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Bagcilar Medical Bulletin (Bağcılar Tıp Bülteni) (BMB) is a periodical scientific publishing of Health Sciences University, İstanbul Bağcılar Training and Research Hospital. This editorially independent, unbiased, international journal periodically publishes peer-reviewed work in the all medical fields on an international scientific basis. Publication language is English for full text and Turkish and English for abstracts. The journal has been published in English since December issue of 2016 as an e-journal.

The journal is published quarterly in March, June, September and December.

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Tarihçe

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T.C.Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi adına Başhekim Doç. Dr. Ozan Beytemür. (Türkiye Cumhuriyeti Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi, Ortopedi ve Travmatoloji Kliniği, İstanbul, Türkiye).

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BAGCILAR MEDICAL BULLETIN
Bağcılar Tıp Bülteni

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The journal is published quarterly in March, June, September and December.

Original clinical and experimental articles,interesting case studies, and literature reviews made from relevant authors in their brancheswill be accepted for evaluation in BMB.

Bagcilar Medical Bulletin is indexed in **TÜBİTAK/ULAKBİM, EBSCO, Gale, Türk Medline, Turkey Citation Index, DOAJ, ProQuest, J-Gate** and **ScopeMed.**

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Bağcılar Tıp Bülteni/Bagcilar Medical Bulletin (BTB), Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi'nin süreli bilimsel yayınıdır. Uluslararası, hakem değerlendirmeli, İngilizce ve açık erişim olarak yılda 4 sayı (Mart, Haziran, Eylül, Aralık) yayınlanan bilimsel bir dergi olup, tıbbın tüm alanlarındaki bilgi birikiminin uluslararası bilimsel platformda yayılabilmesini amaçlamaktadır. Bu amaçla tıbbın her alanında yapılmış orijinal klinik ve deneysel çalışmalar ve ilginç olgu sunumları ile konusunda uzman yazarların yaptığı literatür derlemeleri yayın için değerlendirmeye alınır.

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Derginin editöryal ve yayın süreçleri ile etik kuralları International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), ve National Information Standards Organization (NISO) gibi uluslararası kuruluşların kurallarına uygun olarak şekillenmektedir. Dergimiz, şeffaf olma ilkeleri ve "Akademik Yayıncılıkta En İyi Uygulamalar İlkeleri" ile uyum içindedir.

Bağcılar Tıp Bülteni, **TÜBİTAK/ULAKBİM, EBSCO, Gale, Türk Medline, DOAJ, Türkiye Atıf Dizini, ProQuest, J-Gate** ve **ScopeMed** tarafından indekslenmektedir.

Dergi Adı (İngilizce): Bagcilar Medical Bulletin

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Bu dergi, araştırmaları kamuya ücretsiz olarak sunmanın daha büyük bir küresel bilgi alışverişini desteklediği ilkesine dayanarak içeriğine anında açık erişim sağlar.

Yazarlar ve telif hakkı sahipleri, Bağcılar Tıp Bülteni'nde yayınlanan makaleler için tüm kullanıcılara ücretsiz olarak erişim sağlar. Makaleler kaynak gösterilmek şartıyla kullanıma açıktır.

Açık Erişim Politikası, Budapeşte Açık Erişim Girişimi'nin (BOAI) kurallarına dayanmaktadır. "Açık erişim" ile, onun ücretsiz erişilebilirliğini kastedilmektedir. Herhangi bir kullanıcının bu makalelerin tam metinlerini okumasına, indirmesine, kopyalamasına, dağıtmasına, yazdırmasına, aramasına veya bağlantı vermesine, indeksleme için taramasına, yazılıma veri olarak iletmesine veya başka herhangi bir yasal amaç için internetin kendisine erişim elde etmekten ayrılamaz olanlar dışında finansal, yasal veya teknik engeller olmadan kullanmasına izin verir. Çoğaltma ve dağıtım üzerindeki tek kısıtlama ve bu alandaki telif hakkının tek rolü, yazarlara çalışmalarının bütünlüğü üzerinde kontrol ve uygun şekilde tanınma ve alıntılanma hakkı vermek olmalıdır.

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Description

Bagcilar Medical Bulletin is a peer-reviewed English journal aiming to publish original research, current review articles, case reports and letters related to all medical fields. The journal is currently published quarterly as an online publication. The articles will become freely available to all readers in pdf format as soon as they have been accepted after peer review. Accepted articles will immediately appear as a part of the issue belonging to that publication period. The journal uses EjManager online manuscript submission, review and tracking system .

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The editorial and publication process of the Journal of the Turkish Academy of Dermatology are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

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- Case reports,
- Reviews,
- Letters to the Editor

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All submissions must be original, unpublished (including as full text in conference proceedings), and not under the review of any other publication synchronously. Each manuscript is reviewed by one of the editors and at least two referees under double-blind peer review process. We reserve the right to use plagiarism detecting software to screen submitted papers at all times. We check for plagiary and fraudulent data, falsification (fabrication or manipulation of research data, tables, or images) and improper use of humans or animals in research. All manuscripts not in accordance with these standards will be removed from the publication. This also contains any possible malpractice discovered after the publication. In accordance with the code of conduct we will report any cases of suspected plagiarism or duplicate publishing.

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All manuscripts submitted to the journal for publication are checked by Crossref Similarity Check powered by "iThenticate" software for plagiarism. If plagiarism is detected, relevant institutions may be notified. In this case, the authors might be asked to disclose their raw data to relevant institutions.

Language

The language of the Bagcilar Medical Bulletin is American English. In addition, abstracts of the articles are published in both English and Turkish, and abstracts in both languages are requested from the authour(s).

Manuscript Organization And Format

All correspondence will be sent to the first-named author unless otherwise specified. Papers should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the Journal it is being submitted (i.e., original research article,brief research article, review article, case report or letter to the editor). In addition, a Copyright Transfer Form, Author Contribution Form and ICJME Form for Disclosure of Potential Conflicts of Interest must be submitted. Authors will be notified of the receipt of their paper and the number assigned to it. The number should be included in all further correspondence. All parts of the manuscript, including case reports, quotations, references, and tables, must be double-spaced throughout. All four margins must be at least 2.5 cm. The manuscript should be arranged in the following order, with each item beginning a new page: 1) title page, 2) abstract, 3) text, 4) acknowledgement 5) references, and 6) tables and/or figures. All pages must be numbered consecutively.

Title Page

On the title page, include full names of authors, academic or professional affiliations, and complete address with phone, fax number(s) and e-mail address (es) of the corresponding author. Acknowledgments for personal and technical assistance should be indicated on the title page.

Abstract and Keywords

Title of the manuscript in English should be written in English abstract, and a Turkish title must be for Turkish abstract.. All articles should include abstract and keywords. For abstracts are most distinct parts of an article and take place on the electronic databases, author should be sure that abstract represents the content of the article accurately. Abstract should inform about the basis of the study and include the purpose, basic procedures (selection of cases and laboratory animals, observatory and analytical methods), key findings and conclusions. New and significant apects of the study or observations should be stated. Up to 3-10 key words in English and in Turkish should be in accordance with National Library of Medicine's Medical Subjects Subheadings (MeSH).

Manuscript Types

Original Research

Original research articles report substantial and original scientific results within the journal scope. Original research articles comprised of Abstract, Key Words, Introduction, Material and Methods, Results, Discussion, Conclusion, References and Table/ Figures. The abstract should be structured as the following.

INSTRUCTIONS TO AUTHORS

Abstract

The abstract should be no longer than 500 words and structured as follows: objective, method, results, and conclusions. Objective -the primary purpose of the article; Material and Method(s) -data sources, design of the study, patients or participants, interventions, and main outcome measures; Results -key findings; Conclusions -including direct clinical applications.

Keywords

Up to 3-10 key words in English and in Turkish should be in accordance with National Library of Medicine's Medical Subjects Subheadings (MeSH).

Introduction

This section should contain a clear statement of the general and specific objectives as well as the hypotheses which the work is designed to test. It should also give a brief account of the reported literature. The last sentence should clearly state the primary and secondary purposes of the article. Only, the actual references related with the issues have to be indicated and data or findings related with the current study must not be included in this section.

Materials and Methods

This section should contain explicit, concise descriptions of all procedures, materials and methods used in the investigation to enable the reader to judge their accuracy, reproducibility, etc. This section should include the known findings at the beginning of the study and the findings during the study must be reported in results section. Ethics Committee Approval of the research and written Informed Consent obtained from the participants should be indicated.

The selection and description of the participants

The election, source of population, inclusion and exclusion criteria of the people who participate to experimental or clinical study must be clearly defined in this section. The particular study sample must be explained by the authors (i.e., why the study is performed in a definite age, race or sex population, etc.).

Technical information

The methods, apparatus (the manufacturer's name and address in parentheses), and procedures in sufficient detail must be defined to allow others to reproduce the results. References to established methods, including statistical methods (see below) must be given and brief descriptions for methods that have been published but are not well-known must be provided; new or substantially modified methods must be described, the reasons for using them must be given, and their limitations of the methods must be evaluated. The all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration must be identified. Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

Statistics

The statistical methods must be described with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. If possible, findings should be quantified and presented with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size must be avoided. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. The computer software used must be specified.

Results

The results should be presented in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. The all the data in the tables or illustrations should not be repeated in the text; only the most important observations must

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be emphasized or summarized. Extra or supplementary materials and technical detail can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Discussion

The findings of the study, the findings and results which support or do not support the hypothesis of the study should be discussed, results should be compared and contrasted with findings of other studies in the literature and the different findings from other studies should be explained. The new and important aspects of the study and the conclusions that follow from them should be emphasized. The data or other information given in the Introduction or the Results section should not be repeated in detail.

Conclusions

Conclusions derived from the study should be stated. For experimental studies, it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice. The conclusions should be linked with the goals of the study but unqualified statements and conclusions not adequately supported by the data should be avoided. New hypotheses should be stated when warranted, but should be labeled clearly as such.

Tables, Graphics and Illustrations

Tables, graphics and illustrations should be numbered in Arabic numerals in the text. The places of the illustrations should be signed in the text. Detailed information is under the related heading in below.

Brief Research

Brief researches are similar to original research in that they follow the same format and guidelines, but they consider small-scale research or research that is in early stages of development. These may include preliminary studies that has a simple research design or a small sample size and that have produced limited pilot data and initial findings that indicate need for further investigation. Brief researches are much shorter than manuscripts associated with a more advanced, larger-scale research project. They are not meant to be used for a short version of an article about research that would otherwise qualify for a full original research manuscript or for publishing material on research that lacks significance, is not rigorous or, if expanded, would not qualify for a full article or for research.

Case Report

Case reports consider new, interesting and intriguing case studies in detail. They should be unique and present methods to overcome any health challenge by use of novel tools and techniques and provide a learning source for the readers. Case reports comprise of: Abstract (unstructured summary), Key-words, Introduction, Case Report, Discussion, Reference, Tables and Figures. Written informed consent of the patient should be obtained and indicated in the manuscript.

Review

Review articles are written by individuals who have done substantial work on the subject or are considered experts in the field. The Journal invites authors to write articles describing, evaluating and discussing the current level of knowledge regarding a specific subject in the clinical practice.

The manuscript should have an unstructured abstract representing an accurate summary of the article, key words, introduction, conclusion. Authors submitting review article should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

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Letter to the Editor is short and decisive manuscript. They should be preferably related to articles previously published in the Journal or views expressed in the Journal. The letter should not include preliminary observations that need a later study for validation.

Tables

Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text. Each table should be typed or printed with double spacing on a separate sheet of paper. The tables should be numbered consecutively in the order of their first citation in the text and a brief title for each table should be supplied. Any internal horizontal or vertical lines should not be used and a short or an abbreviated heading should be given to each column. Authors should place explanatory matter in footnotes, not in the heading. All nonstandard abbreviations should be explained in footnotes, and the following symbols should be used in sequence: *,†,‡,§,ǁ,¶,**,††,‡‡. The statistical measures of variations, such as standard deviation and standard error of the mean should be identified. Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully. Additional tables containing backup data too extensive to publish in print may be appropriate for publication in the electronic version of the journal, deposited with an archival service, or made available to readers directly by the authors. An appropriate statement should be added to the text. Such tables should be submitted for consideration with the paper so that they will be available to the peer reviewers.

Illustrations (Figures)

Figures should be either professionally drawn and photographed, or submitted as digital prints in photographic-quality. In addition to requiring a version of the figures suitable for printing, authors are asked for electronic files of figures in a format (for example, JPEG or GIF) that will produce high-quality images in the Web version of the journal; authors should review the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. For X-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, sharp, glossy, black-and-white or color photographic prints should be sent, usually 127 x 173 mm. Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication. Figures should be made as self-explanatory as possible, since many will be used directly in slide presentations. Titles and detailed explanations belong in the legends--not on the illustrations themselves. Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background. Photographs of potentially identifiable people must be accompanied by written permission to use the photograph. Figures should be numbered consecutively according to the order in which they have been cited in the text. If a figure has been published previously, the original source should be acknowledged and written permission from the copyright holder should be submitted to reproduce the figure. Permission is required irrespective of authorship or publisher except for documents in the public domain. Accompanying drawings marked to indicate the region to be reproduced might be useful to the editor. We publish illustrations in color only if the author pays the additional cost.

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Units of Measurement

Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples. Temperatures should be in degrees Celsius, blood pressures should be in millimeters of mercury. Authors must consult the Information for Authors of the particular journal and should report laboratory information in both local and International

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System of Units (SI). Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

Abbreviations and Symbols

Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

Acknowledgement(s)

All forms of support, including individual technical support or material support must be acknowledged in the author's footnote before references.

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Original papers and reviews have no specific word limitation. A case report must be strictly limited to 1000 words excluding abstract and have minimal figures, tables, and references. Letters to the Editor (maximum of 500 words, including references; no tables or figures) will be considered if they include the notation "for publication." A letter must be signed by all of its authors. Letters critical of an article published in the journal must be received within 12 weeks.

Preparation of Manuscripts

The Bagcilar Medical Bulletin follows the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals". Upon submission of the manuscript, authors are to indicate the type of trial/research and provide the checklist of the following guidelines when appropriate:

CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285: 1987-91),

PRISMA for preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.),

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.),

STROBE statement-checklist of items that should be included in reports of observational studies,

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

CARE guidelines are designed to increase the accuracy, transparency, and usefulness of case reports. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; the CARE Group. The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development.)

References

Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible. On the other hand, extensive lists of references to original work on a topic can use excessive space on the printed page. Small numbers of references to key original papers often serve as well as more exhaustive lists, particularly since references can

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now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently. Using abstracts as references should be avoided.

References to papers accepted but not yet published should be designated as "in press" or "forthcoming"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source. Citing a "personal communication" should be avoided unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, written permission and confirmation of accuracy from the source of a personal communication must be obtained.

Reference Style and Format

The Uniform Requirements style for references is based largely on an American National Standards Institute style adapted by the National Library of Medicine for its databases. Authors should consult NLM's Citing Medicine for information on its recommended formats for a variety of reference types. References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used in the list of Journals in National Library of Medicine sources. Accuracy of citation is the author's responsibility. All references should be cited in text. Type references in the style shown below. If there are more than 6 authors, list them followed by et al. Abbreviations of journal names should conform to the style used in National Library of Medicine. If a journal is not indexed in National Library of Medicine's MEDLINE/PubMed, it should not be abbreviated.

Examples for References:

1. For articles in journals:

For the published article from the journal which placed and abbreviated in MEDLINE:

Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3:171-178.

2. For the supplement:

For the published article from the journal which placed and abbreviated in MEDLINE:

Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

3. For articles in press:

Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

4. For the citations from books:

Books edited by one editor:

McKnight TL. Obesity Management in Family Practice. 1st ed., NewYork: Springer, 2005:47-51.

For the citation from a section of book edited by editor(s):

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

If the authors of the cited section are the editors of the book:

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Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. First ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

For the citation from a translated book:

McGuffin P, Owen MJ, Gottsman II. Psikiyatri Genetiği ve Genomiği. Abay E, Görgülü Y (Çevirenler) 1st ed., Istanbul: Nobel Tıp Kitabevleri, 2009:303-341.

5. For the citation from thesis:

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6. For the citation from posters:

Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 201, Antalya, 2011:102.

7. Online Article:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 2006 Jul 4 [cited 2007 Jan 4];145(1):62-9. Available from:http://www.annals.org/cgi/reprint/145/1/62.pdf

SUBMISSION TO JOURNAL

All new manuscripts must be submitted through the Bagcilar Medical Bulletin online manuscript submission and peer review system. Complete instructions are available at the website (). A cover letter should accompany with manuscripts, including the knowledge of:

•The findings of previous same studies should be informed and should be cited. The copies of previous same studies should be sent with manuscripts that might help to the editor in the decision process.

•The knowledge of "all authors have read and accepted the study in its form, all authors meet the criteria for being in authorship" should be stated.

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SUBMISSION CHECKLIST

It is hoped that this list will be useful during the final checking of an article prior to sending it to the journal's editor for review. Please consult this Guide for Authors, for further details of any item.

Ensure that the following items are present:

• Cover letter to the editor

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- Acknowledgement of "the paper is not under consideration for publication in another journal"

- Disclosure of any commercial or financial involvement

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-Permission of previous published material if used in the present manuscript

-Acknowledgement of the study "in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of in 2000.

-Statement that informed consent was obtained after the procedure(s) had been fully explained.

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-Indicating whether the institutional and national guide for the care and use of laboratory animals was followed as in “Guide for the Care and Use of Laboratory Animals”.

-Title page

-The title of the manuscript both in Turkish and in English

-All authors and their affiliations

-All authors’ e-mail address, full postal address, GSM phone, business telephone and fax numbers

-Abstracts (400-500 words) Both in Turkish and in English

-Keywords: 3 to 10 words (in Turkish and in English)

-Body text

-Acknowledgement

-Reference

-All tables (including title, description, footnotes)

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Peer Review, Publication Ethics and Malpractice Statement

Peer- Review

Submission is considered on the conditions that papers are previously unpublished and are not offered simultaneously elsewhere; that authors have read and approved the content, and all authors have also declared all competing interests; and that the work complies with the ethical approval requirements and has been conducted under internationally accepted ethical standards. If ethical misconduct is suspected, the Editorial Board will act in accordance with the relevant international rules of publication ethics (i.e., COPE guidelines).

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The editor of the journal strives to meet the needs of readers and authors, and to provide a fair and appropriate peer-review process. The editor is also responsible for deciding which articles submitted to the journal should be published and guided by the policies subjected to legal requirements regarding libel, copyright infringement, and plagiarism. The editor might discuss such policies, procedures, and responsibilities with reviewers while making publication decisions. The editor is responsible for the contents and overall quality of the publication.

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YAZARLARA BİLGİ

Hakem Değerlendirmesi, Yayın Etiği ve Kötüye Kullanım

Hakem Değerlendirmesi

Makalelerin daha önce yayınlanmamış olması ve aynı anda başka bir yere gönderilmemiş olması koşuluyla başvuru kabul edilir; yazarlar, içeriği okuduğunu, onayladığını, tüm yazarların çıkar çatışmalarını beyan ettiğini, çalışmanın etik onaya uygun olduğunu ve uluslararası kabul görmüş etik standartlarda yürütüldüğünü kabul eder. Etik suistimalden şüphelenilmesi durumunda, Yayın Kurulu ilgili uluslararası yayın etiği kurallarına (COPE yönergelerine) uygun olarak hareket edecektir.

Derginin yayın politikaları, Bilim Konseyi Editörleri tarafından önerilen kurallarda belirtildiği gibi yürütülür ve ICMJE Biyomedikal Dergilere Gönderilen Makaleler için Tekdüzen Gereklilikler: Biyomedikal Yayın için Yazma ve Düzenleme'de yansıtılır. Buna göre yazarlar, gözden geçirenler ve editörlerin bu bildirimde yer alan etik davranışa ilişkin en iyi uygulama kılavuzlarına uymaları beklenmektedir.

Gönderilen yazılar çift-kör hakem değerlendirmesine tabi tutulur. Dergide yayımlanacak yazıların seçimine rehberlik eden bilim kurulu, derginin seçilmiş uzmanlarından ve gerekirse ilgili araştırma alanında ulusal ve uluslararası uzmanlardan seçilmiş uzmanlardan oluşur. Tüm yazılar editör, bölüm yardımcı editörleri ve en az üç dahili ve harici uzman hakem tarafından incelenir. Tüm araştırma makaleleri de bir istatistik editörü tarafından yorumlanır.

