in most of the studies (37). In a

study by Çerçer and Nazik (2018), it was found that aromatherapy applied during childbirth was effective in coping with birth pain and increasing the level of comfort and satisfaction (40).

Conclusion and Recommendations

This review article examines the areas of aromatherapy application during pregnancy, birth and postpartum, how it is applied and for what purposes it is applied. The areas of aromatherapy use in the perinatal period are used to reduce the rates of fatigue, stress and anxiety in women and to increase psychological well-being, and the method of application and the type of essential oil applied vary. The limited number of data in the literature on the areas of aromatherapy application in the perinatal period may affect the rate of use, and it would be beneficial to increase evidence-based studies in this field, contribute to the literature and for health professionals, especially midwives, to follow current information on this subject and improve themselves.

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Review Article

Nursing Approach in Spinal Muscular Atrophy

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Abstract

Spinal muscular atrophy is an important genetic disease that affects motor neurons in the spine, causing muscle weakness, particularly in infancy. Spinal muscular atrophy occurs with a deletion of the survival motor neuron gene and is one of the leading causes of early death in infants. Although some drugs are used for the treatment of spinal muscular atrophy in the world and in Turkey, there is still no treatment method that provides complete recovery. The limited treatment options for spinal muscular atrophy, its inaccessibility, and the poor prognosis of the disease negatively affect the quality of life of individuals and their families. All stages of the disease, starting from the diagnosis process, are very difficult for the patient and his family. A multidisciplinary approach is needed to help patients and their families cope with these difficulties. This approach includes areas such as medical care, rehabilitation, psychosocial support, and education. It is essential that nurses, as key members of the health care team, improve the patient's quality of life, manage symptoms, and support the individual and family in this process. In particular, supporting the patient and family in their care and educating them about their care needs is one of the most important roles of nurses. With this review, an attempt has been made to discuss the diagnostic methods, treatment process, and nursing approaches of spinal muscular atrophy disease, which is a current problem in the world and Turkey.

Key words: *Spinal muscular atrophy, Genetics diseases, Nursing care*

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Introduction

It is an autosomal recessive disease caused by a defect in SMN1, one of the survival motor neuron types. (1). Irreversible loss of the anterior horn cells in the spinal cord and brain stem nuclei. Often seen in the early stages of life, this disease is one of the leading genetic causes of death in infants and young children. Patients usually experience growth retardation, lung disease, scoliosis, and joint contractures, and slowed weight gain that persists from birth into adulthood (2,3). SMA, a pediatric neuromuscular disease, affects 1 in 11,000 live births worldwide. In Türkiye, the annual number of new cases is estimated to be between 130-180 (average: 150) and approximately 3000 SMA patients are being monitored (4).

SMA involves the individual and the family; it requires a multidisciplinary approach because it is a disease that affects biopsychosocial, spiritual, and intellectual aspects. In this interdisciplinary approach, effective treatment and care services are provided to SMA patients to improve the quality of life of individuals and their families. The role of the nurse, who is an important member of the multidisciplinary team, is to integrate the patient and family into society by providing high-quality care and to provide guidance and quality care by analyzing the data collected (5, 6).

Aim

The aim of this review is to discuss the diagnosis and treatment methods of SMA, which is a current problem in the world and Turkey, and the nursing approaches to the disease.

Spinal Muscular Atrophy Types and Symptoms

Spinal Muscular Atrophy (SMA) is an often autosomal recessive neuromuscular disease that results from mutations in the survival motor neuron (SMN) gene and progresses with progressive degeneration (7, 8). The disease is classified according to the age of onset of symptoms and the maximum motor function achieved. The International Spinal Muscular Atrophy Consortium classifies SMA into five clinical types according to the maximum motor function achieved. These are type 0 (Prenatal SMA), type 1 SMA (Werdnig-Hoffmann disease), type 2 SMA (Intermediate type/ also called Dubowitz disease), type 3 SMA (Kugelberg-Welander disease), and type 4 SMA (Adult type) (9). The most common symptoms of the disease vary depending on the type of disease. In brief, the types of SMA and their common symptoms are as follows.

Type 0 SMA (Prenatal SMA): This is the form of SMA that begins before birth.