İnsan ve Hayvan Araştırmaları

Deneysel, klinik, ilaç ve insan çalışmaları için, etik kurul onayı ve çalışma protokolünün uluslararası anlaşmalara uygunluğuna dair bir beyan (World Medical Association of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," Ekim 2013) gereklidir. Deneysel hayvan çalışmalarında yazarlar, izlenen prosedürlerin hayvan haklarına uygun olduğunu (Laboratuvar Hayvanlarının Bakım ve Kullanım Kılavuzu) belirtmeli ve hayvan Etik Kurul Onayı almalıdır. Etik Kurul Onayı belgesi, makale ile birlikte Bağcılar Tıp Bülteni'ne gönderilmelidir.

Etik Kurul Onayı ile yukarıda belirtilen uluslararası kılavuzlara uyum ve hastanın aydınlatılmış onamının alındığına dair beyan "Materyal ve Yöntem" bölümünde belirtilmeli ve kullanılan veri/medyanın hastanın kimliğini ortaya çıkarabileceği durumlarda vaka raporları gerekmektedir. Yazarlar, kurumlar arasında çıkar çatışması beyanı, herhangi bir mali veya maddi desteğin kabulünün belirtilmesi makale gönderen yazarlar için zorunludur ve bu açıklama makalenin sonunda yer almalıdır. Hakemler, yazarlar veya kurumlar ile aralarında herhangi bir potansiyel çıkar çatışması varsa, bunu rapor etmelidir.

18 yaşın altındaki kişiler için, her iki ebeveynin veya kişinin yasal vasisi veya velisinin imzasını içeren bir onay formu gönderilmelidir.

İntihal ve Etik Suistimal

Bağcılar Tıp Bülteni, tüm makaleleri yayınlanmadan önce "iThenticate" kullanarak intihal taramasına tabi tutar. Dergi, iThenticate raporlarına göre benzerlik oranı %15'in üzerinde olan makaleleri kabul etmemektedir.

Yazarların aşağıda yazılanlar gibi her türlü intihal ve etik suistimalden kaçınmaları önemlidir:

İntihal: Başka bir yazarın yayınındaki bir içeriğin tamamını veya bir kısmını kaynak göstermeden yeniden yayınlamak.

Fabrikasyon (Uydurma): Var olmayan veri ve bulguları/sonuçları yayınlamak.

Çoğaltma: Bir makalenin farklı dillerde yeniden yayınlanmasını içeren başka bir yayından alınan verileri kullanmak.

Dilimleme (Salamizasyon): Bir çalışmanın sonuçlarını bölerek birden fazla yayın oluşturma.

Veri Manipülasyonu/Yanlışlığı: Yanlış bir izlenim vermek için araştırma verilerini manipüle etmek veya kasıtlı olarak çarpıtmak.

İntihal, fabrikasyon, çoğaltma, veri manipülasyonu ve dilimleme gibi etik olmayan uygulamaları ve yazarlık hediye etme, uygunsuz teşekkür ve COPE akış şemalarına uygun olmayan referanslar gibi uygulamalarla inceleme sürecini etkilemeye yönelik çabaları onaylamıyoruz.

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Gönderilen yazılar ayrıca otomatik yazılım tarafından intihal ve yayın değerlendirmesine tabi tutulur. Yazarlar, çalışma sonuçlarını tamamen veya kısmen özet şeklinde yayınlayıp yayınlamadıklarını bildirmekle yükümlüdür.

A. YAYINCININ GÖREVLERİ:

Etik Olmayan Yayınlama Davranışının Ele Alınması

Yayıncı, iddia edilen veya kanıtlanmış bilimsel suistimal, hileli yayın veya intihal durumlarında, söz konusu makaleyi editörlerle yakın iş birliği içinde değiştirmek için tüm uygun önlemleri alacaktır. Bu, en ciddi durumda, etkilenen çalışmanın bir yanlışlık sonucu yayınlanmasını, ifşa edilmesini veya geri çekilmesini içerir. Yayıncı, editörlerle birlikte, araştırma suistimalinin meydana geldiği makalelerin yayınlanmasını tespit etmek ve önlemek için makul adımları atacak ve hiçbir koşulda bu tür kötüye kullanımın gerçekleşmesine teşvik etmeyecek veya bilerek izin vermeyecektir.

Editöryal Özerklik

Bağcılar Tıp Bülteni, herhangi birinin veya ticari ortakların etkisi olmaksızın editöryal kararların özerkliğini sağlamayı taahhüt eder.

Fikri Mülkiyet ve Telif Hakkı

Bağcılar Tıp Bülteni, dergide yayınlanan makalelerin mülkiyetini ve telif haklarını korur ve her makalenin yayınlanmış kaydını tutar. Dergi, yayınlanan her makalenin bütünlüğünü ve şeffaflığını sağlar.

Bilimsel Suistimal

Bağcılar Tıp Bülteni'nin yayıncısı, hileli yayın veya intihal ile ilgili gerekli tüm önlemleri almaktadır.

B. EDİTÖRLERİN GÖREVLERİ:

Yayın Kararı ve Sorumluluğu

Dergi editörü, dergideki her şeyi kontrol altında tutar, okuyucuların ve yazarların ihtiyaçlarını karşılamaya çalışır. Editör ayrıca dergiye gönderilen makalelerin hangilerinin yayınlanması gerektiğine karar vermekten ve hakaret, telif hakkı ihlali ve intihal ile ilgili yasal gerekliliklere tabi politikalar tarafından yönlendirilmekten sorumludur. Editör, yayın kararları verirken hakemlerle tartışabilir. Yayının içeriğinden ve genel kalitesinden editör sorumludur. Editör, adil ve uygun bir hakemlik süreci sağlamalıdır.

Nesnellik

Dergiye gönderilen makaleler her zaman önyargısız olarak değerlendirilir.

Gizlilik

Editör, gönderilen bir makaleyle ilgili herhangi bir bilgiyi, editör kadrosu, hakemler ve yayıncı dışında hiç kimseye açıklamamalıdır.

Çıkar Çatışmaları ve İfşa

Bağcılar Tıp Bülteni, yazarlar, hakemler ve editörler gibi taraflar arasında herhangi bir çıkar çatışmasına izin vermez. Gönderilen bir makaledeki yayınlanmamış materyaller, yazarın açık izni olmaksızın hiç kimse tarafından kullanılmamalıdır.

Yayımlanan Eserlerde Temel Hatalar

Yazarlar, yayınlanan çalışmada önemli hatalar veya yanlışlıklar tespit edilirse, derhal dergi editörlerini veya yayıncısını bilgilendirmek ve makaleyi düzeltmek veya geri çekmek üzere onlarla iletişim sağlamakla yükümlüdür. Editörler veya yayıncı, yayınlanan bir çalışmanın önemli bir hata veya yanlışlık içerdiğini üçüncü bir taraftan öğrenirse, yazarlar makaleyi derhal düzeltmeli, geri çekmeli veya dergi editörlerine makalenin doğruluğuna dair kanıt sağlamalıdır.

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C. HAKEMLERİN GÖREVLERİ:

Değerlendirme

Hakemler, yazarların kökeni, cinsiyeti, cinsel yönelimi veya politik felsefesini gözetmeksizin yazıları değerlendirir. Hakemler ayrıca değerlendirme sırasında gönderilen yazılar için adil bir kör hakem incelemesi sağlar.

Gizlilik

Gönderilen makalelerle ilgili tüm bilgiler gizli tutulur. Hakemler, editör tarafından izin verilmedikçe başkalarıyla tartışılmamalıdır.

Çıkar Çatışmaları ve İfşa

Hakemlerin yazarlar, fon sağlayıcılar, editörler vb. taraflarla ilgili herhangi bir çıkar çatışması yoktur.

Editöre Katkı

Hakemler, editöre karar vermede ve makaleyi geliştirmede yardımcı olabilir.

Nesnellik

Daima objektif bir değerlendirme yapılır. Hakemler görüşlerini uygun destekleyici argümanlarla açıkça ifade eder.

Kaynakların Onaylanması

Hakemler, yazarların atıfta bulunmadığı ilgili yayınlanmış bir çalışmayı tanımlamalıdır. Hakemler ayrıca, makale ile kişisel bilgilerine sahip oldukları diğer yayınlanmış makaleler arasındaki önemli benzerlikleri veya örtüşmeleri editörün dikkatine sunarlar.

D. YAZARLARIN GÖREVLERİ:

Raporlama Standartları

Gönderilen bir makale orijinal olmalı ve yazarlar, makalenin daha önce herhangi bir dergide yayınlanmamış olmasını sağlamalıdır. Araştırmanın verileri makalede tam anlamıyla sunulmalıdır. Bir makale, başkalarının çalışmayı yeniden kopyalamasına izin vermek için gerekli ayrıntı ve referansları içermelidir.

Özgünlük

Çalışmalarını dergiye göndermek isteyen yazarlar, çalışmalarının tamamen özgün olduğundan emin olmalıdır. Literatürden alınan kelime ve cümleler uygun şekilde alıntılanmalıdır.

Çoklu Yayınlar

Yazarlar, aynı çalışmayı başka bir dergide yayınlanmak veya değerlendirilmek üzere göndermemiş olmalıdır. Aynı çalışmanın birden fazla dergiye aynı anda gönderilmesi kabul edilemez ve etik dışı bir davranış olarak nitelendirilir.

Kaynakların Belirtilmesi

Başkalarının çalışmalarının uygun bir şekilde alıntılanması gerekir. Yazarlar, çalışmayı belirlemede etkili olan yayınlara atıfta bulunmalıdır. Çalışmanın sürecini kapsayan tüm kaynaklar belirtilmelidir.

Makale Yazarlığı

Bir makalenin yazarlığı, çalışmaya kayda değer bir katkı yapmış olanlarla sınırlı olmalıdır. Başkaları araştırmaya katılmışsa, katkıda bulunanlar olarak listelenmelidir. Yazarlık aynı zamanda bir derginin editörü ile iletişim halinde olan bir sorumlu yazarı da içerir. Sorumlu yazar, tüm uygun ortak yazarların bir makaleye dahil edilmesini sağlamalıdır.

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Çıkar Çatışmaları ve İfşa

Tüm finansal destek kaynakları açıklanmalıdır. Tüm yazarlar, çalışmalarını oluşturma sürecinde (varsa) çıkar çatışmasını ifşa etmelidir. Gönderilen bir çalışma için bireylerden veya kurumlardan alınan mali yardımlar veya diğer destekler, Bağcılar Tıp Bülteni Yayın Kurulu'na açıklanmalıdır. ICMJE Potansiyel Çıkar Çatışması Bildirim Formu, olası bir çıkar çatışmasını açıklamak için katkıda bulunan tüm yazarlar tarafından doldurulmalı ve gönderilmelidir. Derginin Yayın Kurulu, editörler, yazarlar veya hakemler arasında olası bir çıkar çatışması durumlarında COPE ve ICMJE yönergeleri kapsamında hareket eder.

Mali veya şahsi fayda sağlayan koşullar, bir çıkar çatışması doğurur. Bu durum, bilimsel sürecin ve yayınlanan makalelerin güvenilirliği, bilimsel çalışmaların planlanması, uygulanması, yazılması, değerlendirilmesi, düzenlenmesi ve yayınlanması sırasında çıkar çatışmalarının objektif olarak ele alınması ile doğrudan ilişkilidir.

Finansal ilişkiler en kolay tespit edilen çıkar çatışmalarıdır ve derginin, yazarların ve bilimin güvenilirliğini zedelemesi kaçınılmazdır. Bu çatışmalara bireysel ilişkiler, akademik rekabet veya entelektüel yaklaşımlar neden olabilir. Yazarlar, çalışmanın tüm verilerine ulaşmalarını veya makalelerini analiz etme, yorumlama, hazırlama ve yayınlama olanaklarını kısıtlayan kâr veya başka bir avantaj elde etme düşüncesiyle sponsorlarla anlaşmalardan mümkün olduğunca kaçınmalıdır. Editörler, çalışmaları değerlendirirken aralarında ilişki olabilecek kişileri bir araya getirmekten kaçınmalıdır. Makaleler hakkında nihai kararı verecek olan editörlerin, karar verecekleri konulardan hiçbiriyle kişisel, mesleki veya mali bağı olmamalıdır. Yazarlar, makalelerinin bağımsız bir değerlendirme süreci ile etik ilkeler çerçevesinde değerlendirilmesini sağlamak için olası çıkar çatışmalarını yayın kuruluna bildirmelidir.

Editörlerden birinin herhangi bir yazıda yazar olması durumunda editör, makale değerlendirme sürecinden çıkarılır. Herhangi bir çıkar çatışmasını önlemek için makale değerlendirme süreci çift kör olarak yapılmaktadır. Çift kör değerlendirme sürecinden dolayı Baş Editör dışında hiçbir yayın kurulu üyesine, uluslararası danışma kurulu üyesine veya hakemlere, makalenin yazarları veya yazarların kurumları hakkında bilgi verilmemektedir.

Yayın ekibimiz tüm bu durumları göz önünde bulundurarak değerlendirme sürecinin tarafsız bir şekilde yürütülmesi için özveriyle çalışmaktadır.

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Bağcılar Tıp Bülteni (Bagcilar Medical Bulletin), tıbbın her alanında araştırma makalelerini, güncel derleme yazılarını, olgu sunumlarını ve editöre mektupları İngilizce tam metin ve Türkçe özle yayınlayan hakemli bir dergidir. Dergi online olarak yılda 4 sayı yayınlanmaktadır. Tüm makaleler kabul edilir edilmez, online olarak pdf formatında bu web sitesinde, o dönemdeki sayının bir makalesi olarak yer alacaktır. Dergi Galenos Yayınevi tarafından yayımlanmaktadır.

Editoryal Politikalar ve Hakem Süreci

Yayın Politikası

Bağcılar Tıp Bülteni, yayınlanmak üzere gönderilen yazıları aşağıda belirtilen şekillerde kabul eder:

-Orijinal araştırmalar,

-Kısa araştırmalar,

-Olgu sunumları,

-Derlemeler,

-Editöre mektup

Dergi, Türkiye'de yapılan araştırmaların uluslararası bilim arenasına duyurulması, uluslararası bilim çevrelerince paylaşılması ve bu bağlamda Türkiye'nin tanıtılmasına katkıda bulunmayı misyon edindiğinden özellikle orijinal araştırma niteliğindeki yazıları yayınlamaya öncelik vermektedir. Dergide yayınlanacak derleme türündeki yazılar editör tarafından konu ile ilgili çalışan yetkin kişilere hazırlatılmaktadır.

Genel İlkeler

Daha önce yayınlanmamış ya da yayınlanmak üzere başka bir dergide halen değerlendirmede olmayan ve her bir yazar tarafından onaylanan makaleler dergide değerlendirilmek üzere kabul edilir. Yayın kurulu, yazarların iznini alarak yazıda değişiklikler yapabilir. Editör ve dil editörleri dil, imlâ ve kaynakların National Library of Medicine MEDLINE/PubMed Resources'da belirtildiği gibi yazılmasında ve ilgili konularda tam yetkilidir.

Eğer makalede daha önce yayınlanmış alıntı yazı, tablo, resim vs. mevcut ise makale yazarı, yayın hakkı sahibi ve yazarlarından yazılı izin almak ve bunu makalede belirtmek zorundadır. Gerekli izinlerin alınıp alınmadığından yazar(lar) sorumludur.

Bilimsel toplantılarda sunulan özet bildiriler, makalede belirtilmesi koşulu ile kaynak olarak kabul edilir. Editör, dergiye gönderilen makale biçimsel esaslara uygun ise, gelen yazıyı yurtiçinden ve/veya yurtdışından en az iki hakemin değerlendirmesinden geçirtir, hakemler gerek gördüğü takdirde yazıda istenen değişiklikler yazarlar tarafından yapıldıktan sonra yayınlanmasına onay verir. Makale yayınlanmak üzere dergiye gönderildikten sonra yazarlardan hiçbirinin ismi, tüm yazarların yazılı izni olmadan yazar listesinden silinemez ve yeni bir isim yazar olarak eklenemez ve yazar sırası değiştirilemez. Yayına kabul edilmeyen makale, resim ve fotoğraflar yazarlara geri gönderilmez.

Yazar Hakları

Makalelerinin telif haklarını dergiye devreden yazarlar, yayınladıkları yazıdaki yazılarını diğer çalışmalarında kısmen veya tamamen, herhangi bir revizyon veya değişiklik yapmadan kullanma ve uygun gördükleri takdirde kitap haline getirme hakkını saklı tutarlar. Dergideki, CC BY-NC-ND 4.0 Lisansıvnda ve derginin Açık Erişim politikasında belirtildiği gibi açıkça yayınlanmalıdır. Makale, yazar tarafından bir kitap bölümü olarak veya bir koleksiyonda veya derlemede yeniden kullanılacaksa veya ticari amaçlarla bir kitap haline getirilecekse, atama veya feragat etme hakkını saklı tutan Dergi'den izin alınması gerekir. Bu yeniden kullanım için bedel ve dergide asıl yayına açıkça verilmek üzere uygun bir atıf yapılması gerekmektedir.

Yazarların Soru mluluğu

Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır. Yazar makalenin orijinal olduğu, daha önce başka bir yerde yayınlanmadığı ve başka bir yerde, başka bir dilde yayınlanmak üzere değerlendirmede olmadığı konusunda teminat

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sağlamalıdır. Uygulamadaki telif kanunları ve anlaşmaları gözetilmelidir. Telife bağlı materyaller (örneğin tablolar, şekiller veya büyük alıntılar) gerekli izin ve teşekkürle kullanılmalıdır. Başka yazarların, katkıda bulunanların çalışmaları ya da yararlanılan kaynaklar uygun biçimde kullanılmalı ve referanslarda belirtilmelidir.

Gönderilen makalede tüm yazarların akademik ve bilimsel olarak doğrudan katkısı olmalıdır, bu bağlamda "yazar" yayınlanan bir araştırmanın kavramsallaştırılmasına ve desenine, verilerin elde edilmesine, analizine ya da yorumlanmasına belirgin katkı yapan; yazının yazılması ya da bunun içerik açısından eleştirel biçimde gözden geçirilmesinde görev yapan; yazının yayınlanmak üzere nihai halini onaylayan ve çalışmanın herhangi bir bölümünün doğruluğuna ya da bütünlüğüne ilişkin soruların uygun şekilde soruşturulduğunun ve çözümlendiğinin garantisini vermek amacıyla çalışmanın her yönünden sorumlu olmayı kabul eden kişi olarak görülür. Fon sağlanması, ya da araştırma grubunun genel süpervizyonu tek başına yazarlık hakkı kazandırmaz. Yazar olarak gösterilen tüm bireyler sayılan tüm ölçütleri karşılamalıdır ve yukarıdaki ölçütleri karşılayan her birey yazar olarak gösterilebilir. Çok merkezli çalışmalarda grubun tüm üyelerinin yukarıda belirtilen şartları karşılaması gereklidir. Yazarların isim sıralaması ortak verilen bir karar olmalıdır. Tüm yazarlar yazar sıralamasını Telif Hakkı Devir Formunda imzalı olarak belirtmek zorundadırlar. Yazarların tümünün ismi yazının başlığının altındaki bölümde yer almalıdır.

Yazarlık için yeterli ölçütleri karşılamayan ancak çalışmaya katkısı olan tüm bireyler Teşekkür (Acknowledgement) kısmında sıralanmalıdır. Bunlara örnek olarak ise sadece teknik destek sağlayan, yazıma yardımcı olan ya da sadece genel bir destek sağlayan kişiler verilebilir. Finansal ve materyal destekleri de belirtilmelidir.

Yazıya materyal olarak destek veren ancak yazarlık için gerekli ölçütleri karşılamayan kişiler "klinik araştırıcılar" ya da "yardımcı araştırıcılar" gibi başlıklar altında toplanmalı ve bunların işlevleri ya da katılımları "bilimsel danışmanlık yaptı", "çalışma önerisini gözden geçirdi", "veri topladı" ya da "çalışma hastalarının bakımını üstlendi" şeklinde belirtilmelidir. Teşekkür (Acknowledgement) kısmında belirtilen bu ifadeler için bu bireylerden de yazılı izin alınması gerekmektedir.

Bütün yazarlar, araştırmanın sonuçlarını ya da bilimsel değerlendirmeyi etkileyebilme potansiyeli olan finansal ilişkiler, çıkar çatışması ve çıkar rekabetini beyan etmelidirler. Bir yazar kendi yayınlanmış yazısında belirgin bir hata ya da yanlışlık tespit ederse, bu yanlışlıklara ilişkin düzeltme ya da geri çekme için yayın yönetmeni ile hemen temasa geçme ve işbirliği yapma sorumluluğunu taşır. Yazarların katkısını belirten Yazar Katkı Formu ve çıkar çatışması olup olmadığını belirten ICMJE Potansiyel Çıkar Çatışması Beyan Formu makale ile birlikte gönderilmelidir. Yazarların görevleri ve sorumlulukları ICMJE yönergelerine dayandırılmaktadır.

Editör ve Hakem Sorumlulukları ve Değerlendirme Süreci

Editörler, makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Yayına gönderilen makalelerin adil bir şekilde çift taraflı kör hakem değerlendirmesinden geçmelerini sağlarlar. Gönderilen makalelere ilişkin tüm bilginin, makale yayınlanana kadar gizli kalacağını garanti ederler. Editörler içerik ve yayının toplam kalitesinden sorumludurlar. Gereğinde hata sayfası yayınlamalı ya da düzeltme yapmalıdırlar.

Genel Yayın Yönetmeni; yazarlar, editörler ve hakemler arasında çıkar çatışmasına izin vermez. Hakem atama konusunda tam yetkiye sahiptir ve Bağcılar Tıp Bülteni'nde yayınlanacak makalelerle ilgili nihai kararı vermekle yükümlüdür. Dergide yayın etiği hususunda COPE yönergeleri izlenmektedir.

Hakemler makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Araştırmayla ilgili, yazarlarla ve/veya araştırmanın finansal destekçileriyle çıkar çatışmaları olmamalıdır. Değerlendirmelerinin sonucunda tarafsız bir yargıya varmalıdırlar. Hakemler yazarların atıfta bulunmadığı konuyla ilgili yayınlanmış çalışmaları tespit etmelidirler. Gönderilmiş yazılara ilişkin tüm bilginin gizli tutulmasını sağlamalı ve yazar tarafında herhangi bir telif hakkı ihlali ve intihal fark ederlerse Genel Yayın Yönetmeni`ne raporlamalıdırlar. Hakem, makale konusu hakkında kendini vasıflı hissetmiyor ya da zamanında geri dönüş sağlaması mümkün görünmüyorsa, Baş Editör`e bu durumu bildirmeli ve hakem sürecine kendisini dahil etmemesini istemelidir.

Editör makalelerle ilgili bilgileri (makalenin alınması, içeriği, gözden geçirme sürecinin durumu, hakemlerin eleştirileri ya da varılan sonuç) yazarlar ya da hakemler dışında kimseyle paylaşmaz.

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Değerlendirme sürecinde editör hakemlere gözden geçirme için gönderilen makalelerin, yazarların özel mülkü olduğunu ve bunun imtiyazlı bir iletişim olduğunu açıkça belirtir. Hakemler ve yayın kurulu üyeleri topluma açık bir şekilde makaleleri tartışamazlar. Hakemlerin kendileri için makalelerin kopyalarını çıkarmalarına izin verilmez ve editörün izni olmadan makaleleri başkasına veremezler. Hakemler gözden geçirmelerini bitirdikten sonra makalenin kopyalarını yok etmeli ya da editöre göndermelidirler. Dergimiz editörü de reddedilen ya da geri verilen makalelerin kopyalarını imha etmelidir.

Yazarın ve editörün izni olmadan hakemlerin gözden geçirmeleri basılamaz ve açıklanamaz. Hakemlerin kimliğinin gizli kalmasına özen gösterilmelidir. Bazı durumlarda editörün kararıyla, ilgili hakemlerin makaleye ait yorumları aynı makaleyi yorumlayan diğer hakemlere gönderilerek hakemlerin bu süreçte aydınlatılması sağlanabilir. Değerlendirme süreciyle ilgili COPE yönergeleri izlenmektedir.

Açık Erişim İlkesi

Açık erişimli bir yayın olan Bağcılar Tıp Bülteni dergisinin tüm içeriği okura ya da okurun dahil olduğu kuruma ücretsiz olarak sunulur. Okurlar, yayıncı ya da yazardan izin almadan dergi makalelerinin tam metnini okuyabilir, indirebilir, kopyalayabilir, dağıtabilir, basabilir, arayabilir ve link sağlayabilir.

Yayın Etiği

İlke ve Standartlar

Bağcılar Tıp Bülteni yayın etiğinde en yüksek standartlara bağlıdır ve Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) ve International Committee of Medical Journals (ICJME) tarafından geliştirilen yayın etiği ilkelerini ve tavsiyelerini gözetir.

Gönderilen tüm makaleler orijinal, yayınlanmamış (konferans bildirilerindeki tam metinler de dahil) ve başka bir dergide değerlendirme sürecinde olmamalıdır. Her bir makale editörlerden biri ve en az iki hakem tarafından çift kör değerlendirmeden geçirilir. Gönderilen makaleleri intihal yazılımı ile denetleme hakkımız haklıdır. İntihal, veride hile ve tahrif (araştırma verisi, tabloları ya da imajlarının manipülasyonu ve asılsız üretimi), insan ve hayvanların araştırmada uygun olmayan kullanımı konuları denetimden geçmektedir. Bu standartlara uygun olmayan tüm makaleler yayından çıkarılır. Buna yayından sonra tespit edilen olası kuraldışı, uygunsuzluklar içeren makaleler de dahildir. Yayın etiği kurallarına bağlı olarak, intihal şüphesini ve duplikasyon durumlarını rapor edeceğimizi belirtiriz. Olası bilimsel hatalı davranışları ve yayın etiği ihlali vakalarını ele alırken COPE Ethics Flowcharts izlenir.

İnsan ve Hayvan Hakları, Bilgilendirilmiş Olur, Çıkar Çatışması

Bağcılar Tıp Bülteni, yayınladığı makalelerin ticarî kaygılardan uzak ve konu ile ilgili en iyi etik ve bilimsel standartlarda olması şartını gözetmektedir. Makalelerin etik kurallara uygunluğu yazarların sorumluluğundadır.

Bağcılar Tıp Bülteni, 2013 yılında revize edilen Helsinki Deklarasyonu “Ethical Principles for Medical Research Involving Human Subjects”e ve 2006 yılında revize edilen WMA Statement on Animal Use in Biomedical Research’e uymayı prensip edinmiştir. Bu yüzden dergide yayınlanmak üzere gönderilen yazılarda, klinik deneylere katılan denekler ile ilgili olarak yukarıda belirtilen etik standartlara uyulduğunun mutlaka belirtilmesi gerekmektedir. Ayrıca deneyin türüne göre gerekli olan yerel veya ulusal etik komitelerden alınan onay yazıları yazı ile birlikte gönderilmelidir. Bununla birlikte deneye katılan kişi/hastalardan, hastalar eğer temyiz kudretine sahip değilse vâsilerinden yazılı bilgilendirilmiş onam alındığını belirten bir yazı ile beraber tüm yazarlar tarafından imzalanmış bir belgenin editöre gönderilmesi gerekmektedir.

Hastalardan izin alınmadan mahremiyet bozulamaz. Hastaların ismi, isimlerinin baş harfleri ya da hastane numaraları gibi tanımlayıcı bilgiler, fotoğraflar ve soy ağacı bilgileri vb. bilimsel amaçlar açısından çok gerekli olmadıkça ve hasta (ya da anne-baba, ya da vâsisi) yazılı bilgilendirilmiş onam vermedikçe basılmazlar. Özellikle olgu bildirimlerinde, çok gerekli olmadıkça hasta ile ilgili tanımlayıcı ayrıntılar çıkarılmalıdır. Örneğin, fotoğraflarda göz bölgesinin maskelenmesi kimliğin gizlenmesi için yeterli değildir. Eğer veriler kimliğin gizlenmesi için değiştirildiyse yazarlar bu değişikliklerin bilimsel anlamı etkilemediği konusunda güvence vermelidirler. Olgu sunumlarında yer verilen hastalardan bilgilendirilmiş onam alınmalıdır. Bilgilendirilmiş onam alındığı da makalede belirtilmelidir.

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Bu tip çalışmaların varlığında yazarlar, makalenin YÖNTEM(LER) bölümünde bu prensiplere uygun olarak çalışmayı yaptıklarını, kurumlarının etik kurullarından ve çalışmaya katılmış insanlardan "bilgilendirilmiş onam" aldıklarını belirtmek zorundadırlar.

Çalışmada "hayvan" kullanılmış ise yazarlar, makalenin YÖNTEM(LER) bölümünde "Guide for the Care and Use of Laboratory Animals" doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadırlar. Hayvan deneyleri rapor edilirken yazarlar, laboratuvar hayvanlarının bakımı ve kullanımı ile ilgili kurumsal ve ulusal rehberlere uyup uymadıklarını yazılı olarak bildirmek zorundadırlar.

Editör ve yayıncı, reklam amacı ile dergide yayınlanan ticari ürünlerin özellikleri ve açıklamaları konusunda hiçbir garanti vermemekte ve sorumluluk kabul etmemektedir. Eğer makalede doğrudan veya dolaylı ticarî bağlantı veya çalışma için maddî destek veren kurum mevcut ise yazarlar; kaynak sayfasında, kullanılan ticarî ürün, ilaç, ilaç firması vb. ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar) bildirmek zorundadır.

Buna göre, yazar, hakem ya da editör sorumluluklarını aşırı düzeyde ve/veya haksızlığa yol açabilecek düzeyde etkileyebilecek ya da etkileyebileceği olası bir çıkar rekabeti içindeyse, çıkar çatışması söz konusudur ve bunun açıklanması gerekir. Açıklanması öngörülen çıkar çatışması tipleri, finansal bağlar, akademik taahhütler, kişisel ilişkiler, politik ya da dini inançlar, kurumsal bağlantılardır. Çıkar çatışması söz konusuysa bu makalede açıklanmalıdır.

Dergiye yayımlanmak üzere gönderilen tüm yazılar editör ve hakemlerin uzmanlığı ile Crossref Similarity Check "iThenticate" programı ve internet üzerinden arama motorlarında taranarak, intihal kontrolünden geçmektedir. İntihal taraması sonucuna göre yazılar reddedilebilir. İntihal tespit edilmesi halinde, ilgili kurumlara yazarlar hakkında ihbar yapılabilir. Bu durumda yazarlar sorumlu kurumlara çalışmalarının ham sonuçlarını teslim etmek zorunda kalabilir.

Dil

Bağcılar Tıp Bülteni'nin yayın dili Amerikan İngilizcesi'dir. Ayrıca makalelerin özleri hem İngilizce, hem Türkçe yayınlanır. Her iki dildeki özler yazarlardan istenir.

Yazıların Hazırlanması

Aksi belirtilmedikçe gönderilen yazılarla ilgili tüm yazışmalar ilk yazarla yapılacaktır. Gönderilen yazılar, yazının yayınlanmak üzere gönderildiğini ve Bağcılar Tıp Bülteni'nin hangi bölümü (Orijinal Araştırma, Kısa Araştırma, Olgu Sunumu, Derleme, Editöre Mektup) için başvurulduğunu belirten bir mektup, yazının elektronik formunu içeren Microsoft Word 2003 ve üzerindeki versiyonları ile yazılmış elektronik dosya ile tüm yazarların imzaladığı 'Telif Hakkı Devir Formu', Yazar Katkı Formu ve ICMJE Potansiyel Çıkar Çatışması Beyan Formu eklenerek gönderilmelidir. Yazıların alınmasının ardından yazarlara makalenin alındığı, bir makale numarası ile bildirilecektir. Tüm yazışmalarda bu makale numarası kullanılacaktır. Makaleler sayfanın her bir kenarından, 5 cm kenar boşluğu bırakılarak ve çift satır aralıklı yazılmalıdır. Makalelerde aşağıdaki sıra takip edilmelidir ve her bölüm yeni bir sayfa ile başlamalıdır: 1) başlık sayfası, 2) öz, 3) metin, 4) teşekkür / 5) kaynaklar ve 6) tablo ve/veya şekiller. Tüm sayfalar sırayla numaralandırılmalıdır.

Başlık

Başlık sayfasında, yazarların adları, akademik ünvanları ve yazışılacak yazarın tam adres, telefon ve faks numaraları ile e-mail adresi mutlaka bulunmalıdır. Yazıların Türkçe özlerinde mutlaka Türkçe başlık da yer almalıdır.

Öz ve Anahtar Sözcükler

Makalenin İngilizce başlığı İngilizce özde, Türkçe başlığı da Türkçe özde yer almalıdır. Bütün makaleler öz ve anahtar kelime içermelidir. Özler bir makalenin birçok elektronik veri tabanında yer alan en belirgin kısmı olduğundan, yazarlar özün makalenin içeriğini doğru olarak yansıttığından emin olmalıdır. Öz çalışmanın temeliyle ilgili bilgi vermeli ve çalışmanın amacını, temel prosedürleri (olguların ya da laboratuvar hayvanlarının seçimi, gözlemsel ve analitik yöntemler), ana bulguları (mümkünse özgül etki büyüklüklerini ve istatistiksel anlamlılıklarını vererek) ve temel çıkarımları içermelidir. Çalışmanın ya da gözlemlerin yeni ve önemli yönleri belirtilmelidir. Anahtar sözcükler, her türlü yazıda Türkçe ve İngilizce özlerin altındaki sayfada 3-10 adet verilmelidir.

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Anahtar sözcük olarak National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (Medical Subject Headings, MeSH) yer alan terimler kullanılmalıdır. MeSH'de yer alan terimlerin Türkçe karşılıklarına Türkiye Bilim Terimleri'nden erişilebilir.

Makale Türleri

Orijinal Araştırma

Orijinal araştırma makaleleri derginin kapsamına uygun konularda önemli, özgün bilimsel sonuçlar sunan araştırmaları raporlayan yazılardır. Orijinal araştırma makaleleri, Öz, Anahtar Kelimeler, Giriş, Yöntem ve Gereçler, Bulgular, Tartışma, Sonuçlar, Kaynaklar bölümlerinden ve Tablo, Grafik ve Şekillerden oluşur. Öz bölümü araştırma yazılarında aşağıda belirtilen formatta yapılandırılmış olmalıdır.

Öz

Araştırma yazılarında Türkçe ve İngilizce özler en fazla 500 kelime olmalı ve şu şekilde yapılandırılmalıdır: Amaç/Objective: Yazının birincil ve asıl amacı; Yöntem ve Gereçler/Material and Method(s): Veri kaynakları, çalışmanın iskeleti, hastalar ya da çalışmaya katılanlar, görüşme/değerlendirmeler ve temel ölçümler; Bulgular/Results: Ana bulgular; Sonuç(lar)/Conclusion(s):Doğrudan klinik uygulamalar, çıkartılacak sonuçlar belirtilmelidir.

Anahtar Kelimeler

National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (Medical Subject Headings, MeSH) yer alan terimler kullanılmalıdır, en az üç anahtar kelime belirtilmelidir.

Giriş

Giriş/Introduction bölümünde konunun önemi, tarihçe ve bugüne kadar yapılmış çalışmalar, hipotez ve çalışmanın amacından söz edilmelidir. Hem ana hem de ikincil amaçlar açıkça belirtilmelidir. Sadece gerçekten ilişkili kaynaklar gösterilmeli ve çalışmaya ait veri ya da sonuçlardan söz edilmemelidir.

Yöntem ve Gereçler

Yöntem ve Gereçler/Material and Methods bölümünde, veri kaynakları, hastalar ya da çalışmaya katılanlar, ölçekler, görüşme/değerlendirmeler ve temel ölçümler, yapılan işlemler ve istatistiksel yöntemler yer almalıdır. Yöntem bölümü, sadece çalışmanın planı ya da protokolü yazılırken bilinen bilgileri içermelidir; çalışma sırasında elde edilen tüm bilgiler bulgular kısmında verilmelidir. Yöntem ve Gereçler bölümünde olguların seçimi ve tanımlanması hakkında bilgi, teknik bilgi ve istatistik hakkında bilgi yer almalıdır. Araştırmanın Etik Kurul Onayı ve katılımcılardan alınan yazılı Bilgilendirilmiş Onam belirtilmelidir.

Olguların Seçimi ve Tanımlanması

Gözlemsel ya da deneysel çalışmaya katılanların (hastalar, hayvanlar, kontroller) seçimi, kaynak popülasyon, çalışmaya alınma ve çalışmadan dışlanma ölçütleri açıkça tanımlanmalıdır. Yaş ve cinsiyet gibi değişkenlerin çalışmanın amacıyla olan ilişkisi her zaman açık olmadığından yazarlar çalışma raporundaki kullanımlarını açıklamalıdır; örneğin yazarlar niçin sadece belli bir yaş grubunun alındığını ya da neden kadınların çalışma dışında bırakıldığını açıklamalıdır. Çalışmanın niçin ve nasıl belli bir şekilde yapıldığı açık bir şekilde belirtilmelidir. Yazarlar etnisite ya da ırk gibi değişkenler kullandıklarında bu değişkenleri nasıl ölçtüklerini ve geçerliklerini açıklamalıdır.

Teknik Bilgi

Diğer çalışmacıların sonuçları yineleyebilmesi için yöntem ve kullanılan araçlar (üretici firma ve adres paragraf içinde belirtilerek) ayrıntılı bir şekilde belirtilmelidir. Önceden kullanılan bilinen yöntemler için (istatistiksel yöntemler dahildir) kaynak gösterilmeli, basılmış ama iyi bilinmeyen bir yöntem için kaynak verilmeli ve yöntem açıklanmalıdır. Aynı şekilde yeni ya da belirgin olarak modifiye edilmiş yöntemler tanımlanmalı ve kullanılma nedenleri belirtilip kısıtlılıkları değerlendirilmelidir. Kullanılan tüm ilaç ve

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kimyasallar doğru olarak tanımlanıp jenerik isimleri, dozları ve kullanım biçimleri belirtilmelidir. Gözden geçirme yazısı gönderen yazarlar veriyi bulma, seçme, ayırma ve sentezleme yöntemlerini belirtmelidir. Bu yöntemler aynı zamanda özde de yer almalıdır.

İstatistik

İstatistiksel yöntem, orijinal veriye erişebilecek bilgili bir okuyucunun rapor edilen sonuçları onaylayabileceği bir ayrıntıda belirtilmelidir. Mümkünse, bulgular niceliksel hale getirilmeli ve hata ölçümleri (güvenlik aralıkları gibi) sunulmalıdır. Etki büyüklüğünü vermeyen, p değerlerinin kullanımı gibi, salt istatistiksel hipotez sınamasına dayanılmamalıdır. Çalışma deseni ve istatistiksel yönteme dair kaynaklar sayfalar belirtilerek mümkün olduğu sürece standart kaynaklar olmalıdır. İstatistiksel terimler, kısaltmalar ve semboller tanımlanmalıdır. Kullanılan bilgisayar programı belirtilmelidir.

Bulgular

Ana bulgular istatistiksel verilerle desteklenmiş olarak eksiksiz verilmeli ve bu bulgular uygun tablo, grafik ve şekillerle görsel olarak da belirtilmelidir. Bulgular yazıda, tablolarda ve şekillerde mantıklı bir sırayla önce en önemli sonuçlar olacak şekilde verilmelidir. Tablo ve şekillerdeki tüm veriyi yazıda vermemeli, sadece önemli noktaları vurgulanmalıdır. Ekstra materyal ve teknik bilgi ek kısmında verilerek yazının akışının bozulmaması sağlanmalı, alternatif olarak bunlar sadece elektronik versiyonda yer almalıdır.

Tartışma

Tartışma/Discussion bölümünde o çalışmadan elde edilen veriler, kurulan hipotez doğrultusunda hipotezi destekleyen ve desteklemeyen bulgular ve sonuçlar irdelenmeli ve bu bulgu ve sonuçlar literatürde bulunan benzeri çalışmalarla kıyaslanmalı, farklılıklar varsa açıklanmalıdır. Çalışmanın yeni ve önemli yanları ve bunlardan çıkan sonuçları vurgulanmalıdır. Giriş ya da sonuçlar kısmında verilen bilgi ve veriler tekrarlanmamalıdır.