Usually, the first clinical finding is that the baby has little or no movement in the womb. The baby has generalized weakness, hypotonia, and respiratory failure from birth. In these cases where mental development is not affected, symptoms due to fetal hypokinesia such as polyhydramnios, intrauterine growth retardation, multiple joint contractures (arthrogryposis), skeletal abnormalities, and pulmonary hypoplasia may occur during the intrauterine period (10). Perinatal death occurs with widespread motor and sensory neuron loss in these patients (11).

Type 1 SMA (Werdnig-Hoffmann Disease): Babies with this type appear within the first six months of life; they look like rag dolls, cannot hold their heads up, cannot sit unsupported, have severe respiratory distress (cannot survive without mechanical respiratory support), and usually die in the second year of life (12, 13).

Type 2 SMA (Intermediate Type): Type 2 SMA occurs after the first six months of life and disease complications become evident. These patients can sit, crawl, or stand without assistance, but cannot walk. These patients are prone to respiratory infections. Scoliosis, hand, foot, and chest wall deformities are common. Tendon contraction may result in limited joint movement. Their prognosis is better and their life expectancy is longer than that of type 1 SMA patients. However, impairment of breathing and swallowing may alter the course of the disease (12-14).

Type 3 SMA (Kugelberg-Welander Disease): The disease shows symptoms after the 18th month of an individual's life and is characterized by difficulty or inability to walk. Individuals usually require a wheelchair between the ages of 20 and 30. It is the mildest form of SMA seen in childhood (14, 15).

Type 4 SMA (Adult Type): This is the mildest type of SMA. Life expectancy is not or only slightly affected by this disease (16). SMA Type 4 develops in adulthood and, who also presents with proximal limb girdle weakness (17). The common symptom of the disease is loss of strength in the arms and legs (18).

Spinal Muscular Atrophy in The World and Turkey

The incidence of SMA disease in the world is 1/11,000; The carrier rate varies between 1/40-60 (4). It occurs in 1 in 5000 to 10,000 births in Europe and the carrier frequency is 1 in 50 (19). Although carrier rates vary by ethnic group, the highest carrier rate is in Caucasians (1/37 or 2.7%) and the lowest in Hispanics (1/125 or %0,8). The gender distribution of SMA is similar in girls and boys (20). Genetically, SMA is second only

to cystic fibrosis as a cause of death in children; it is second only to Duchenne muscular dystrophy as a cause of death in children (21). Although the incidence and carrier rates of SMA disease in Turkey are not known, considering that there have been approximately 1,200,000 live births in recent years, it is estimated that the annual number of new cases is between 130-180 (average: 150). Approximately 3000 individuals with SMA are being monitored in Türkiye (4).

Spinal Muscular Atrophy Diagnosis and Treatment Options

Diagnostic methods in spinal muscular atrophy: The first step in making a diagnosis in a patient with SMA findings as a result of clinical evaluation is the detection of homozygous deletions in exon 7 of the SMN1 gene in the survival motor neuron. Losses in this gene are the molecular pathology observed in 95% of patients. In the case of compound heterozygosity, the clinical diagnosis cannot be confirmed but is supported by exon 7 deletion testing alone. In this situation; SMN1 sequence analysis should be performed to look for point mutations such as missense, sense, nonsense, and splice site mutations. If no deletion is detected, electromyography should be performed to evaluate motor neuron damage. In the case of motor neuron damage, changes in SMN1 copy number are quickly and reliably determined by real-time Polymerase Chain Reaction (PCR) or Multiplex Ligation Dependent Probe Amplification (MLPA) techniques (10, 22). The phenotypic variability in SMA patients is also associated with the copy number of the SMN2 gene. SMN2 copy number correlates with disease severity. As the SMN2 copy number decreases, the severity of the disease increases (11). People with 5 or more copies of SMN2 may have no symptoms (11, 23).

Treatment methods for spinal muscular atrophy: While until recently the treatment of SMA disease consisted of respiratory and nutritional support, methods to increase SMN protein levels in disease-related cell types and tissues, particularly in the presymptomatic period, are now being used through small molecule, oligonucleotide, and gene replacement approaches (24, 25). Drugs commonly used in treatment; a gene replacement therapy called Zolgensma, nusinersen (Spinraza), and risdiplam (Evyrsdi) (8). Another treatment method is cell replacement therapy, which is not yet as common as strategies to increase SMN. However, this method can be used with stem cells (26). Other treatments for SMA include quinazoline enzymes, aminoglycoside antibiotics (tobramycin and amikacin), and stem cell therapy. The

effectiveness of these treatments has not been yet proven (8).

The Effect of Spinal Muscular Atrophy Disease on The Individual and The Family

Spinal muscular atrophy (SMA) is a disease that negatively affects a person's quality of life due to severe symptoms. Caring for a person with the disease, meeting their medical needs, and organizing the family's daily life around the individual makes SMA an important issue in the family. Therefore, the individual and the family need to be emotionally and practically strong to cope with the disease. To manage the disease effectively, the impact of SMA on the individual and the family must first be defined (27).

Effects of spinal muscular atrophy on the individual

Spinal muscular atrophy can cause limitations and restrictions in areas such as musculoskeletal disorders, speech, and communication problems, breathing and swallowing difficulties. These limitations and restrictions experienced by people with SMA have a significant impact on their social lives. Society's lack of awareness of SMA can lead to misunderstanding and prejudice, especially from individuals in a society whose looks, insensitive comments, and exclusionary attitudes make the disease process more difficult for individuals. All of this makes it difficult for individuals to participate in events and social activities, increases the social isolation of the individual, causes disappointment, and leads to feelings of loneliness (28-30). In the literature, it has been found that children with SMA-like chronic diseases are twice as likely to have emotional and behavioral problems. A study conducted in our country found that the perceived quality of life of individuals diagnosed with SMA was lower than that of healthy individuals in all domains (21, 31, 32). In addition, situations such as lack of support in relationships with the social environment are common in these patients (29, 33). Children and adolescents diagnosed with SMA may therefore find it difficult to form peer relationships, which can lead to feelings of exclusion or problems finding friends who understand them (29, 34). There are also serious problems in schools, which are the most important means of socialization. The physical facilities of most schools are not set up for the care of people with SMA and this makes it difficult for people with SMA to attend school (29, 35).

One of the main reasons why patients experience social isolation is the treatment process for SMA. During this process, the inability of individuals to participate in social activities can gradually isolate these

individuals from social life and the social relationships in the individual's life can deteriorate. Therefore, the quality of social support provided to patients during the treatment period is very important and closely related to their level of psychosocial adaptation (36-39). Social support and help, especially from family, friends, and close relatives, help the patient overcome despair and adapt to the illness more easily (40).

Another important issue for patients with SMA is the economic problems caused by the disease. The treatment of SMA disease is usually a multidisciplinary approach in hospitals where there are health professionals who require advanced expertise (41). These hospitals are not located on the periphery but in urban areas. In this case, patients, with the support of their families, have to travel to fully equipped hospitals. This involves additional costs such as transport and accommodation. Physical therapy and rehabilitation programs can also be used in the treatment of SMA. These programs also have economic costs, both in terms of session fees and patient mobilization (42). The cost of the drugs needed to treat the disease is also quite high, making it very difficult for individuals to access medication (43). The combination of all these factors creates serious economic difficulties for individuals and families with SMA (41).

Effects of spinal muscular atrophy on family members

Many chronic diseases, such as SMA, cause serious social, psychological, academic, and economic problems for patients and their families. Family members who are primarily responsible for caring for people with SMA often experience many difficulties in providing care. This can cause great anxiety and stress for family members (44-46). One study reported that parents caring for children with chronic illnesses experience more chronic stress than parents of healthy children (47). In general, the psychological, social, and economic impact of SMA on family members can be summarised as follows.

Psychological effects: Due to the physical limitations and treatment process of SMA, family members experience emotional difficulties such as stress, anxiety, helplessness, loss of self-confidence, depression, and fear of not being able to cope with the patient's death, and these difficulties significantly affect the family's mental health. It can be seen that the emotional distress experienced by parents is influenced by various factors such as economic level, educational level, level of social support, communication difficulties, severity of the illness, age of the patient, chronicity of the illness, level of medical care required and disruption of the family

cycle. The physical limitations experienced by the child during the illness, the economic difficulties experienced, and the restrictions in social life significantly increase the stress level of family members. Many psychiatric disorders can also be associated with this stress. Internalizing disorders, especially depression, are often seen in family members with chronic illness (48,49). In addition to these feelings; shock, anxiety, not accepting the disease, anger, resentment, blaming the spouse, and acceptance in the last stage of the disease are among the emotional changes seen in the family (31, 32, 50).