Sonuçlar

Sonuçlar/Conclusions bölümünde çalışmadan çıkarılan sonuçlar sıralanmalıdır. Deneysel çalışmalar için tartışmaya sonuçları kısaca özetleyerek başlamak, daha sonra olası mekanizmaları ya da açıklamaları incelemek ve bulguları önceki çalışmalarla karşılaştırmak, çalışmanın kısıtlılıklarını özetlemek, gelecekteki çalışmalar ve klinik pratik için uygulamalarını belirtmek faydalıdır. Varılan sonuçlar çalışmanın amacıyla karşılaştırılmalı, ancak elde edilen bulgular tarafından yeterince desteklenmeyen çıkarımlardan kaçınılmalıdır. Yazarlar, eğer elde ettikleri veriler ekonomik veri ve analizler içermiyorsa, ekonomik çıkar ya da faydalarla ilgili yorumlardan özellikle kaçınılmalıdır. Gerektiğinde yeni hipotezler ortaya konmalı, ancak bunların yeni hipotezler olduğu belirtilmelidir.

Tablo, Grafik ve Şekiller

Yazı içindeki grafik, şekil ve tablolar Arap sayıları ile numaralandırılmalıdır. Şekillerin metin içindeki yerleri belirtilmelidir. Ayrıntılı bilgi aşağıda ilgili başlık altında yer almaktadır.

Kısa Araştırma

Kısa Araştırma makaleleri tarz ve format açısından Orijinal Araştırma makaleleri gibidir; ancak daha küçük ölçekli araştırmaları ya da geliştirme çalışmasının erken aşamalarında olan araştırmaları ele alır. Basit araştırma tasarımı kullanan ön çalışmalar, sınırlı pilot veri sağlayan küçük örnek kitle ile yapılan çalışmalar, ileri araştırma gereksinimine işaret eden başlangıç bulguları bu tür araştırmalar kapsamında sayılabilir. Kısa Araştırma makaleleri, büyük ölçekli gelişkin araştırma projelerini konu alan Orijinal Araştırma makalelerinden daha kısadır. Ancak Kısa Araştırma, Orijinal Araştırma makalesi olabilecek kalitede bir araştırma makalesinin kısa versiyonu olarak anlaşılmamalıdır; önem derecesi düşük, titizlikle yapılmamış bir araştırma hakkında bir yayın malzemesi hazırlamak için kullanılmamalıdır ya da genişletildiğinde Orijinal Araştırma makalesi ya da araştırma niteliği kazanmayacak bir içeriği değerlendirecek bir makale türü olarak anlaşılmamalıdır.

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Olgu Sunumu

Olgu sunumu makaleleri özgün vakaları rapor eden yazılardır. Derginin kapsamına giren konulara ilişkin bir problemin üstesinden gelen tedaviyle ilgili, yeni araçlar, teknikler ve metotlar göstererek okuyucular için bilgilendirme sağlamalıdır. Olgu sunumu yazıları Öz (özün araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Olgu Sunumu, Tartışma, Referanslar, gerekirse Tablo ve açıklayıcı bilgilerden oluşur. Olgu sunumunda yazılı bilgilendirilmiş onam alınmalı ve makalede belirtilmelidir.

Derleme

Derleme makaleleri alanında zengin birikime ve atıf alan çalışmalara sahip uzman kişilerce yazılan yazılardır. Klinik pratiğe ilişkin bir konuda mevcut bilgiyi tanımlayan, değerlendiren ve tartışan; geleceğe ilişkin çalışmalara yol gösteren derleme yazıları yazmaları için dergi belirlediği yazarlara davet gönderir. Derleme makaleleri, Öz (özün, araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Sonuç bölümlerinden oluşur. Derleme makale gönderen yazarların, makalede kullandıkları verinin seçimi, alınması, sentezi için kullandıkları yöntemleri tanımlayan bir bölüme de makalede yer vermeleri gerekir. Bu yöntemler Öz bölümünde de belirtilmelidir.

Editöre Mektup

Editöre Mektup, kısa ve net görüş bildiren yazılardır. Dergide daha önce yayınlanmış olan makalelerle ilgili olarak ya da dergide ifade edilmiş görüşlerle ilgili olarak yazılmış olması tercih edilir. Editöre Mektup yazıları, daha sonra yeni bir yazı ile geçerlilik ispatı gerektirebilecek ön görüş bildiren yazılar olmamalıdır.

Tablolar

Tablolar bilgileri etkin bir şekilde gösterir ve ayrıca bilginin istenen tüm ayrıntı seviyelerinde verilmesini sağlar. Bilgileri metin yerine tablolarda vermek genelde metnin uzunluğunu kısaltır.

Her tablo ayrı bir sayfaya çift aralıklı olarak basılmalıdır. Tablolar metindeki sıralarına göre numaralanıp, her birine kısa bir başlık verilmelidir. MS Word 2003 ve üstü versiyonlarında otomatik tablo seçeneğinde "tablo klasik 1" ya da "tablo basit 1" seçeneklerine göre tablolar hazırlanmalıdır. Başlık satırı ve tablo alt üst satırları dışında tablonun içinde başka dikey ve yatay çizgiler kullanılmamalıdır. Her sütuna bir başlık verilmelidir. Yazarlar açıklamaları başlıkta değil, dipnotlarda yapmalıdır. Dipnotlarda standart olmayan tüm kısaltmalar açıklanmalıdır. Dipnotlar için sırasıyla şu semboller kullanılmalıdır: (*,†,‡,§,ǁ,¶,**,††,‡‡).

Varyasyonun standart sapma ya da standart hata gibi istatistiksel ölçümleri belirtilmelidir. Metin içinde her tabloya atıfta bulunulduğuna emin olunmalıdır. Eğer yayınlanmış ya da yayınlanmamış herhangi başka bir kaynaktan veri kullanılıyorsa izin alınmalı ve onlar tam olarak bilgilendirilmelidir. Çok fazla veri içeren tablolar, çok yer tutar ve sadece elektronik yayınlar için uygun olabilir ya da okuyuculara yazarlar tarafından doğrudan sağlanabilir. Böyle bir durumda uygun bir ifade metne eklenmelidir. Bu tip tablolar, hakem değerlendirmesinden geçmesi için makaleyle beraber gönderilmelidir.

Şekiller

Şekiller ya profesyonel olarak çizilmeli ve fotoğraflanmalı ya da fotoğraf kalitesinde dijital olarak gönderilmelidir. Şekillerin basıma uygun versiyonlarının yanı sıra JPEG ya da GIF gibi elektronik versiyonlarda yüksek çözünürlükte görüntü oluşturacak biçimlerde elektronik dosyaları gönderilmeli ve yazarlar göndermeden önce bu dosyaların görüntü kalitelerini bilgisayar ekranında kontrol etmelidir.

Röntgen, CT, MRI filmleri ve diğer tanısal görüntülemeler yüksek kalitede basılmış olarak gönderilmelidir. Bu nedenle şekillerin üzerindeki harfler, sayılar ve semboller açık ve tüm makalede eşit ve yayın için küçültüldüklerinde bile okunabilecek boyutlarda olmalıdır. Şekiller mümkün olduğunca tek başlarına anlaşılabilir olmalıdır. Fotomikrografik patoloji preparatları iç ölçekler içermelidir. Semboller, oklar ya da harfler fonla kontrast oluşturmalıdır. Eğer insan fotoğrafı kullanılacaksa, ya bu kişiler fotoğraftan tanınmamalıdır ya da yazılı izin alınmalıdır (Etik bölümüne bakınız).

Şekiller metinde geçiş sıralarına göre numaralandırılmalıdır. Eğer önceden yayınlanmış bir şekil kullanılacaksa, yayın hakkını elinde bulunduran bireyden izin alınmalıdır. Toplum alanındaki belgeler hariç yazarlığa ve yayıncıya bakılmadan bu izin gereklidir.

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Basılacak bölgeyi gösteren ek çizimler editörün işini kolaylaştırır. Renkli şekiller editör gerekli gördüğünde ya da sadece yazar ek masrafı karşılarsa basılır.

Şekillerin Dipnotları

Ayrı bir sayfadan başlayarak şekiller için tablo başlıkları ve dipnotları tek aralıklı olarak ve Arap sayıları ile hangi şekle karşı geldikleri belirtilerek yazılmalıdır. Semboller, oklar, sayılar ya da harfler şeklin parçalarını belirtmek için kullanıldığında, dipnotlarda her biri açıkça tanımlanmalıdır. Fotomikrografik patoloji preparatlarında iç ölçek ve boyama tekniği açıklanmalıdır.

Ölçüm Birimleri

Uzunluk, ağırlık ve hacim birimleri metrik (metre, kilogram, litre) sistemde ve bunların onlu katları şeklinde rapor edilmelidir. Sıcaklıklar Celsius derecesi, kan basıncı milimetre civa cinsinden olmalıdır. Ölçü birimlerinde hem lokal hem de Uluslararası Birim Sistemleri (International System of Units, SI) kullanılmalıdır. İlaç konsantrasyonları ya SI ya da kütle birimi olarak verilir, alternatif olarak parantez içinde de verilebilir.

Kısaltmalar ve Semboller Sadece standart kısaltmaları kullanın, standart olmayan kısaltmalar okuyucu için çok kafa karıştırıcı olabilir. Başlıkta kısaltmadan kaçınılmalıdır. Standart bir ölçüm birimi olmadıkça kısaltmaların uzun hali ilk kullanılışlarında açık, kısaltılmış hali parantez içinde verilmelidir.

Teşekkür(ler)

Yazının sonunda kaynaklardan önce yer verilir. Bu bölümde kişisel, teknik ve materyal yardımı gibi nedenlerle yapılacak teşekkür ifadeleri yer alır.

Kelime Sayısı Sınırlandırması

Türkçe ve İngilizce özler en fazla 500 kelime olmalıdır. Orijinal makaleler ve derleme yazılarında özel bir kelime sayısı sınırlandırması yoktur. Olgu sunumları öz /abstract hariç 1000 kelime ile sınırlandırılmalı ve en az sayıda şekil, tablo ve kaynak içermelidir. Editöre mektuplar (en fazla 1000 kelime, tablosuz ve şekilsiz) olmalı ve mektup, tüm yazarlar tarafından imzalanmış olmalıdır. Bağcılar Tıp Bülteni`nde yayınlanmış olan bir yazı ile ilgili eleştiri ya da değerlendirme niteliğindeki mektuplar sözü edilen yazının yayınlanmasından sonraki 12 hafta içinde alınmış olmalıdır.

Makale Hazırlığı

"Bağcılar Tıp Bülteni", Tıp Dergilerinde Bilimsel Çalışmaların Yürütülmesi, Raporlanması, Düzenlenmesi ve Yayınlanmasına İlişkin Yönergeleri takip eder "(Uluslararası Tıp Dergisi Editörleri Komitesi ICMJE). Makalenin sunulması üzerine, yazarlar deneme/araştırma türünü belirtmeli ve uygun olduğunda aşağıdaki kuralların kontrol listesini sağlamalıdır:

Randomize çalışmalar için CONSORT beyanı (CONSORT Grubu için Moher D, Schultz KF, Altman D. CONSORT beyanı paralel grup randomize çalışmaların raporlarının kalitesini iyileştirmek için önerileri gözden geçirdi. JAMA 2001; 285: 1987-91),

Sistematik gözden geçirmeler ve meta-analizler için tercih edilen raporlama maddeleri için PRISMA (Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Grubu. Sistematik İncelemeler ve Meta-Analizler için Tercih Edilen Raporlama Maddeleri: PRISMA Beyanı. PLoS Med 2009; 6 (7): e1000097.),

Tanısal doğruluk çalışmalarının raporlanması için STARD kontrol listesi (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, vd, STARD Grubu için. Teşhis doğruluğu çalışmalarının eksiksiz ve doğru raporlanmasına yönelik: STARD girişimi, Ann Intern Med 2003; 138: 40-4.),

STROBE gözlemsel çalışma raporlarında yer alması gereken maddelerin kontrol listesi,

Gözlemsel çalışmaların meta-analizi ve sistemik incelemeleri için MOOSE yönergeleri (Stroup DF, Berlin JA, Morton SC, vd.) Epidemiyolojideki gözlemsel çalışmaların meta-analizi: Epidemiyoloji (MOOSE) grubundaki gözlemsel çalışmaların Meta-analizini bildirme önerisi JAMA 2000; 283: 2008-12),

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CARE kuralları, vaka raporlarının doğruluğunu, şeffaflığını ve kullanışlılığını artırmak için tasarlanmıştır. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Grubu. CARE Yönergeleri: Konsensüs Tabanlı Klinik Vaka Raporlama Rehberinin Geliştirilmesi).

Kaynaklar

Kaynaklarla İlgili Genel Konular

Gözden geçirme yazıları okuyucular için bir konudaki kaynaklara ulaşmayı kolaylaştıran bir araç olsa da, her zaman orijinal çalışmayı doğru olarak yansıtmaz. Bu yüzden mümkün olduğunca yazarlar orijinal çalışmaları kaynak göstermelidir. Öte yandan, bir konuda çok fazla sayıda orijinal çalışmanın kaynak gösterilmesi yer israfına neden olabilir. Birkaç anahtar orijinal çalışmanın kaynak gösterilmesi genelde uzun listelerle aynı işi görür. Ayrıca günümüzde kaynaklar elektronik versiyonlara eklenebilmekte ve okuyucular elektronik literatür taramalarıyla yayınlara kolaylıkla ulaşabilmektedir.

Özler kaynak olarak gösterilmemelidir. Kabul edilmiş ancak yayınlanmamış makalelere atıflar "basımda" ya da "çıkacak" şeklinde verilmelidir; yazarlar bu makaleleri kaynak gösterebilmek için yazılı izin almalıdır ve makalelerin basımda olduğunu ispat edebilmelidir. Gönderilmiş ancak yayına kabul edilmemiş makaleler, "yayınlanmamış gözlemler" olarak gösterilmeli ve kaynak yazılı izinle kullanılmalıdır. Genel bir kaynaktan elde edilemeyecek temel bir konu olmadıkça "kişisel iletişimlere" atıfta bulunulmamalıdır. Eğer atıfta bulunulursa parantez içinde iletişim kurulan kişinin adı ve iletişimin tarihi belirtilmelidir. Bilimsel makaleler için yazarlar bu kaynaktan yazılı izin ve iletişimin doğruluğunu gösterir belge almalıdır.

Referans Stili ve Formatı

Tek tip kurallar esas olarak National Library of Medicine, tarafından uyarlanmış olan bir ANSI standart stilini kabul etmiştir. Kaynak atıfta bulunma örnekleri için yazarlar NIH Samples of Formatted References for Authors of Journal Articles sitesine başvurabilirler. Dergi isimleri National Library of Medicine kaynağında yer alan şekilleriyle kısaltılmalıdır. Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise parantez içinde belirtilmelidir. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır.

Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise () şeklinde parantez içinde referans numarası belirtilmelidir. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır.

Kaynakların doğruluğundan yazar(lar) sorumludur. Tüm kaynaklar metinde belirtilmelidir. Kaynaklar aşağıdaki örneklerdeki gibi gösterilmelidir. Altı yazardan fazla yazarı olan çalışmalarda ilk altı yazar belirtilmeli, sonrasında "ve ark." ya da "et al." ibaresi kullanılmalıdır. Kaynak dergi adlarının kısaltılması National Library of Medicine'de belirtilen kısaltmalara uygun olmalıdır. National Library of Medicine'da indekslenmeyen bir dergi kısaltılmadan yazılmalıdır.

Kaynaklar için örnekler aşağıda belirtilmiştir:

1. Dergilerdeki makaleler için örnekler: MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3:171-178.

2. Ek sayı için: MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

3. Baskıdaki makale için: Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

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4. Kitaptan alıntılar:

Tek yazarlı kitaptan alıntı için:

McKnight TL. Obesity Management in Family Practice. 1st ed., New York:Springer, 2005:47-51.

Kitaptan bir bölüm için, editör(ler) varsa:

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

Editörler aynı zamanda kitabın içindeki metin ya da metinlerin yazarı ise: Önce alınan metin ve takiben kitabın ismi yine kelimeler büyük harfle başlatılarak yazılır.

Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. 1st ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

Çeviri Kitaptan Alıntı için:

McGuffin P, Owen MJ, Gottsman II. Psikiyatri Genetiği ve Genomiği. Abay E, Görgülü Y (translation editors) 1st ed., Istanbul: Nobel Tıp Kitabevleri, 2009:303-341.

5. Tezden alıntı için: Keçeli F. Yeme bozukluğu hastalarında obsesif kompulsif bozukluk ve kişilik bozukluğu. Thesis, T.C. Sağlık Bakanlığı Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, Istanbul:2006.

6. Kongre bildirileri için: Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 201, Antalya, 2011:102.

7. Online Makale:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 4 Temmuz 2006 [Atıf tarihi:4 Ocak 2007];145(1):62-9. Erişim adresi:http://www.annals.org/cgi/reprint/145/1/62.pdf

Makalenin Dergiye Gönderilmesi

Çevrimiçi gönderim (online submission) ile birlikte Bağcılar Tıp Bülteni web sitesinin (www.ijfed.org) ilgili kısımlarındaki talimatlara uyarak makale gönderilebilmekte, hakem süreçleri de bu yolla yapılabilmektedir.

Makalelere eşlik eden ve aşağıdaki bilgileri içeren bir kapak mektubu olmalıdır.

• Aynı ya da çok benzer çalışmadan elde edilen raporların daha önce yayına gönderilip gönderilmediği mutlaka belirtilmelidir. Böyle bir çalışmaya özgül olarak atıfta bulunulmalı ve ayrıca yeni makalede de eskisine atıfta bulunulmalıdır. Gönderilen makaleye bu tip materyalin kopyaları da eklenerek editöre karar vermesinde yardımcı olunmalıdır.

• Eğer makalenin kendisinde ya da yazar formunda belirtilmemişse çıkar çatışmasına neden olabilecek mâli ya da diğer ilişkileri belirten bir ifade olmalıdır.

• Makalenin tüm yazarlar tarafından okunup kabul edildiğini, önceden belirtilen şekilde yazarlık ölçütlerinin karşılandığını, her yazarın makalenin dürüst bir çalışmayı yansıttığına inandığını belirten bir ifade olmalıdır. Mektup editöre yardımcı olabilecek tüm diğer bilgileri içermelidir. Eğer makale önceden başka bir dergiye gönderilmişse önceki editörün ve hakemlerin yorumları ve yazarların bunlara verdiği cevapların gönderilmesi faydalıdır. Editör, önceki yazışmaların gönderilmesini hakem sürecini dolayısıyla yazının yayınlanma sürecini hızlandırabileceğinden istemektedir.

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Bağcılar Tıp Bülteni

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ORIGINAL RESEARCH

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Evaluation of Birth Satisfaction in Caesarean Section with General Anesthesia and Spinal Anesthesia

Genel Anestezi ve Spinal Anestezi Uygulanan Sezaryen Doğumlarda Doğum Memnuniyetinin Değerlendirilmesi

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Abstract

Objective: This study aims to investigate the effects of general and spinal anesthesia methods on the birth satisfaction of women in cesarean deliveries with the birth satisfaction scale (BSS) and to determine the factors affecting birth satisfaction.

Method: This descriptive cross-sectional study included 350 women who delivered by cesarean section under general and spinal anesthesia in a tertiary healthcare institution between June 2022 and November 2022. The patients were divided into groups S (spinal anesthesia) and G (general anesthesia). The data collection form and the "BSS" were filled in by face-to-face interview technique on the day of discharge to women who had a cesarean section.

Results: A total of 350 women who had a cesarean section, 228 (65.1%) in group S and 122 (34.9%) in group G, participated in the study. While 59.7% (n=209) of the women were primary school graduates, 6.9% (n=24) were university graduates. The mean BSS score was significantly higher in group S compared to group G (108±13 vs. 104±12, p=0.005). The preference for spinal anesthesia in university graduates and general anesthesia in illiterate women was significantly higher (p=0.021). When evaluated according to educational status, BSS scores were significantly higher in university graduates (p=0.002).

Conclusion: Birth satisfaction scores were high in women with a cesarean section under spinal anesthesia. In addition, preference for spinal anesthesia and BSS scores were high in university graduate

Öz

Amaç: Bu çalışmanın amacı, sezaryen doğumlarda genel ve spinal anestezi yöntemlerinin kadınların doğum memnuniyetine olan etkisinin doğum memnuniyet ölçeği (BSS) ile araştırılması ve doğum memnuniyetine etki eden faktörlerin belirlenmesidir.

Yöntem: Tanımlayıcı kesitsel tipteki bu çalışmaya Haziran 2022 ile Kasım 2022 tarihleri arasında tersiyer bir sağlık kuruluşunda genel ve spinal anestezi altında sezaryen ile doğum yapan 350 kadın dahil edildi. Hastalar grup S (spinal anestezi) ve grup G (genel anestezi) olarak iki gruba ayrıldı. Sezaryen doğum yapan kadınlara taburcu olacakları gün yüz yüze görüşme tekniği ile veri toplama formu ve "BSS" doldurduldu.