Social impact: Family members may find it difficult to balance their social and work lives with the needs of SMA. Families of people with SMA spend most of their time caring for their loved ones who need support, while also meeting their own basic needs. In this case, family members may have difficulty coping with the burden of caregiving. It is known that women/mothers who are primarily involved in caregiving experience serious problems. These problems include having to care for the patient all the time, sleeping less, not having free time, not being able to rest, and putting their own needs on hold due to regular and continuous follow-up medical care (51).

Economic impact: The treatment and care of SMA is generally costly. Expenses such as medical care, medications, therapies, and special equipment can seriously affect the family's financial situation. In addition, situations such as caregiving family members leaving their jobs or working part-time can cause economic problems. The main economic problems experienced in this process are high costs of medical care; high costs of medicines, special equipment (such as wheelchairs and ventilators), and therapies (physical, occupational, and respiratory); high travel and accommodation costs to access health services; costs of home care; loss of work and income; limited social assistance; and limited coverage of health insurance (41, 52, 53).

Patients and their families can generally benefit from resources such as psychological support, social services, and financial assistance to help them cope with all these effects, and fundraising campaigns can be organized with the permission of the Governor's Office, particularly to help families financially (29).

Raising Awareness in Society

Spinal muscular atrophy is treated symptomatically as there is no proven cure (18). The fact that the disease cannot be treated under current conditions indicates the importance of prenatal or preimplantation genetic diagnosis, and it is

extremely important to raise public awareness about this issue and to develop social policies that support this vulnerable group (54). In this section of the article, the screening and diagnostic methods that the public should know about SMA disease and the social policies will be emphasized. These headings can be briefly summarised as follows.

Scanning methods

Studies of current treatments for SMA have shown that the best outcomes are achieved in patients who begin treatment before clinical signs and motor neuron loss occur (10, 55). For this reason, early diagnosis and genetic screening are extremely important for the prognosis of the disease. The Ministry of Health has put forward some strategies to start appropriate treatment in babies diagnosed through the newborn screening program, to raise awareness in society to reduce consanguineous marriages, and to prevent the economic burden it imposes on society (21).

The Ministry of Health aims to inform and guide potential spouses about detailed genetic counseling services and prenatal diagnosis options through the Premarital SMA Carrier Screening Programme. SMA carrier screening is available to couples who apply for a premarital health report and to currently married couples who request it. The real-time PCR method is used as the carrier screening test; blood samples for screening are taken at the family medicine units where the potential spouses are registered. The blood samples collected are sent to the screening laboratory designated by the provincial health directorates on the designated days. The screening results are reported to family doctors through the system and individuals can access their results through e-Nabız. First, a sample is taken from the male spouse who is to be screened. If the result is "normal", the prospective spouse is informed and removed from the follow-up. If the result is "suspect", the screening test is also performed on the female spouse candidate. If both spouses are carriers, they should be given detailed counseling about the risks and referred to a medical geneticist (21). Genetic counseling and prenatal or pre-implantation diagnostic testing options can be offered to carrier couples to ensure a healthy child. Embryo selection during in vitro fertilization (IVF) using pre-implantation diagnostics can reduce both carrier and disease rates in subsequent generations (56).

Prenatal diagnosis

In spinal muscular atrophy (SMA), as in other genetic diseases, it is recommended that couples who are both carriers have prenatal diagnosis. For autosomal recessive genetic diseases such as SMA, carrier

couples have a 25% risk of having a child with the disease for each fetus in each pregnancy. Prenatal diagnostic tests can be carried out from the 10th week of pregnancy by chorionic villus sampling and from the 15th week of pregnancy by amniocentesis. If there is an affected child, the mother and father should be genetically screened (22).

Social policies

Another issue that society should be aware of in SMA is how families should deal with the economic difficulties caused by the disease. Under Article 5 of Law 2860 on fundraising, those in need can collect aid by obtaining a receipt, placing boxes in certain places, opening bank accounts, issuing a fundraising appeal, organizing a lottery, organizing cultural shows and exhibitions, organizing sports events, trips and entertainment, or using systems that process information automatically or electronically. According to Article 7 of the same Law, if the authority authorized to grant the permit covers more than one district of a province, the governor of that province shall be taken into consideration, and if it is within the borders of a district, the district governor of that district. If the fundraising activity covers more than one province, permission must be obtained from the governor of the province in which the natural or legal persons who will carry out the fundraising activity are established, and the governor who grants permission must inform the other governors and the Ministry of the Interior. Transactions related to fundraising activities can also be produced by association units (57).