Bulgular: Çalışmaya grup S'de 228 (%65,1) ve grup G'de 122 (%34,9) olmak üzere toplam 350 sezaryen doğum yapmış kadın katıldı. Kadınların %59,7'si (n=209) ilkokul mezunu iken %6,9'u (n=24) yükseköğrenim mezunu idi. Grup S'de BSS skor ortalaması grup G'ye kıyasla anlamlı olarak yüksek saptandı (108±13 vs. 104±12, p=0,005). Üniversite mezunu kadınlarda spinal anestezi ve okur-yazar olmayan kadınlarda genel anestezi tercihi anlamlı olarak yüksekti (p=0,021). Eğitim durumuna göre değerlendirildiğinde üniversite mezunlarında BSS skorları anlamlı olarak yüksek bulundu (p=0,002).

Sonuç: Spinal anestezi altında sezaryen doğum yapan kadınlarda doğum memnuniyet skorları yüksek saptanmıştır. Ek olarak üniversite mezunu kadınlarda spinal anestezi tercihi ve BSS skorları yüksek bulunmuştur. Eğitim seviyesi düşük kadınların spinal anestezi hakkında

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Abstract

women. Informing women with low educational levels about spinal anesthesia and eliminating any concerns may increase the preference for spinal anesthesia and the satisfaction of delivery.

Keywords: Cesarean section, childbirth, general anesthesia, satisfaction, spinal anesthesia

Öz

bilgilendirilmeleri ve varsa endişelerin giderilmesi spinal anestezi tercihini ve doğum memnuniyetini artırabilir.

Anahtar kelimeler: Doğum, genel anestezi, memnuniyet, sezaryen, spinal anestezi

Introduction

Pregnancy and childbirth are among the most important and unique experiences that affect women's lives physically, psychologically, and socially. In birth satisfaction, the training received in preparation for birth, the pain experienced during the birth process, the care and needs of women, the mode of delivery, and the sense of individual control of the birth are of great importance. In addition, it is effective for pregnant women not to be included in the decision-making process and to receive support from someone they trust during delivery (1-3). The determination of birth satisfaction is crucial as it indicates maternal care quality and shows the well-being of the newborn and mother.

The satisfaction level of women from obstetric services in health institutions from various regions of is between 54 and 90% (4,5). Positive birth experience increases women's self-confidence and contributes positively to establishing stronger relationships with their children and planning for future births. Negative birth experience; is associated with inadequacy in breastfeeding and maternal attachment, postpartum depression, neglect of child care, sexual reluctance, and fear of the subsequent birth (6).

Cesarean section rates are increasing in Turkey and the rest of the world. Spinal anesthesia; has advantages such as the faster recovery of gastrointestinal functions after surgery, providing postoperative analgesia, lower risk of drug toxicity for mother and baby, early mobilization in the postoperative period, and early communication between mother and baby (7). In addition, complications have been reported to be higher in general anesthesia (8). For all these reasons, the preference for spinal anesthesia is increasing in cesarean deliveries.

This study aims to investigate the effect of general and spinal anesthesia methods on the birth satisfaction of women in cesarean deliveries with the "birth satisfaction scale (BSS)'' and to determine the factors affecting the level of birth satisfaction.

Materials and Methods

This prospective descriptive cross-sectional study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital (date: 06.04.2022, number: 90). The work was started following the principles of the Declaration of Helsinki. Verbal and written consent was obtained from all women who gave birth in the study.

The Design, Universe, and Sample of the Study

Women who gave birth by cesarean section between June 2022 and November 2022 at the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital and agreed to participate in the study were included.

Inclusion criteria for the study;

• Eighteen years of age and older who had a cesarean section under general and spinal anesthesia in the hospital where the research was conducted,

• Not having a high-risk pregnancy, not having health problems in herself or her baby, not being treated in the postnatal intensive care unit for herself or her baby,

• Not a refugee or a citizen of another country, fluent in Turkish and with no communication problems,

• Primiparous and multiparous women who agreed to participate in the study and had elective cesarean delivery during working hours were included (Figure 1).

In the hospital where the study was conducted, the number of cesarean deliveries in 2021 was 3248, and the number of vaginal deliveries was 3033. The study's sample size: According to the sample size formula used when the universe is known, it was calculated as 343 at a 95% confidence interval by using the Epi info 7.2.5 program. A total of 350 women who had cesarean delivery under spinal and general anesthesia were included in the study. The patients were divided into groups G (general anesthesia group) and S (spinal anesthesia group), and their BSS scores were analyzed. At the same time, socio-

demographic characteristics affecting birth satisfaction in the whole population were investigated.

Data Collection and Data Collection Tools

Questionnaire forms were applied to the women who agreed to participate in the study, on the day of discharge, in their rooms, and when alone by using the face-to-face interview technique. The researchers prepared the data collection form, and the "BSS" was used to collect the data (Table 1). In the data collection form, women's socio-demographic data (age, number of births, educational status, employment status) and obstetric and neonatal clinical data (gestational week, visual analog scale score at the 6th-hour postoperative, APGAR score of the newborn at 1 and 5 minutes) were questioned.

BSS

Martin and Fleming (9) developed the BSS in 2009 to evaluate the birth satisfaction of women. The scale was prepared in English and consisted of 30 items. BSS is a five-point Likert-type scale scored according to the answers given. "I strongly agree" is 5 points; "I agree" is 4 points; "I neither agree nor disagree" is 3 points; "I disagree" is 2 points; "I strongly disagree" is 1 point.

The total number of points taken from the scale varies between 30 and 150. Items 4, 8, 12, 15, 16, 17, 19, 20, 21, 23, 25, and 29 of the BSS are scored in reverse order. As the score obtained from the scale increases, the level of birth satisfaction increases, and the scale has no cut-off value. When the scale was created, validity and reliability studies

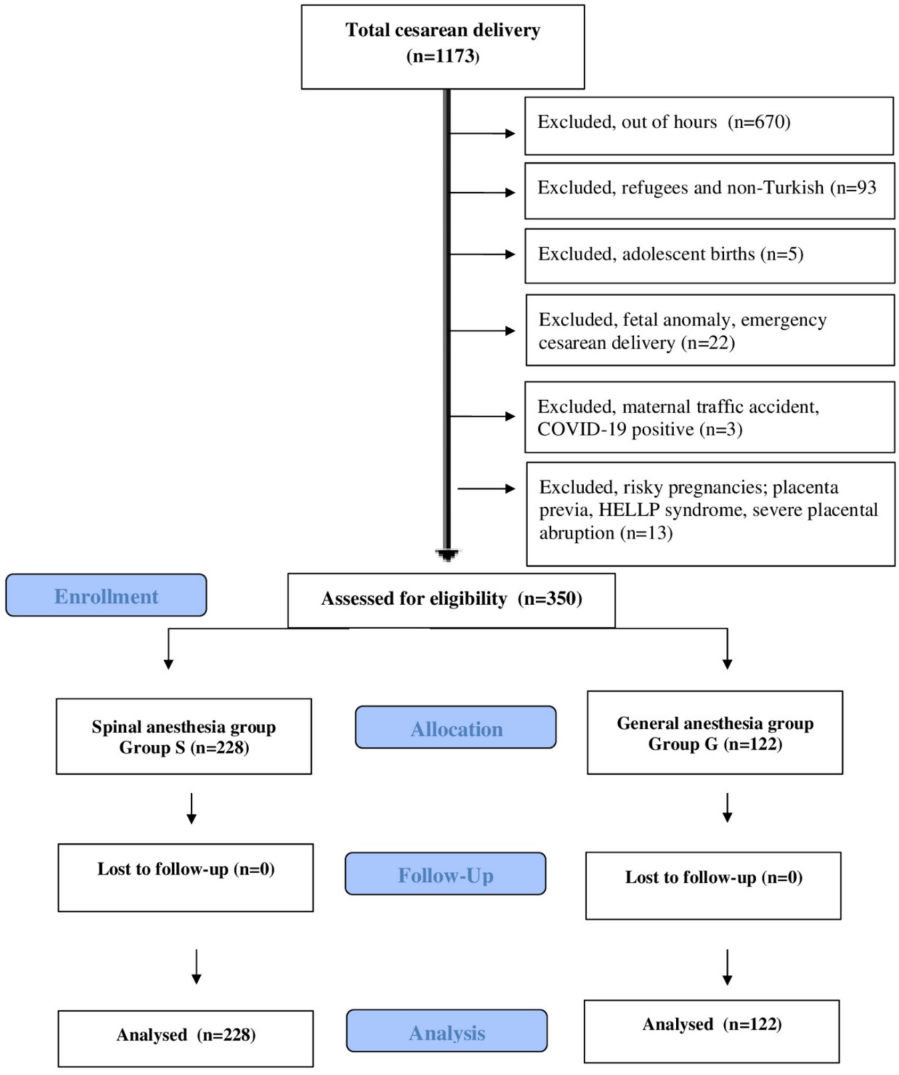

Figure 1. Flow chart of the study

COVID-19: Coronavirus disease-2019

were not carried out, and central themes and sub-themes were determined in line with the literature review results. Three overarching themes were selected in the scale:

1. Quality of care provision

2. Women's attributes

3. Stress experienced during labor (Table 2).

Turkish validity and reliability of BSS Cetin et al. (10). Cronbach's alpha coefficient was determined as 0.62.

Table 1. Items of the birth satisfaction scale

1) I coped well with my birth.
2) The delivery room staff encouraged me to make decisions about how I wanted my birth to progress.
3) I was well prepared for my labour, i.e., read a lot of literature and/or attended parenthood education classes.
4) I found giving birth a distressing experience.
5) I came through childbirth virtually unscathed
6) I gave birth to a healthy normal baby.
7) During labour I received outstanding medical care.
8) I received a lot of medical intervention, i.e., induction, forceps, section etc.
9) I had a swift and speedy labour.
10) I felt well supported by my partner during labour and birth.
11) I was encouraged to hold my baby for a substantial amount of time after birth.
12) My birth experience was considerably different from what I intended.
13) I had the same midwife throughout the entire process of labour and delivery.
14) I felt that the delivery room was unthreatening and comfortable.
15) I felt very anxious during my labour and birth.
16) I felt out of control during my birth experience.
17) I felt it was better not to know in advance about the processes of giving birth.
18) I was not distressed at all during labour.
19) I felt mutilated by my birth experience.
20) My baby was avoidably hurt during birth.
21) The staff provided me with insufficient medical care during my birth.
22) I had a natural labour, i.e., minimal medical intervention.
23) I thought my labour was excessively long.
24) I felt well supported by staff during my labour and birth.
25) I was separated from my baby for a considerable period of time after my birth.
26) My birth proceeded as I planned it.
27) The staff communicated well with me during labour.
28) The delivery room was clean and hygienic.
29) Giving birth was incredibly painful.
30) Labour was not as painful as I imagined.

In our study, the total Cronbach's alpha coefficient for BSS was 0.82, 0.68 for the first theme, 0.62 for the second theme, and 0.72 for the third theme. The general validity of the BSS was tested, and its items were found to be suitable and sufficient for factor analysis (KMO=0.75, p<0.001).

Statistical Analysis

SPSS 26.0 (SPSS Inc., Chicago, USA) program was used to analyze the data. Descriptive data are expressed as the number of patients, percentage, mean, standard deviation, and range. The conformity of the variables to the normal distribution was evaluated analytically (Shapiro-Wilks test) and visually (histogram). Mann-Whitney U and Kruskal-Wallis H tests were used to analyze non-normally distributed quantitative data. Mann-Whitney U test was used in the analysis of the scale data. The chi-square test was used in the analysis of categorical data. The Bonferroni test was used as a post-hoc test to determine the difference between groups in categorical data. The statistical significance limit was accepted as p<0.05.

Results

A total of 350 women, 228 (65.1%) in group S and 122 (34.9%) in group G participated in the study. While the mean age and distribution range of the cases were 29.4±5.5 (18-44) in group S, it was 28.8±4.9 (18-38) in group G. The mean parity was 2.2±1.2 in group S and 2.1±1.3 in group

Table 2. Themes and sub-themes affecting birth satisfaction

Themes	Sub-themes	Questions
Quality of care provision	Home assessment	12 and 26
	Birth environment	14 and 28
	Sufficient support	10 and 24
	Relationships with health care professionals	13 and 27
Women's personal attributes	Ability to cope during labour	1 and 15
	Feeling in control	2 and 16
	Preparation for childbirth	3 and 17
	Relationship with baby	11 and 25
Stress experienced during labour	Distress experienced during labour	4 and 18
	Obstetric injuries	5 and 19
	Perception of medical care	7 and 2
	Receipt of an obstetric intervention	8 and 22
	Pain experienced	29 and 30
	Long labour	9 and 23
	Health of baby	6 and 20

G. When examined according to their educational status, 59.7% (n=209) of the population were primary school graduates. In comparison, 6.9% (n=24) were university graduates. When evaluated according to employment status, 87.7% (n=307) of the entire population was not working. The mean gestational week of both groups was 38±1.3. While newborns' mean 1st minute (min) APGAR scores were 6.9±0.6 in group S, it was 6.7±0.7 in group G. The mean post-operative 6th-hour visual analog scale (VAS) scores were 5.1±1.9 in group S and 5.6±2.1 in group G. The mean BSS scores and range of distribution, were 108±13 (66-137) in group S, while it was 104±12 (71-130) in group G (Table 3).

When the BSS themes were evaluated, there was no significant difference between the groups' quality of care delivery (p=0.152). The personal attitudes of the women and the satisfaction levels of their stress experiences during the birth process were significantly higher in group S (p=0.003 and p=0.031, respectively) (Table 4).

When the evaluation was made between groups, BSS scores in group S were significantly higher than in group G (p=0.005). The mean age, number of births, and women's employment rates were higher in group S, although insignificant (p=0.619, p=0.519, p=0.147, respectively). The rate of university graduates in group S and the rate of illiterate women in group G were significantly higher (p=0.021). In group S, newborns' APGAR scores (1st and 5th min) were significantly higher, while post-operative 6th-hour VAS scores were significantly lower (p=0.036, p=0.032, p=0.037, respectively).

When the factors affecting birth satisfaction levels were investigated, the mean BSS scores of women aged 30-44 were higher than those aged 18-29, although insignificant (p=0.201). When compared according to education levels, the highest BSS scores were among university graduate women, and the lowest BSS scores were among high school graduate women. There was a significant difference between BSS scores according to education level (p=0.002).

Table 3. Socio-demographic data by groups, some clinical features, and BSS scores

	All population (n=350)	Group S (n=228)	Group G (n=122)	p-value
Age (years)	29.2±5.3 (18-44)	29.4±5.5 (18-44)	28.8±4.9 (18-38)	0.619*
Parity, n	2.2±1.2 (1-6)	2.2±1.2 (1-6)	2.1±1.2 (1-6)	0.644*
Educational status, n (%)	10 (16.7%)	4 (13.3%)	6 (20.0%)	**0.021†**
Illiterate	63 (18)	32 (14)	31 (25.4)	
Primary education	209 (59.7)	144 (63.1)	65 (53.4)	
High school	54 (15.4)	33 (14.5)	21 (17.2)	
University and postgraduate	24 (6.9)	5 (16.7%)	5 (4)	
Working status, n (%)				0.147†
Working	43 (12.3)	33 (14.4)	10 (8.2)	
Housewife	307 (87.7)	195 (85.6)	112 (91.8)	
Gestational week, n	38±1.3 (35-41)	38±1.3 (35-41)	38±1.3 (36-41)	0.662*
APGAR score (1st min), n	6.8±0.7 (3-8)	6.9±0.6 (4-8)	6.7±0.7 (3-8)	**0.036***
APGAR score (5st min), n	8.7±0.5 (4-9)	8.8±0.5 (6-9)	8.6±0.5 (4-9)	**0.032***
VAS score (post-op 6th hour)	5.3±2 (1-9)	5.1±1.9 (2-8)	5.6±2.1 (1-9)	**0.037***
BSS score, n	106±13 (66-137)	108±13 (66-137)	104±12 (71-130)	**0.005***

Data are given as mean ± standard deviation, range, number of patients (n), and percentage.
APGAR: Neonatal scoring system, VAS: Visual analog scale, BSS: Birth satisfaction scale,*Mann-Whitney U test, †chi-squared test

Table 4. Birth satisfaction scale theme and total score averages

	All population (n=350)	Group S (n=228)	Group G (n=122)	p-value
Theme				
Quality of care provision	3.70±0.5	3.72±0.5	3.67±0.4	0.152*
Women's personal attibutes	3.48±0.5	3.55±0.5	3.34±0.5	**0.003***
Stress experienced during labor	3.49±0.4	3.54±0.4	3.41±0.5	**0.031***
Total	3.42±0.4	3.46±0.4	3.34±0.3	**0.005***

Data are given as mean ± standard deviation, *Mann-Whitney U test

The BSS scores of illiterate women were significantly higher than those of high school graduate women. The BSS scores of university graduate women were considerably higher than high school graduate women (adj. p=0.019 and p=0.004, respectively). Although not substantial, BSS scores were high in workers and multiparous women (p=0.153, p=0.425, respectively) (Table 5).

Discussion

The experiences of women in the intrapartum and postpartum period and their satisfaction with the health services they receive have become increasingly important. Many scales, such as the birth satisfaction and postpartum comfort scales, have been developed and used for this purpose (9,11). The delivery type is a critical factor affecting women's satisfaction with birth. Çelik and Çelik (11) reported that those who gave vaginal birth had higher postpartum comfort than those who had a cesarean section. The same study said that postpartum comfort was higher in those who had a cesarean section with regional anesthesia than in those with a cesarean section with general anesthesia. Fleming et al. (12) evaluated labor satisfaction with BSS in their study and reported that the mean BSS score was 128.9±9. The same survey emphasized that those who had a vaginal delivery had higher birth satisfaction than those who had a cesarean section. In our research, spinal anesthesia was applied in most of the cesarean deliveries (65.1%) that participated in the study, consistent with the literature. The birth satisfaction score of the whole population was 106±13. At the same time, the birth satisfaction scores of those who had a cesarean section in group S were significantly higher than those of group G (BSS score 108±13 vs. 104±12, p=0.005).

Pain is one of the negative experiences in childbirth. Problems experienced in the postpartum period, and the birth process, can affect birth satisfaction. Huang et al. (13) determined that the pain experienced in the postpartum period negatively affects birth satisfaction by preventing the mother's comfort, performing the baby, and self-related care activities. A study conducted with primiparous and multiparous women reported that one-third of women had problems in the postpartum period. The most common problem is a pain in the operation area and standing up during cesarean deliveries (14). In our study, the BSS scale was used to evaluate birth satisfaction. When the themes of the BSS were compared between the groups, no significant difference was observed in the quality of care. On the other hand, in the sub-headings of stress level during delivery and attitudes of pregnant women, birth satisfaction scores were found to be significantly higher in the spinal anesthesia group. Following the literature, we think pain palliation in postpartum is essential for birth satisfaction in cesarean deliveries.

It has been reported that maternal age may affect birth satisfaction (1,2,6). However, studies also report that age does not significantly affect birth satisfaction (15-17). In our study, although the mean age of the spinal anesthesia group was higher than the general anesthesia group, no

Table 5. Socio-demographic characteristics affecting the birth satisfaction scale score

	n	%	BSS score	p-value
Age range				0.201*
18-29	194	55.4	105.5±12.3	
30-44	156	4.46	107.6±13.5	
Parity				0.425*
Primiparous	122	34.8	105.6±12.7	
Multiparous	228	65.2	106.9±13	
Educational status				**0.002†**
Illiterate	63	18	108.3±12[a]	
Primary education	209	59.7	106.2±12.9	
High school	54	15.5	101.8±12.9[ab]	
University and postgraduate	24	6.8	114.1±11.6[b]	
Working status				0.153*
Working	43	12.3	110.6±12.4	
Housewife	307	87.7	105.8±12.9	

Data are given as mean ± standard deviation, BSS: Birth satisfaction scale, *Mann-Whitney U test, †Kruskal-Wallis test, [a]The BSS scores of illiterate patients were significantly higher than those of high school graduate patients (Adj. p=0.019), [b]BSS scores of university graduate patients were significantly higher than high school graduate patients (adj. p=0.004)

significant difference was found. Although the BSS scores of women aged 30-44 in the entire population were high, no significant difference was observed.

Parity can also affect birth satisfaction. Bilgin et al. (15) reported that the level of birth satisfaction in multiparous women is higher than in primiparous women. In our study, BSS scores were significantly higher in group S. The mean parity in this group was higher than in general anesthesia, although it was insignificant. In our study, although BSS scores in multiparous puerperal women were higher than those in primiparous, no significant difference was observed. The fact that multiparous and older women are more experienced in both spinal anesthesia and childbirth than primiparous women and are more effective in decision-making is effective in spinal anesthesia preference and birth satisfaction.

One of the factors that affect women's birth satisfaction is education. It has been reported in some studies that education status does not affect birth satisfaction (15,17). However, studies also note that increased education level increases birth satisfaction (16,18). In our research, illiterate women had a significantly higher preference for general anesthesia; similarly, a priority for spinal anesthesia was considerably higher in university graduates. Our study also found that education level greatly affected birth satisfaction (p=0.002). While the mean BSS scores in higher education graduates were 114.1±11.6, the mean BSS scores in the whole population were 106±13.

One of the factors that may affect birth satisfaction is the working status of women. Studies report that working status does not affect women's birth satisfaction (2,18). However, Goodman et al. (18) said working women had higher labor satisfaction. In our study, the rate of working women in the spinal anesthesia group was high, although it was insignificant. When the whole population was evaluated, the BSS scores of working women were higher than those who did not, although insignificant (BSS score =110.6±12.4 vs. 105.8±12.9, p=0.153).

Study Limitations

The main limitation of our study is that it is single-centered, and the sample size is relatively small. Additionally, it is not a randomized controlled trial. The anesthesiologist informed the patients about general and spinal anesthesia, and the decisions were left to the patients, and groups were formed. Since general anesthesia is mainly preferred in our clinic for risky pregnancies such as placenta previa, HELLP syndrome, and pregnant with fetal anomalies, these pregnant were not included in the study. Birth satisfaction scores may have been lower in these pregnant women.

Conclusion

In conclusion, this study found that the birth satisfaction scores of women who had a cesarean section under spinal anesthesia were significantly higher than those who had general anesthesia. In addition, the educational status of women affects their anesthesia preferences and birth satisfaction scores. Informing women with low education levels about spinal anesthesia and eliminating their fears and concerns may enable them to prefer it. Thus, it can increase satisfaction with the birth process, essential in women's lives.

Ethics

Ethics Committee Approval: This prospective descriptive cross-sectional study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital (date: 06.04.2022, number: 90). The work was started following the principles of the Declaration of Helsinki.

Informed Consent: Verbal and written consent was obtained from all women who gave birth in the study.

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Authorship Contributions

Surgical and Medical Practices: H.Ç.A., K.A., Ş.Ç.Y., Concept: H.Ç.A., K.A., Ş.Ç.Y., Design: H.Ç.A., K.A., Ş.Ç.Y., Data Collection or Processing: H.Ç.A., Ş.Ç.Y., Analysis or Interpretation: H.Ç.A., K.A., Literature Search: K.A., Writing: H.Ç.A., K.A.

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ORIGINAL RESEARCH

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Tips for 6 Months After COVID-19 Pneumonia: Acute Inflammatory Parameters

COVID-19 Pnömonisinden 6 Ay Sonrası için İpuçları: Akut Dönem Enflamatuvar Parametreleri

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Abstract

Objective: In our study, we aimed to investigate the long-term effects of the acute phase parameters of C-reactive protein, procalcitonin, D-dimer, lymphocyte, thrombocyte and ferritin on the respiratory function parameters in patients hospitalized due to Coronavirus disease-2019 (COVID-19) pneumonia.

Method: The present study was carried out with the retrospective evaluation of patients with COVID-19 pneumonia, who were hospitalized in Medipol University Hospital between March 2020 and June 2021, and who were 6 months to 1 year after discharge. The relationship between pulmonary function test results and acute period laboratory findings of 52 patients who applied for control purposes 6 months after discharge was examined.

Results: Diffusing capacity for carbon monoxide (DLCO) (pred) value in 26 patients (50%), total lung capacity (TLC) value in 9 patients (17.3%), and residual volume (RV) (pred) value in 10 patients (19.2%) were below 80%. As a result of multiple linear regression analysis in our study, the maximum D-dimer level and maximum procalcitonin level were determined by DLCO (% pred) (adjusted R^2 =0.645; p<0.001), TLC (% pred) (adjusted R^2 =0.582; p=0.003) and RV (% pred) (adjusted R^2 =0.560; p=0.001) values and were independent determinants in predicting these values.

Conclusion: High D-dimer and procalcitonin levels in the acute period in patients with COVID-19 pneumonia may predict losses in respiratory function parameters such as DLCO, TLC, RV in the longer term than 6 months. Long-term follow-up of these patients is important in terms of respiratory function.

Keywords: COVID-19, D-dimer, DLCO

Öz

Amaç: Çalışmamızda Koronavirüs hastalığı-2019 (COVID-19) nedeniyle hastaneye yatırılan hastalarda akut faz parametrelerinden C-reaktif protein, prokalsitonin, D-dimer, lenfosit, trombosit ve ferritinin solunum fonksiyon parametreleri üzerine uzun dönem etkilerini araştırmayı amaçladık.

Yöntem: Çalışmamız Medipol Üniversite Hastanesi'nde Mart 2020-Haziran 2021 tarihleri arasında servise yatırılan ve taburculuk sonrası 6 ay ila 1 yıl zaman geçmiş olan COVID-19 pnömonisi hastalarının geriye dönük olarak değerlendirmesi ile gerçekleştirildi. Taburculuktan 6 ay sonrasında kontrol amaçlı başvurmuş olan 52 hastanın solunum fonksiyon test sonuçları ile akut dönem laboratuvar bulguları arasındaki ilişki incelendi.

Bulgular: Hastaların 26'sında (%50) karbon monoksit difüzyon kapasitesi (DLCO) (% pred), 9'unda (%17,3) total akciğer kapasitesi (TLC) (% pred) ve 10'unda (%19,2) rezidüel hacim (RV) (% pred) %80'in altındaydı. Çalışmamızda çoklu doğrusal regresyon analizi sonucunda maksimum D-dimer düzeyi ve maksimum prokalsitonin düzeyinin DLCO (% pred) (düzeltilmiş R^2 =0,645; p<0,001), TLC (% pred) (düzeltilmiş R^2 =0,582; p=0,003) ve RV (%pred) (düzeltilmiş R^2 =0,560; p=0,001) değerleri ile anlamlı bir ilişkiye sahip olduğu ve bu değerleri öngörmede bağımsız birer belirleyici olduğu saptandı.

Sonuç: COVID-19 pnömonisi hastalarında akut dönemde yüksek seyreden D-dimer ve prokalsitonin seviyeleri 6 aydan uzun dönemde DLCO, TLC, RV gibi solunum fonksiyon parametrelerindeki kayıpları öngörebilir. Bu hastaların solunum fonksiyonu açısından uzun dönem takibi önemlidir.

Anahtar kelimeler: COVID-19, D-dimer, DLCO

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Introduction

A coronavirus known as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is the cause of Coronavirus disease-2019 (COVID-19). COVID-19 due to SARS-CoV-2 affects multiple organs and has serious effects on lung function (1). Pathophysiological changes such as capillary damage, hyaline membrane formation, alveolar epithelial damage, alveolar septal fibroplasia occurs (2). With these changes, 5-10% of COVID-19 patients develop crucial illnesses, including acute respiratory distress syndrome (ARDS). ARDS causes pulmonary dysfunction with residual volume loss (2,3). Also, these pathological changes in the lungs are associated with impaired diffusion capacity. Correspondingly, a high prevalence of impaired diffusing capacity for carbon monoxide (DLCO) has been found in patients who are more likely to develop pulmonary fibrosis (4). Parameters reflecting inflammation such as C-reactive protein (CRP), D-dimer, lymphocyte, and ferritin in the acute phase of COVID-19 pneumonia have been found to be related in literature in terms of prognostic prediction (5-7). In the review of Ponti et al. (8), low lymphocyte count, increase in inflammatory parameters such as CRP and D-dimer were found to be associated with severe prognosis in the acute phase in COVID-19 patients. In a recent meta-analysis; lymphopenia, thrombocytopenia and increases in inflammatory parameters such as CRP, procalcitonin, D-dimer, ferritin count in the acute period were associated with mortality (9). Inflammatory parameters showing the severity of the disease can give an idea about the long-term effects of the disease. However, as far as we know, a limited number of studies in the literature investigate the relationship between acute phase laboratory findings and long-term respiratory function in COVID-19 pneumonia. The aim of our study was to investigate the relationship of acute phase parameters CRP, procalcitonin, D-dimer, lymphocyte, platelet and ferritin with respiratory function parameters longer than 6 months after discharge in patients with COVID-19 pneumonia.

Materials and Methods

This single-center, retrospective cohort study; was carried out with the retrospective evaluation of COVID-19 pneumonia patients hospitalized in Medipol University Hospital between March 2020 and June 2021. The sample of our study consisted of COVID-19 pneumonia patients aged 18-65 years, who were followed up in the service, with SARS-CoV-2 polymerase chain reaction positivity in the nasopharyngeal swab and who had viral infection related findings in thorax computed tomography. In order to exclude physiological changes in respiratory function that may occur with aging, patients aged 65 and over were excluded (10).

Inclusion criteria were being between the ages of 18-65, being hospitalized with COVID-19 pneumonia, having spent at least 6 months and maximum 1 year after discharge, and having completed pulmonary function tests at the control visit. Exclusion criteria were to have any other chronic lung disease and/or heart failure, to have a history of hospitalization after discharge, to have an active infection at the time of control visit and to be pregnant.

Seven hundred and ten inpatients in the ward were screened and the data of 110 patients who met the inclusion and exclusion criteria were evaluated through the hospital registry system. The data of 52 patients, 24 females and 28 males, who had all their data accessible and who completed the pulmonary function tests at the control visit, were included in the study. Demographic and clinical information, laboratory findings and pulmonary function test results were recorded.

All tests were performed by the same investigator and a pulmonologist was the observer. Spirometric measurements, diffusion capacities and plethysmography measurements were made on the Vyntus body device. For spirometry, flow-volume curves were obtained through and the greatest volume of the three manoeuvres was expressed as the percentage of predicted normal and used for analysis. Plethysmography was performed with the panting maneuver method in a closed cabin.

All pulmonary function test measurements were expressed as percentages of predicted normal values. Spirometry and body plethysmography tests were performed in accordance with the European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines (11). DLCO was evaluated with a single breath technique in accordance with the ATS/ERS guidelines (12). The percentage of predicted values in spirometry, DLCO, and were calculated according to the Global Lung Function Initiative reference values (13). Written and verbal consent was obtained from all patients before the test.

Statistical Analysis

Statistical analyzes of all data were performed with SPSS Statistics Version 26 (IBM Statistical Package for the Social Science, New York, USA) program. Descriptive data were

given as mean ± standard deviation or percent (%). Normal distribution was evaluated with the Shapiro-Wilk test. One-Way Spearman correlation analysis was performed to determine the relationship between respiratory parameters and laboratory test parameters, and the Spearman correlation coefficient (r) value is given in the results section. Laboratory test parameters that were found to be significantly associated with respiratory parameters according to One-Way Spearman correlation analysis were evaluated with multiple linear regression analysis. As a result of the regression analysis, the regression coefficient was given with the standardized β coefficient value. The significance level was taken as $p<0.05$ for all statistical analyses.

Results

Seven hundred and ten patients were screened for compliance with the inclusion criteria. Fifty-two patients who met the inclusion criteria were included in the study. Demographic and clinical characteristics of the patients, respiratory parameters and laboratory test parameters are given in Table 1.

DLCO (pred) was below 80% in 26 (50%) patients, TLC in 9 (17.3%) patients (pred), and RV (pred) in 10 (19.2%) patients. The results of the One-Way correlation analysis of respiratory parameters and laboratory test parameters of the patients are given in Table 2.

There was no correlation between maximum CRP level, minimum lymphocyte level and minimum platelet level with any respiratory parameter ($p>0.05$). Maximum D-dimer level with DLCO (% pred) ($r=-0.305$, $p<0.001$), TLC (% pred) ($r=-0.270$, $p=0.002$) and RV (% pred) ($r=-0.299$, $p=0.004$), there was a significant negative correlation.

There was no relationship between the maximum D-dimer level and other respiratory parameters ($p>0.05$). There was a significant positive correlation between maximum ferritin level and PEF (% pred) ($r=0.324$, $p=0.019$) and FEF75 (% pred) ($r=0.316$, $p=0.023$). There was no correlation between the maximum ferritin level and other respiratory parameters ($p>0.05$). There was a negative and significant relationship between maximum procalcitonin level with DLCO (% pred) ($r=-0.368$, $p<0.001$), TLC (% pred) ($r=-0.289$, $p=0.010$) and RV (% pred) ($r=-0.269$, $p=0.021$).

The results of multiple linear regression analysis of respiratory parameters and laboratory test parameters of the patients are given in Table 3. When the independent

Table 1. Demographic/clinical/laboratory parameters of the patients

	Mean ± standard deviation (n=52)	Min-max
Age (years)	49.13±9.04	32-65
Gender		
Woman (n)	24 (46.2%)	
Male (n)	28 (53.8%)	
BMI (kg/m²)	30.79±4.81	22-42
Smoking		
Never (n)	39 (75%)	
Ex smoker (n)	11 (21.2%)	
Active smoker (n)	2 (3.8%)	
Comorbidities		
Hypertension (n)	11 (21.2%)	
Diabetes (n)	11 (21.2%)	
Other systemic diseases (n)	10 (19.2%)	
Respiratory parameters		
FEV_1 (% pred)	99.73±17.50	60-154
FVC (% pred)	99.83±16.74	51-149
FEV_1/FVC (%)	82.66±5.05	72-99
PEF (% pred)	90.35±25.02	36-155
FEF_{25} (% pred)	80.73±32.30	32-174
FEF_{50} (% pred)	97.85±29.28	49-176
FEF_{75} (% pred)	95.85±26.04	38-158
DLCO (% pred)	79.65±21.34	55-119
DLCO/VA (% pred)	93.92±24.12	64-130
TLC (% pred)	84.50±20.17	53-112
RV (% pred)	87.71±25.66	46-125
RV/TLC (% pred)	97.35±28.63	54-148
FRC (% pred)	88.86±31.66	53-143
Laboratory test parameters		
Max CRP level (mg/dL)	93.38±70.33	10-295
Max D-dimer level (ng/mL)	1520.38±4051.20	241-29846
Min lymphocyte level (10^3/µL)	889.61±385.40	270-1890
Min platelet level (10^3/µL)	184.28±66.78	85-406
Max ferritin level (mg/L)	1057.69±1179.80	49-5081
Max procalcitonin level (ng/mL)	0.53±2.63	0.02-19.14
Length of stay in hospital (days)	7.88±8.12	2-61
Time after discharge (months)	9±1.81	6-12

BMI: Body mass index, FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity, PEF: Peak flow rate, FEF_{25}: 25% of forced expiratory flow, FEF_{50}: 50% of forced expiratory flow, FEF_{75}: Forced expiratory flow 75% of current, DLCO: Carbon monoxide diffusion capacity, DLCO/VA: Carbon monoxide diffusion coefficient of alveolar volume, TLC: Total lung capacity, RV: Residual volume, FRC: Functional residual capacity, CRP: C-reactive protein

variables (maximum ferritin level and maximum procalcitonin level) that were significantly associated with the FEF75 (% pred) value were included in the multiple linear regression analysis model, it was seen that a model consisting of these variables was not a significant determinant (Adjusted R^2=0.021, p>0.05). Independent variables (maximum D-dimer level and maximum procalcitonin level) that were significantly associated with the DLCO (% pred) value were evaluated by including them in the multiple linear regression analysis model.

As a result of multiple linear regression analysis, it was determined that both maximum D-dimer level (β=-0.611) and maximum procalcitonin level (β=-0.701) were independent predictors of DLCO (% pred) value and were significant in predicting DLCO (% pred) value. (Adjusted R^2=0.645, p<0.001). Independent variables (maximum D-dimer level and maximum procalcitonin level) significantly associated with TLC (% pred) value were evaluated by multiple linear regression analysis. It was determined that both maximum D-dimer level (β=-0.347) and maximum procalcitonin level (β=-0.380) were

Table 2. Results of One-Way correlation analysis of respiratory parameters and laboratory test parameters

	Maximum CRP level		Maximum D-dimer		Minimum lymphocyte		Minimum platelet		Maksimum ferritin		Maximum procalsitonin	
	r	p	r	p	r	p	r	p	r	p	r	p
FEV_1 (% pred)	-0.103	0.469	0.098	0.490	-0.122	0.388	0.035	0.804	0.071	0.616	0.067	0.638
FVC (% pred)	-0.115	0.415	0.099	0.485	-0.167	0.237	-0.036	0.798	-0.056	0.693	0.069	0.629
FEV_1/FVC (%)	-0.082	0.561	-0.098	0.492	0.058	0.685	0.141	0.318	0.001	0.996	-0.030	0.832
PEF (% pred)	0.076	0.593	0.103	0.469	0.009	0.949	0.152	0.281	0.324	0.019	0.109	0.444
FEF_{25} (% pred)	-0.129	0.361	-0.006	0.964	-0.007	0.960	0.085	0.549	0.146	0.302	0.069	0.628
FEF_{50} (% pred)	0.082	0.561	0.062	0.663	-0.087	0.539	0.059	0.675	0.264	0.058	0.170	0.228
FEF_{75} (% pred)	0.103	0.468	0.203	0.148	-0.024	0.868	0.154	0.277	0.316	0.023	0.353	0.002
DLCO (% pred)	-0.005	0.969	-0.305	<0.001	-0.232	0.098	0.090	0.524	0.204	0.147	-0.368	<0.001
DLCO/VA (% pred)	0.031	0.826	0.050	0.727	-0.143	0.311	0.193	0.169	0.236	0.092	-0.079	0.577
TLC (% pred)	-0.092	0.517	-0.270	0.002	-0.137	0.334	-0.074	0.604	0.027	0.852	-0.289	0.010
RV (% pred)	0.029	0.836	-0.299	0.004	-0.116	0.411	-0.235	0.094	0.085	0.550	-0.269	0.021
RV/TLC (% pred)	0.028	0.845	-0.057	0.687	-0.066	0.643	-0.118	0.406	0.026	0.853	-0.088	0.534
FRC (% pred)	0.048	0.736	0.052	0.712	-0.138	0.330	0.024	0.864	0.013	0.926	-0.006	0.966

FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity, PEF: Peak flow rate, FEF_{25}: 25% of forced expiratory flow, FEF_{50}: 50% of forced expiratory flow, FEF_{75}: Forced expiratory flow 75% of current, DLCO: Carbon monoxide diffusion capacity, DLCO/VA: Carbon monoxide diffusion coefficient of alveolar volume, TLC: Total lung capacity, RV: Residual volume, FRC: Functional residual capacity, CRP: C-reactive protein

Table 3. Results of multiple linear regression analysis of respiratory and laboratory parameters

Dependent variable	Independent variable	β	R^2	Adjusted R^2	p
FEF_{75} (% pred)					
	Maximum ferritin level	-0.091	0.028	0.021	0.103
	Maximum procalcitonin level	-0.074			0.084
DLCO (% pred)					
	Maximum D-dimer level	-0.611	0.711	0.645	**<0.001**
	Maximum procalcitonin level	-0.701			**<0.001**
TLC (% pred)					
	Maximum D-dimer level	-0.347	0.695	0.582	**0.003**
	Maximum procalcitonin level	-0.380			**0.002**
RV (% pred)					
	Maximum D-dimer level	-0.420	0.607	0.560	**0.001**
	Maximum procalcitonin level	-0.311			**0.002**

PEF: Peak flow rate, FEF_{75}: 75% of forced expiratory flow, DLCO: Diffusion capacity of carbon monoxide, TLC: Total lung capacity, RV: Residual volume

independent predictors of TLC (% pred) value and were significant in predicting TLC (% pred) value (Adjusted R^2=0.582, p=0.003, p=0.002).

Independent variables (maximum D-dimer level and maximum procalcitonin level) significantly associated with RV (% pred) value were evaluated by multiple linear regression analysis. It was determined that both maximum D-dimer level (β=-0.420) and maximum procalcitonin level (β=-0.311) were independent predictors of RV (% pred) value and were significant in predicting RV (% pred) value (Adjusted R^2=0.560, p=0.001, p=0.002).