Roles and Responsibilities of The Nurse in Spinal Muscular Atrophy

A multidisciplinary approach is key to managing the treatment and care of people with SMA. The care of a person with SMA is a complex phenomenon involving multiple dimensions and different healthcare professionals, and therefore care should be considered as part of a multidisciplinary approach (3). Despite advances in the treatment of SMA, there is currently no definitive cure for the disease, so treatment and care focus on preventing complications from muscle weakness and improving quality of life. This is where nursing care becomes even more important. Care in SMA includes management of respiratory failure, nutritional support, rehabilitation, orthopedic care, and psychosocial care (58). The main purpose of the care provided to a child with spinal muscular atrophy and their family is to ensure that the person with SMA progresses towards a normal life to the best of their ability and to help the child and family cope with the disease (8). The care that should be given to the patient varies according to the bedridden status of the child. Care is

explained in three categories: care for SMA patients who cannot sit, who can sit, and who can walk.

Nursing care for sma patients who cannot sit

The main problem in SMA patients who cannot sit is respiratory problems. Nurses should be aware of the respiratory problems that patients have/could have and have a good knowledge of the respiratory protocols to be applied. To manage respiratory problems, respiratory function should be reviewed with clinical assessment every 3 months initially. To maintain airway patency, mechanical cough assistance devices should be used and chest physiotherapy should be given to all SMA patients. Aspiration of airway secretions is important for SMA patients who cannot sit and should be performed regularly (59). Children with type 1 SMA need mechanical ventilation support to survive. (60). In addition, non-invasive positive pressure ventilation (NIV) should be used in all symptomatic infants and in patients who are unable to sit up before signs of respiratory failure appear. Continuous positive airway pressure should not be used continuously in chronic respiratory failure in SMA. A tracheostomy is an option for ventilation when non-invasive positive pressure ventilation is inadequate or unsuccessful. The option of tracheostomy should be considered individually with the family, taking into account the patient's clinical condition, prognosis, and impact on quality of life (59). Pulse oximetry should be used at home to assess the patient during sleep and to provide non-invasive ventilation if necessary (8). Nurses should provide training and support to parents and carers in the effective use of aspirators, non-invasive respiratory support devices, and medical equipment, explain the situations that require intervention, and carry out assessments through regular home visits (61).

For SMA patients who cannot sit, nutrition and safe swallowing are among the most important issues to consider. The first step in assessing a patient's nutritional status is to perform a swallowing test as soon as possible after diagnosis (3). If the swallowing reflex is inadequate, short-term nasogastric or nasojejunal tube feeding should be used until a long-term gastrostomy tube is placed. About nutrition in acute care, nurses should be aware of metabolic acidosis, abnormalities in fatty acid metabolism, and hyper/hypoglycemia, avoid prolonged starvation of the patient, provide nutrition with a protein source within 6 hours of an acute episode, avoid fluid-electrolyte imbalance and inform the family (14).

Finally, for these bedridden patients, active/passive exercises should be performed in bed and the family should be taught how to do these exercises so that they can apply them later to prevent pressure ulcers (62).

Nursing care for sma patients who can sit

The first thing nurses should be aware of in patients with SMA who can sit in respiratory function. Respiratory assessments of patients who can sit should be performed every 6 months. As part of this clinical assessment, it is important to assess cough function and perform a sleep study if nocturnal hypoventilation is suspected. Care practices to ensure airway patency are similar to those in the non-sitting group. As in patients with SMA who cannot sit, non-invasive positive pressure ventilation (NIV) should be used in all symptomatic patients. In these cases, where tracheostomy support is less common than in those who cannot sit, nebulized bronchodilators can be used if there is a high suspicion of asthma or if there is significant clinical improvement after use. However, nurses should be cautious when using nebulized mucolytics and avoid long-term use. Nurses should provide these patients with annual influenza and pneumococcal vaccinations (59).

SMA patients who can sit should be assessed for obesity and impaired glucose metabolism if they are overweight. If necessary, an appropriate dietary program should be designed to ensure weight control and the patient should be informed (3).