Discussion

In our study, we determined that maximum D-dimer level and maximum procalcitonin level were independent predictors of long-term DLCO (% pred), TLC (% pred), RV (% pred) values and were significant in predicting these values. In COVID-19 pneumonia, the lungs are the most affected organ due to alveolar epithelial destruction, capillary damage/bleeding, hyaline membrane formation, alveolar septal fibrous proliferation (14).

These effects are mostly determined as decrease in diffusion capacity (DLCO) and loss of total capacity (TLC) (14). Depending on the severity of the disease, changes occur in inflammatory parameters such as fibrinogen degradation products, lymphocyte, D-dimer, thrombocyte, CRP, procalcitonin, and ferritin (15-17).

In COVID-19 pneumonia, respiratory function losses, which progress with loss of diffusion (DLCO), can be detected even 6 months after discharge from the service (18,19). Despite these understandings of the long-term effects of COVID-19 on lung function, there is a lack of analysis of risk factors for long-term effects. Risk factors for long-term losses in respiratory function parameters, especially DLCO, have been investigated in a limited number of studies in hospitalized patients due to COVID-19 pneumonia. In their study, Zhao et al. (1) found that high D-dimer levels predicted DLCO loss in long-term follow-up. Santus et al. (20) found that D-dimer was the most important parameter predicting impaired DLCO during the service period and 6-week follow-up. A similar result was also found in a meta-analysis evaluating long-term DLCO loss (3).

In our study, we found that D-dimer elevation reflects the decrease in DLCO, consistent with the literature. Moreover, it reflected not only DLCO but also RV and TLC reductions. High D-dimer and procalcitonin values in COVID-19 pneumonia maintain their importance in this respect in long-term follow-up as well as in the acute period in patient follow-up in the service.

Bursac et al. (21) found a significant relationship between the initial CRP elevation and the decrease in DLCO in long-term follow-up. His extensive research with emphasis on other laboratory parameters is limited. In a study conducted with 60 patients 3-6 months after discharge, it was found that high CRP, high D-dimer, and low lymphocyte values in the acute period predict impaired DLCO (22).

Although our study was different from this study, the maximum CRP, minimum lymphocyte, platelet and ferritin values in the acute period did not reflect the long-term effects of pulmonary function, generally consistent with the literature. However, we also found that the maximum procalcitonin level was also significant in predicting DLCO, TLC and RV losses in long-term follow-up. Regarding other respiratory functions, laboratory findings do not reflect long-term pulmonary functional involvement, again in line with the literature. However, as it was emphasized at the beginning of the article, our results are remarkable since DLCO is the most important parameter with the highest loss. More studies are needed to be presented for discussion regarding these parameters.

Study Limitations

Our study has some limitations. First of all, the low number of patients evaluated is among these limitations. However, the exclusion of chronic lung diseases and other comorbid conditions in which respiratory functions are affected and the inclusion of patients with all available data are strengths in terms of both the long-term effects of the disease and its evaluation with laboratory findings. As far as we know, there is no research on risk factors for the pulmonary effects of the disease longer than 6 months in our country. Our research can shed light on long-term follow-up strategies with laboratory findings and different parameters.

Conclusion

It may be important to follow-up patients with high D-dimer and procalcitonin levels in COVID-19 pneumonia, not only in the acute period but also in the long-term, especially in terms of respiratory functions. In patients with COVID-19 pneumonia, the elevation of these parameters during the acute infection period may predict the decrease in DLCO (% pred), TLC (% pred), and RV (% pred) parameters after 6-12 months later. While respiratory function loss is observed even in cases

evaluated for up to 1 year, longer follow-up is required, especially in patients with COVID-pneumonia who are hospitalized and followed up.

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Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, with the approval of İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee, dated 25.05.2022 and numbered E-10840098-772.02-3116.

Informed Consent: Written and verbal consent was obtained from all patients before the test.

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Authorship Contributions

Concept: E.A., Design: E.A., Data Collection or Processing: G.K., Analysis or Interpretation: E.A., G.K., Drafting Manuscript: E.A., G.K., Critical Revision of Manuscript: E.A., G.K., Final Approval and Accountability: E.A., G.K., Writing: E.A., G.K.

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ORIGINAL RESEARCH

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Evaluation of Post-cesarean Section Surgical Site Infections Before and During the COVID-19 Pandemic: Retrospective, Tertiary Center Experience

Sezaryen Sonrası Cerrahi Alan Enfeksiyonlarının COVID-19 Pandemisi Öncesi ve Sırasında Değerlendirilmesi: Retrospektif, Tersiyer Merkez Deneyimi

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Abstract

Objective: Surgical site infection (SSI) significantly causes maternal morbidity requiring hospitalization. This study aimed to determine the clinical and laboratory results of patients who developed SSI after cesarean section at the peak of Coronavirus disease-2019 (COVID-19).

Method: Sixty patients who developed SSIs after cesarean section were included in the study retrospectively. They were divided into two groups. Thirty patients recruited at the peak of COVID-19 were the "pandemic group" and thirty patients recruited in previous years were the "pre-pandemic group". Age, parity, presence of comorbidity, emergency or elective cesarean section, use of drain in operation, postoperative hemoglobin, hematocrit and leukocyte values, presence of superficial or deep incisional infection, time from discharge to wound infections, wound growth culture, antibiotic duration, length of hospital stay, and the need for suture performed were analyzed between the two groups.

Results: While superficial incisional infection was observed in 71.7% (n=43) of the patients with SSI, deep incisional infection was observed in 28.3% (n=17). It was observed that there was an increase in deep incisional infection rates and the need for suturation in SSIs during the pandemic period, but there was no significant difference (p=0.390). There was no significant difference in hemoglobin, hematocrit, and leukocyte values. However, it was observed that all patients with deep incisional infections were sutured (p<0.001).

Conclusion: SSI causes prolonged hospital stays, poor delivery experience, and patient dissatisfaction. Demographic characteristics of patients and surgical factors are essential in determining the risk.

Öz

Amaç: Cerrahi alan enfeksiyonu (CAE) hastaneye yatış gerektiren önemli bir derecede maternal morbiditeye neden olur. Bu çalışma, Koronavirüs hastalığı-2019'un (COVID-19) zirve yaptığı dönemde sezaryen sonrası CAE gelişen hastaların klinik ve laboratuvar sonuçlarını belirlemeyi amaçladı.

Yöntem: Sezaryen sonrası insizyonel CAE gelişen 60 hasta retrospektif olarak çalışmamıza dahil edildi. İki gruba ayrıldılar. COVID-19'un pik yaptığı dönemde toplanan otuz hasta pandemi grubu kabul edildi ve önceki yıllarda görülen otuz hasta pandemi öncesi grup olarak kabul edildi. Yaş, parite, ek hastalık varlığı, acil veya elektif sezaryen, operasyonda dren kullanımı, postoperatif hemoglobin, hematokrit ve lökosit değerleri, yüzeysel veya derin insizyonel enfeksiyon varlığı, taburculuktan yara gelişimine kadar geçen süre, yara üreme kültürü, antibiyotik süresi, hastanede kalış süresi ve sütüre edilip edilmediği gibi parametreler iki grup arasında analiz edildi.

Bulgular: CAE gözlenen hastaların %71,7'sinde (n=43) yüzeyel insizyonel enfeksiyon görülürken, %28,3'ünde (n=17) derin insizyonel enfeksiyon görüldü. Pandemi döneminde CAE'de derin insizyonel enfeksiyon oranlarında ve sütürasyon ihtiyacında artış olduğu ancak anlamlı bir fark olmadığı görüldü (p=0,390). Hemoglobin, hematokrit ve lökosit değerlerinde anlamlı fark gözlenmedi. Ancak derin insizyonel enfeksiyonu olan hastaların tümünün sütüre edildiği görüldü (p<0,001).

Sonuç: CAE, hastanede kalış süresinin uzamasına, kötü doğum deneyimine ve hasta memnuniyetsizliğine neden olur. Hastaların demografik özellikleri ve cerrahi faktörler riskin belirlenmesinde esastır.

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Abstract

This study shows that although there is an increase in the frequency of deep incisional infections during the pandemic, post-cesarean section infections are not affected by the pandemic in terms of clinical and laboratory features.

Keywords: Cesarean section, morbidity, pandemic, surgical site infections

Öz

Bu çalışma, pandemi döneminde derin insizyonel enfeksiyonlarının sıklığında artış olmasına rağmen, sezaryen sonrası enfeksiyonların klinik ve laboratuvar özellikleri açısından pandemiden etkilenmediğini göstermektedir.

Anahtar kelimeler: Cerrahi alan enfeksiyonları, morbidite, pandemi, sezaryen

Introduction

Surgical site infections (SSI) are observed in the incision line or manipulated organs/areas and occur within the first 30 days after the operation. In the presence of a foreign body (prosthesis, implant, etc.), this period increases to one year. While SSIs cause surgery-related morbidity and mortality, they also severely burden countries' economies because of prolonged hospital stays.

By the middle of the 19th century, the incidence of SSIs reached 90%. This rate decreased with the discovery of antibiotics and the principles of asepsis/antisepsis by Joseph Lister (1). Today, the prevalence of SSI, the most critical complication of cesarean section operations, varies between 3% and 15% (2). It ranks third among infections requiring hospitalization (3).

Standard definitions for diagnosing SSI have been determined by the Centers for Disease Control and Prevention. They are classified as superficial infection, deep infection, and organ/space infection if involving structures deeper than muscle and fascia space (4). With COVID-19 infection, there was a period when potential morbidity and mortality increased. Therefore, new proposals specific to the pandemic were planned. As elective operations were postponed due to the COVID-19 pandemic, cesarean section surgery became one of the most frequently performed procedures.

This study aims to analyze the clinical and laboratory outcomes of SSIs after cesarean sections performed during the most intense COVID-19 compared to infections seen in previous years and to show the possible effects of the pandemic.

Materials and Methods

Ethical approval for this retrospective study was obtained from the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (28.07.2022/181). The study was initiated by the principles of the Declaration of Helsinki. The consent form was obtained from the patients before hospitalization.

Incisional CAE is considered purulent discharge, redness or swelling from the wound, and wound dehiscence, involving the skin and subcutaneous tissues within the first 30 days after the procedure. In the clinic, preoperative antibiotic prophylaxis is routinely administered to all patients at a dose of 1 g cefazolin 30-60 minutes before the incision. A total of 60 patients with diagnosed SSI who underwent elective and emergency cesarean sections between January 2018 and May 2022 were included in the study. The study sample was divided into two groups; the patients admitted between January 2018 and March 2020 were considered as the pre-pandemic group (n=30), and the patients between March 2020 and May 2022 were considered as the pandemic group (n=30). Demographic data such as age, parity, presence of additional disease, and clinical parameters such as emergency or elective cesarean section, use of drains in operation, presence of superficial or deep incisional infection, and organism cultured from wound swabs were compared in two groups. Laboratory parameters such as hemoglobin, hematocrit, and leukocyte values obtained within 24-48 hours after the operation and the duration of the antibiotic used, the duration of hospitalization, the time from discharge to wound development, and the need for suturing were compared. In managing SSI, one group had to be sutured, while one group was treated conservatively. The distribution of these parameters in the suturation group was also examined. The conservative group (n=21) consisted of patients who did not require secondary suturing and were treated only with antibiotics, and the re-suturing group (n=39) consisted of patients who underwent secondary suturing.

Statistical Analysis

All statistical analyses were performed using the Statistical Program for Social Sciences (SPSS) version 16.0 (SPSS Inc., Chicago, IL). The Shapiro-Wilk test was used to assess the normality of the distribution of variables. Independent t-tests were used to compare parameters with normal

distribution, and data were presented as mean ± standard deviation. In contrast, the Mann-Whitney U test was used to compare parameters with the non-normally distribution, and data were presented as medians. Fisher's Exact and chi-square tests were used to compare qualitative data. p-values less than 0.05 were considered statistically significant.

Results

A total of 60 patients diagnosed with SSI within 30 days postoperatively were included in the study. Preoperative antibiotic prophylaxis was determined in all patients. The mean age of the patients was 30.6±6.1 years and ranged from 19 to 41. The mean number of deliveries was 2.0±1.7 and all patients were multiparous. Ten patients (16.7%) had one or more additional diseases, such as hypertensive disease, anemia, and obesity. While comorbidity was observed more in the pandemic group, it did not reach a significant value. It was observed that the emergency or elective occurrence of the operation and the use of drains were similar between the two groups. While superficial incisional infections were observed in 71.7% (n=43) of the patients; deep incisional infections were observed in 28.3% (n=17). Although there was an increase in the frequency of deep incisional infections with the pandemic, it did not reach a significant difference (p=0.390). Cultures taken from wound swabs showed growth in 38.3% (n=23) of the patients. Reproducing organisms increased with the pandemic, but no significant difference was found. When the distribution of the patients who developed infections at the wound site after the operation were examined, Gram (+) bacteria were found in 48.3% of the patients, Gram (-) bacteria in 43%, and fungal growth in 8.7%. *Staphylococcus aureus* was the most frequently isolated pathogen, and *Enterococcus faecalis* was the second pathogen. Re-suturing was performed in 65% (n=39) of the patients who developed SSI, while only antibiotic treatment was applied in 35% (n=21) (Table 1).

When the laboratory results were examined, no significant difference was observed between hemoglobin, hematocrit, and leukocyte values (Table 2). The mean day on which SSI was diagnosed was 12.2±11.0 postoperative day. The mean duration of antibiotics was 14.0±5.7 days, and the average length of stay was 7.1±5.0 days. There was no significant difference in the duration of antibiotics and the length of stay between pre-pandemic and pandemic groups.

The clinical parameters of the patients treated conservatively, and those who needed suturing are compared in Table 3. Parameters such as age, deep incisional infection rate, presence of growth in wound culture, blood leukocyte values, hospital admission time after discharge, duration of antibiotics usage, and hospital stays were observed at higher rates in the group requiring suturing; however, no significant difference was found.

Table 1. Demographic data and distribution of clinical characteristics of the patients with surgical site infections, and comparison of study groups

	Total (n=60)	Pre-pandemic group (n=30)	Pandemic group (n=30)	p-value
Age (mean ± SD)	30.6±6.1	29.1±6.2	32.1±5.8	0.707
Parity (mean ± SD)	2.0±1.7	1.3±1.4	2.8±1.7	**0.001**
Comorbidity (n, %)	10 (16.7%)	4 (13.3%)	6 (20.0%)	0.488
Cesarean section (n, %)				0.793
Emergency	25 (41.7%)	12 (40.0%)	13 (43.3%)	
Elective	35 (58.3%)	18 (60.0%)	17 (56.7%)	
Drain use (n, %)	8 (13.3%)	5 (16.7%)	3 (10.0%)	0.448
Incisional infection (n, %)				
Superficial	43 (71.7%)	23 (76.7%)	20 (66.7%)	0.390
Deep	17 (28.3%)	7 (23.3%)	10 (33.3%)	
Organism cultured from wound swab	23 (38.3%)	10 (33.3%)	13 (43.3%)	0.426
Management of SSI (n, %)				0.417
Conservative	21 (35%)	12 (40.0%)	9 (30.0%)	
Re-suturing	39 (65%)	18 (60.0%)	21 (70.0%)	

SD: Standard deviation, SSI: Surgical site infections. p-value <0.05 is significant

It was observed that all patients with deep incision infections were sutured (p<0.001).

Discussion

Cesarean section operations are one of the most common abdominal surgeries performed worldwide. SSI complicates 2-5% of all surgeries and 5-12% of cesarean section surgeries (5,6). SSI is the second most common complication of urinary tract infection after delivery (7), and it also burdens the health system by prolonging the hospital stay.

Most SSIs are observed as superficial incisional, less often deep incisional, and organ/space. Wloch et al. (8) reported that superficial incisions were for 88.3% of infections. In our study, 71.7% were superficial, and 28.3% were deep incisional infections. It should be known that superficial infection may spread to deep tissues if the necessary antimicrobial treatment and care are not performed.

Causative microorganisms from wound swabs are often reported as diffuse skin or urogenital tract flora. *Ureaplasma urealyticum* 62%, followed by coagulase-negative *Staphylococcus aureus* 32%, and *Enterococcus faecalis* 28% were detected in cultures obtained from 939 post-cesarean SSIs (9). In a multicenter prospective study investigating SSI frequency and risk factors after cesarean section, causative microorganisms were reported in 39.8% of infections. The common isolated pathogen was found to be *Staphylococcus aureus* (40.4%) (8). Our analysis also has findings supporting this study. Causative microorganisms were reported in 38.3% of the infections, and the most commonly isolated pathogen was *Staphylococcus aureus*. The β-lactam antibiotics used for antimicrobial prophylaxis are suitable for targeting such organisms. Among the first-generation cephalosporins, cefazolin is generally preferred as first-line therapy. Clindamycin is recommended in combination with an aminoglycoside in patients with beta-lactam allergy (10).

In a study evaluating risk factors for SSI, age, high BMI, malnutrition, low socio-economic status, preoperative anemia, and co-morbidities were found to be associated (11). Johnson et al. (12) reported that the risk of SSI increases with age. On the other hand, in some studies in

Table 2. Clinical and laboratory outcomes and comparison of study groups

	Total (n=60)	Pre-pandemic group (n=30)	Pandemic group (n=30)	p-value
Postoperative hemoglobin (g/dL)	10.3±1.6	10.1±1.7	10.4±1.5	0.569
Postoperative hematocrit	31.5±4.8	30.8±5.1	32.3±4.5	0.287 (%)
Postoperative WBC counts (cells/µL)	13.7±6.7	13.2±5.8	14.2±7.6	0.569 (10^3)
Time from discharge to hospitalization (days)	12.2±11.0	13.3±14.2	11.1±6.7	0.988
Lenght of antibiotic use (days)	14.0±5.7	13.2±6.4	14.9±4.7	**0.028**
Lenght of hospital stay (days)	7.1±5.0	7.3±6.1	7.0±3.7	0.645

p-value <0.05 is significant. WBC: White blood cell

Table 3. Clinical characteristics and comparison of the conservative and re-suturing group

	Conservative group (n=21)	Re-suturing group (n=39)	p-value
Age (mean ± SD)	28.6±5.8	31.7±6.1	0.085
Incisional infection (n, %)			
Superficial	21 (100%)	22 (56.4%)	**0.001**
Deep	0	17 (43.6%)	
Organism from wound swab	9 (42.9%)	14 (35.9%)	0.597
Postoperative WBC counts (cells/µL)	11.7±4.3	15.0±7.5	0.161
Time from discharge to (days)	10.6±6.0	13.2±13.1	0.981
Lenght of antibiotic use (days)	13.1±3.9	14.6±6.5	0.300
Lenght of hospital stay (days)	5.5±2.0	8.0±6.0	0.116

SD: Standard deviation, p-value <0.05 is significant, WBC: White blood cell

the literature, the incidence of SSI was found to be more common in young women (<20 years), although the cause is unknown. There was no difference in the length of hospital stay in young women (13,14). In our study, the mean age of the study population was 30.6±6.1, and the mean parity was 2.0±1.7. Drain use, emergency or elective operation, and comorbidity were also evaluated as risk factors, but they were not significant between the groups.

In the clinic, leukocyte values taken from the blood are often checked for infection and complications in the postoperative period. However, available clinical and biological variables are not always associated with the severity of the infection (15). In our study, although there was a slight increase in the laboratory parameters of the patients during the pandemic period, they were not found to be significant.

SSIs usually occur 4-7 days after the operation but can be prolonged to 20 days. In the first 24 hours, it may also occur in the presence of clostridial infection and exotoxin-producing streptococcal infection. The follow-up period should be at least 21 days, preferably extended to 30 days after the operation. The literature showed signs of SSI ten days after surgery (8). In our study, SSI occurred 12.2±11.0 days after surgery, consistent with the literature.

A randomized controlled trial by Quinn et al. (16) conducted that uncomplicated dehiscence, shorter than 2 cm, being sutured unnecessarily, would heal with similar results without sutures. Similarly, in our study, there was no difference between conservative and re-suturing groups regarding clinical outcomes.

Study Limitations

This study has some limitations, some of which are the low number of patients and the fact that conducted in a single center retrospectively.

Conclusion

It is essential to determine the risk factors of post-cesarean infections to take the necessary precautions. At a time when maternal morbidity and mortality increased in the COVID-19 pandemic, no significant difference was observed in the clinical and laboratory outcomes of SSI patients. This may be because of the positive effect of infection control and the compliance of patients and healthcare personnel with the security measures applied during the pandemic.

Ethics

Ethics Committee Approval: Ethical approval for this retrospective study was obtained from the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (28.07.2022/181). The study was initiated by the principles of the Declaration of Helsinki.