Finally, to improve the musculoskeletal system of SMA patients who can sit, stretch movements, manual stretching and orthoses, splint use, active assisted stretching, serial casting, and positioning techniques can be used in collaboration with a physiotherapist. These methods should be explained to parents and their active use should be ensured (3).

Nursing care for ambulatory sma patients

Most outpatients with SMA have normal lung function. However, the nurse should be alert for upper respiratory tract infections, cough activity, and any symptoms of sleep apnoea or hypoventilation (snoring, restlessness, morning headache, daytime sleepiness) in these patients. No preventive measures are recommended for outpatients with SMA. Supportive care should be provided if specific problems are identified on clinical assessment. Nurses should also provide these patients with annual influenza and pneumococcal vaccinations (59).

Swallowing and feeding difficulties are rarely seen in ambulatory patients. If there are feeding problems, they should be assessed and referred to a dietician (3).

The nurse should educate the patient and family about the importance of passive and active stretching techniques and how to perform them to strengthen the musculoskeletal system in ambulatory SMA patients (3).

In all types of SMA, gastrointestinal problems such as gastro-oesophageal reflux, constipation, use of bowel-regulating agents, delayed gastric emptying and vomiting should be assessed, and growth and development should be monitored. Nurses should always work with a dietician to monitor not only weight but also fluid, macro- and micronutrient intake, particularly calcium and vitamin D intake for bone health (3). Nurses should be knowledgeable about all of these practices in the care of SMA patients and should work with the physician and other team members while fulfilling their dependent roles.

Nurses play an important role in improving the quality of life and health outcomes of people with SMA and their families (8). The nurse should plan individualized care and education according to the needs of the child and family, and provide education and support to the family on what to do in an emergency (59). Parents need information, support, and some resources to care for the SMA patient and ensure family unity, and nurses should support the family in this and try to meet their needs. As SMA patients are intellectually normal, verbal, tactile, and auditory stimulation is an important aspect of developmental care. Helping them to see the activities in their environment and transporting and encouraging them with appropriate vehicles (e.g. trolley, electric wheelchair) for changes in the environment increases and expands patients' communication (8).

The nurse should use the roles of caregiver, educator, researcher, manager, decision maker, advocate, communicator and coordinator, rehabilitator, comforter, therapeutic, counselor, collaborator, autonomy, and responsibility in caring for the person with SMA and the family (63, 64). Nurses provide higher-quality care to patients by using these roles throughout the disease process. As the needs of each individual vary, nurses should take on the roles appropriate to the person they are caring for. However, the essential role of nurses is to provide care. In chronic diseases such as SMA, the roles of educator, researcher, advocate, consoler, rehabilitator, and counselor come to the fore in addition to the role of caregiver. Nurses play a key role in disease prevention through counseling, meeting the physical and psychosocial care needs of SMA patients and their families, referring them to resources, and providing support.

Therefore, it is recommended that nurses address the multidimensional care needs of SMA patients and their families and ensure continuity of educational studies on the subject to increase their awareness (8).

Conclusion and Recommendations

Spinal muscular atrophy is an autosomal recessive neuromuscular disease caused by deletions or mutations SMN1 gene in the survival motor neuron. The most common inherited cause of childhood death, SMA is classified into five types (0-4) according to age of onset, severity of motor deterioration, and life expectancy. Type 1 (Werding-Hoffmann) is the most severe form and affects mainly newborn babies (11). Recently, SMA has become a topical issue and the lack of a treatment that completely cures the disease increases the importance of nursing care in treatment. The disease, which affects the motor neurons in the spine causes muscle weakness, and which is particularly severe in SMA type 1 patients, presents a picture that reveals the requirements of nursing care at this point. What is expected of nurses when dealing with rare diseases such as SMA is not to know and recognize all diseases, but to be aware that there are thousands of rare diseases and that millions of people suffer from these diseases, and to be aware that a non-standard approach should be taken to these diseases (65). Nursing care in SMA is the determinant of the patient's prognosis and quality of life. The nurse should plan the best education for the individual and family during this process. Nurses who provide high-level care with a multidisciplinary team should support the family and the individual at every moment of care and should have a close relationship with the patient and their family. To better manage the process, nurses should use their roles as caregivers, educators, researchers, managers, decision-makers, advocates, communicators and coordinators, rehabilitators, comforters, and therapeutics effectively.

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