Informed Consent: The consent form was obtained from the patients before hospitalization.

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Authorship Contributions

Surgical and Medical Practices: H.Ç.A., M.G., Concept: H.Ç.A., K.A., Design: H.Ç.A., Data Collection or Processing: K.A., M.G., Analysis or Interpretation: K.A., M.G., Literature Search: M.G., Writing: H.Ç.A., K.A.

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Clinical Characteristics of Patients with Methyl Alcohol Intoxication Followed up in the Intensive Care Unit and Factors Affecting Mortality

Yoğun Bakım Ünitesinde Takip Edilen Metil Alkol İntoksikasyonlu Hastaların Klinik Özellikleri ve Mortaliteye Etki Eden Faktörler

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Abstract

Objective: Methyl alcohol is a solvent obtained by the fermentation of wood and used in various fields industrially. Due to its cheap and easy accessibility, it is frequently used to manufacture moonshine and can lead to severe morbidity and mortality. This study aims to evaluate the clinical features of patients with methanol intoxication followed in the tertiary center intensive care unit (ICU) and determine the factors affecting mortality.

Method: All patients aged 18 years and older who were followed up in the ICU for methanol intoxication between January 2016 and September 2022 were included in the study. Demographic characteristics, clinical data, and factors affecting mortality were evaluated retrospectively by classifying the patients as discharged and dead.

Results: A total of 32 patients, 11 (34.3%) in the discharged group and 21 (65.7%) in the dead group, were included in the study. The mean age of the whole population was 41.5±8.8 years, and all were male. Of the population, 37.5% had central nervous system findings, 34.3% had visual disturbances, and 15.6% had gastrointestinal system complaints. Renal replacement therapy was administered to 93.7% of the patients, ethyl alcohol or fomepizole to 40.6%, and folate to 28.1%. High anion gap metabolic acidosis (pH<6.95, base excess<-25.2, anion gap>23.2) and high lactate levels (lactate>5.27) were associated with poor outcomes.

Conclusion: Although methanol intoxication is an important public health problem affecting especially young-middle-aged men, it is a significant cause of mortality. We think that developing effective policies can prevent methanol intoxication and related deaths.

Keywords: Acidosis, intensive care unit, intoxications, methanol, mortality

Öz

Amaç: Metil alkol ahşabın fermentasyonu ile elde edilen ve endüstriyel olarak çeşitli alanlarda kullanılan bir çözücüdür. Ucuz ve kolay ulaşılabirliği nedeniyle kaçak içki yapımında sıklıkla kullanılmakta ve ciddi morbidite ile mortaliteye yol açabilmektedir. Bu çalışmanın amacı, üçüncü basamak bir merkezin yoğun bakım ünitesinde (YBÜ) takip edilen metanol intoksikasyonlu hastaların klinik özelliklerini değerlendirmek ve mortalite üzerine etkili faktörleri saptamaktır.

Yöntem: Ocak 2016 ile Eylül 2022 tarihleri arasında YBÜ'de metanol intoksikasyonu nedeniyle takip edilen 18 yaş ve üzeri tüm hastalar çalışmaya dahil edildi. Hastalar taburculuk grubu ve ölen grup olarak sınıflandırılarak demografik özellikler, klinik veriler ve mortaliteye etki eden faktörler retrospektif olarak değerlendirildi.

Bulgular: Çalışmaya taburculuk grubunda 11 (%34,3), vefat eden grupta 21 (%65,7) olmak üzere toplam 32 hasta dahil edildi. Tüm popülasyonun yaş ortalaması 41,5±8,8 yıl ve hepsi erkek idi. Tüm popülasyonun %37,5'inde santral sinir sistemi bulguları, %34,3'ünde görme bozuklukları, %15,6'sında gastrointestinal sistem şikayetleri mevcuttu. Hastaların %93,7'sine renal replasman tedavisi, %40,6'sına etil alkol veya fomepizol, %28,1'ine folat uygulandı. Yüksek anyon açıklı metabolik asidoz (pH<6,95, baz açığı<-25,2, anyon gap>23,2) ve yüksek laktat düzeyleri (laktat>5,27) kötü sonuçlarla ilişkili bulundu.

Sonuç: Metanol intoksikasyonları özellikle genç-orta yaş erkekleri etkileyen, ileri tedavi yöntemlerine rağmen hastaneye geç başvuru ve tedavide gecikme nedeniyle yüksek mortalite oranları görülebilen bir halk sağlığı problemidir. Etkili politikaların geliştirilmesinin ve bu konuda yapılacak çalışmaların hastaların yönetimine ve tedavi protokollerinin iyileştirilmesine katkı sağlayacağını düşünüyoruz.

Anahtar kelimeler: Asidoz, metanol, mortalite, yoğun bakım ünitesi, zehirlenmeler

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Introduction

Methyl alcohol (methanol) is an organic solvent obtained by wood fermentation (1). Since it is used in various industrial dry cleaning processes, glass cleaning solutions, and paint thinner, it is provided legally and efficiently. It is colorless, odorless, and tastes similar to ethyl alcohol but is cheaper than ethyl alcohol (2). Although methyl alcohol toxicity is often seen when it is used in the manufacture of illicit liquor, it can also be consumed for suicide or accidentally when people who are addicted to alcohol consume products such as cologne made from methyl alcohol (3). Although methanol is not toxic, its metabolites, formaldehyde and formic acid are responsible for methanol toxicity, which can lead to severe poisoning and death (4).

Gastrointestinal system findings such as nausea and vomiting, changes in consciousness, shortness of breath, tachypnea, chest pain and visual disturbances, complete vision loss, permanent neurological dysfunction, severe metabolic acidosis, and cardiac arrest can be seen in patients with methanol intoxication (5). The non-specificity of presentation complaints and the inaccessibility of laboratory tests (serum methanol, formic acid level, osmolality analysis) used in every health institution make the diagnosis difficult (6). High anion gap metabolic acidosis, confusion, and visual impairment are essential in diagnosing methanol intoxication (7,8). Antidotes with fomepizole or ethanol in treatment, hemodiafiltration to eliminate toxic metabolites, and buffers with folic acid and sodium bicarbonate are essential (9). Despite advances in treatment, it continues to be one of the significant causes of death due to poisoning due to difficulties in diagnosis and delayed admission to the hospital.

This study aims to evaluate the clinical features of patients with methanol intoxication who were followed up and treated in the ICU of a tertiary center and to investigate the factors affecting mortality.

Materials and Methods

This retrospective cross-sectional study was initiated following the principles of the Declaration of Helsinki after the approval of the Local Ethics Committee of University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital (date: 11.11.2022, number: 211). Patients aged 18 years and older who were followed up with the diagnosis of methyl alcohol intoxication between January 1, 2016, and September 1, 2022, in the ICU of the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital were included in the study. Patients with missing data and referred to another healthcare institution during ICU follow-up were excluded from the study.

Although the best method for the definitive diagnosis of methanol intoxication is the measurement of the methanol level in the blood, the diagnosis was based on the patient's or relative's history, clinical findings, and blood gas values since they could not be examined in the emergency department of our hospital. Suspected alcohol intake history (unlabeled, homemade), abdominal pain, nausea, vomiting, impaired consciousness and vision, high anion gap metabolic acidosis in blood gas analysis, and increased anion gap (pH<7.30, HCO_3< 20 mEq^{-1}, anion gap>10 $mEqL^{-1}$), the diagnosis was made in the emergency department of our hospital. Differential diagnosis was made with other toxic alcohols using anamnesis, clinical findings, and blood gas findings (differential diagnosis was made from ethyl and isopropyl alcohol exposure with the absence of high anion gap metabolic acidosis, from ethylene glycol exposure due to increased anion gap metabolic acidosis and increased osmolar deficit).

Demographic data of the patients, comorbid diseases, reasons for applying to the emergency department, presence of visual complaints based on information obtained from themselves or their relatives in the emergency department or ICU, duration of stay in the ICU, the Glasgow Coma scale (GCS) routinely checked during ICU admission, and Acute Physiology and Chronic Health Assessment-2 (APACHE-2) scores, mechanical ventilation (Mv) requirements, length of stay in MV, laboratory findings and mortality during admission to the emergency department were recorded and analyzed through our hospital's information system and patient files.

Since the treatment plan of patients with methanol intoxication could change according to the patient's clinical condition, laboratory results, and the availability of drugs used in the treatment, there was no routine treatment protocol in our ICU during the study period. Renal replacement therapy (RRT), ethyl alcohol, fomepizole, and folic acid treatments were recorded and analyzed in the discharged and dead groups.

Statistical Analysis

The SPSS 29.0 (SPSS Inc., Chicago, USA) program was used to analyze the data. Descriptive data are expressed as the number of patients, percentage, mean and standard deviation (minimum-maximum). The conformity of

the variables to the normal distribution was evaluated analytically (Shapiro-Wilks test) and visually (histogram). Independent sample t-test was used to analyze normally distributed quantitative data between the two groups, and the Mann-Whitney U test was used to analyze non-normally distributed quantitative variables. The chi-square and Fisher's Exact tests were used to evaluate qualitative data. Multiple logistic regression analysis was used to analyze whether age, GCS, and APACHE-2 scores differed significantly between the groups and were independent risk factors for mortality. ROC curve analysis was performed to estimate mortality from blood gas parameters with significant differences between the groups and to determine cut-off values. The statistical significance limit was accepted as $p<0.05$.

Results

During the six years between January 2016 and September 2022, 32 patients with methyl alcohol intoxication who were followed up and treated in the ICU were included in the study. All of the patients were male. While 34.1% (n=11) of the patients were discharged after treatment, 65.9% (n=21) died. It was determined that methanol intoxication (n=5) was caused by the concomitant intake of ethyl alcohol and methyl alcohol in 15.6% of the population. The discharged group's mean age and distribution range were 36±8 (19-48) years, while the mean age and distribution range of the died group was 44.4±7.9 (34-60) years. The mean length of stay and range of stay in the ICU in the discharged patients were 5.6±5.8 (2-17) days, while it was 5.1±5.7 (1-26) days in the patients who died. While no comorbid disease was observed in the discharge group, comorbid disorder (hypertension, diabetes mellitus, chronic obstructive pulmonary disease) was detected in 23.8% (n=5) of the dead group. The mean GCS score and distribution range at the time of admission to the ICU in the discharged group was 10.2±4 (3-15), while that of the dead group was 3.3±8 (3-6). Mechanical ventilation was applied to 81.2% (n=26) and vasopressors to 68.7% (n=22) of the entire population. RRT was used in 93.7% (n=30) of the whole population, ethyl alcohol or fomepizole in 40.6% (n=13), and folic acid in 28.1% (n=9) of the whole population. It was determined that the treatment protocols were carried out in different sessions according to the clinical condition of the patients and the supply of the drugs used. The mean APACHE-2 score and range of distribution of the discharged group at the time of admission to the ICU were 16.2±4 (10-25), while the mean APACHE-2 score and range of issuance of the died group were 29.9±6 (20-41). Age and APACHE-2 scores of the discharged group were significantly lower than those of the dead group ($p=0.008$, $p<0.001$), while GCS scores were significantly higher ($p<0.001$) (Table 1). However, age, GCS, and APACHE-2 scores were not independent risk factors for mortality ($p=0.234$, $p=0.266$, and $p=0.439$), respectively (Table 2).

Table 1. Demographic data of patients, distribution of some clinical characteristics

Variable	All population (n=32)	Discharged group (n=11)	Dead group (n=21)	p
Age (years)	41.5±8.8	36.0±8.0	44.4±7.9	0.008*
Gender, n (%)				-
Male	32 (100)	21 (100)	11 (100)	
Comorbidity, n (%)	5 (23.8)	0	5 (23.8)	-
GCS score	5.2±5 (3-15)	10.2±4 (3-15)	3.3±8 (3-6)	<0.001†
APACHE-2 score	25.2±8 (10-41)	16.2±4 (10-25)	29.9±6 (20-41)	<0.001†
Duration of ICU (days)	5.3±5 (1-26)	5.6±5 (2-17)	5.1±5 (1-26)	0.667†
Mv, n (%)	26 (81.2)	5 (45.4)	21 (100)	0.01‡
Duration of Mv (days)	5.2±5 (1-26)	5.2±4 (1-10)	5.1±5 (1-26)	0.667†
Vasopressor, n (%)	22 (68.7)	1 (38.7)	21 (100)	<0.001‡
Ethanol and methanol intake, n (%)	5 (15.6)	2 (18.1)	3 (9.3)	-
Treatment				
RRT, n (%)	30 (93.7)	9 (81.8)	21(100)	0.05‡
Ethyl alcohol or fomepizole, n (%)	13 (40.6)	4 (36.3)	9 (40.9)	0.721‡
Folic acid, n (%)	9 (28.1)	3 (27.2)	6 (28.5)	1.000‡

Values are the number of patients (n), percentage, mean, standard deviation and distribution range (minimum-maximum) GCS: Glascow Coma scale, APACHE-2: Acute Physiology and Chronic Health Assessment-2, ICU: Intensive care unit, Mv: Mechanical ventilation, RRT: Renal replacement therapy, *Independent sample t-test, †Mann-Whitney U test, ‡chi-squared test

Considering the complaints of the patients who applied to the emergency department, 37.5% (n=12) had central nervous system findings (confusion, coma, seizures, and cerebrovascular events), 34.3% (n=11) had visual disturbances, 15.6% (n=5) had gastrointestinal system complaints and 12.5% (n=4) cardiac arrest was detected (Table 3). It was determined that the patients applied to the emergency services at the highest rate in the winter (65.6%) and spring (21.8%) seasons (Table 4).

When the biochemical and blood gas values of the patients at the time of admission to the emergency services were examined, creatinine, BE (base excess), anion gap, and lactate levels were significantly higher in the dead group (p=0.016, p<0.001, p=0.016, p<0.001, respectively). pH and HCO_3 values were significantly lower (Table 3).

When the patient's blood gas values were examined at admission to the emergency department, pH and HCO_3 values were significantly lower in the dead group. At the same time, lactate, anion gap, and BE (base excess) levels were significantly higher (p<0.001, p=0.003, p<0.001, p=0.016, and p<0.001, respectively) (Table 5). The ROC curves used to compare blood gas parameters to predict mortality are shown in Figure 1, and the analytical data of these curves are shown in Table 6. According to ROC

Table 2. Multiple logistic regression analysis of factors associated with patients' mortality status

Variables	OR	p	95% CI (min-max)
Age	1.435	0.234	0.791-2.600
GCS	0.509	0.266	0.155-1.672
APACHE-2	1.400	0.439	0.579-3.286
Constant	0.363	0.214	

OR: Odds ratio, CI: Confidence interval, GCS: Glasgow Coma scale, APACHE-2: Acute Physiology and Chronic Health Assessment-2

Table 3. Distribution of methyl alcohol intoxications according to hospitalization findings

Findings of admission to the emergency department	All population (n=32)	Discharged group (n=11)	Dead group (n=21)
Central nervous system findings*, n (%)	12 (37.5)	2 (18.1)	10 (47.6)
Visual impairment**, n (%)	11 (34.3)	3 (27.2)	8 (38.1)
Gastrointestinal system complaints, n (%)	5 (15.6)	5 (45.4)	0
Cardiac arrest, n (%)	4 (12.5)	0	4 (19)

Values are the number of patients (n), percentage, *Confusion, coma, seizures, and cerebrovascular events
**There was no visual finding in 7 (21.8%) of the patients, and it could not be evaluated in 14 (43.7) patients because of unconsciousness

Table 4. Seasons of admission to hospital

Seasons, n (%)	All population (n=32)
Winter	21 (65.6)
Spring	7 (21.8)
Autumn	3 (9.3)
Summer	1(3.1)

Values are the number of patients (n), percentage

Table 5. Some biochemical and blood gas values of methanol intoxications

Variable	All population (n=32)	Discharged group (n=11)	Dead group (n=21)	p
pH	6.8±0.2 (6.4-7.2)	7.1±0.1 (6.8-7.2)	6.7±0.1 (6.4-7.1)	<0.001*
Lactate (mmol/L)	7.46 (4.5)	3.29 (1.9)	9.65 (3.9)	<0.001*
Anion gap (mmol/L)	20±10.9	13.2±15.4	23.5±5.4	0.016*
HCO_3 (mmol/L)	6.6±5.0	9.8±7.3	5.0±1.9	0.003*
BE (mmol/L)	-24.8±8.5	-18.1±10.4	-28.3±4.5	<0.001*
Sodium (mmol/L)	138±5.8	138±3.4	138±4.0	0.938*

Values are the number of patients (n), percentage, mean, standard deviation and distribution range (minimum-maximum), BE: Base excess, HCO_3: Bicarbonate, *Mann-Whitney U test

analysis, mortality estimates of pH, lactate, anion gap, HCO_3, and BE parameters were all statistically significant. Among the predictive values determined by the area under the curve (AUC), the highest predictive value for mortality was found to be pH [AUC: 0.937, 95% confidence interval (CI) 0.855-0.909, p<0.001] and lactate (AUC: 0.935, 95% CI 0.852-1.000, p<0.001). When the cut-off values determined regarding the predictive power of mortality were examined, it was found that the highest sensitivity and specificity belonged to pH and lactate. When the cut-off value for pH is 6.95, the sensitivity is 85.7%, specificity is 90.9%; When the cut-off value for lactate was taken as 5.27 mmol/L, the sensitivity was 81%, and the specificity was 81.8%.

Discussion

Methanol intoxication can be seen as a collective or individual case. Mass intoxication is seen in countries with high alcohol tax rates that result in the illicit alcohol production. Methyl alcohol intoxications in Turkey generally develop with alcoholic beverages prepared and marketed illegally, and middle-aged men are more frequently affected (10). Gulen et al. (11) reported that 95.5% of the patients with methanol intoxication were male, and the mean age was 48.4±13.1. Çetinkaya et al. (12) reported that 88.8% of the patients were male, and the median age was 38. Although the surviving patients were younger than the deceased patients, no significant difference was observed (12). In our study, all patients were male, and the mean age of the whole population was 41.5±8.8, consistent with the literature. However, the mean age of the discharged group was found to be significantly lower than the dead group.

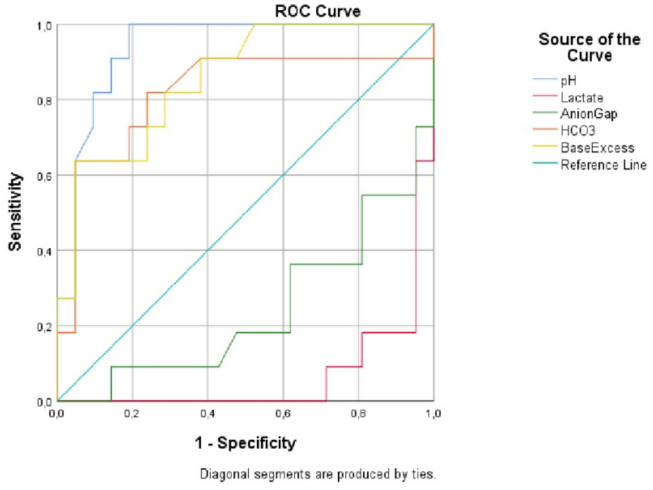

Figure 1. Comparison of blood gas parameters pH, lactate, anion gap, HCO_3, and base excess for predicting mortality

Methyl alcohol reacts enzymatically with alcohol dehydrogenase and turns into its metabolites, formaldehyde, and formic acid. Formic acid causes cellular dysfunction and end-organ damage by inhibiting cytochrome c oxidase in the electron transport chain (13). Clinical signs and symptoms related to methanol poisoning can be seen between 40 minutes and 72 hours, depending on the type of exposure, amount of methanol, and ethanol, the antidote. The diagnosis is made by the patient's and their relatives history, metabolic acidosis with an increased anion gap, increased osmotic gap, and methanol level measurement (14,15). However, methanol levels can only be studied in some centers. Since the methanol level could not be studied in our hospital, the diagnosis was made in the emergency department based on clinical findings, the history of the patient and his relatives, the presence of metabolic acidosis with an increased anion gap, and exclusion from other causes. Kute et al. (16) reported that the most common complaints of patients with methanol intoxication were gastrointestinal complaints (83.5%) and visual disturbances (60.4%). From Turkey, Özkarataş and Yeşilnacar (3) reported the most common complaint at admission as GIS findings, and Babuş et al. (10) and Gulen et al. (11) reported visual complaints. In our study, the most common (37.5%) CNS findings (confusion, coma, seizures, and cerebrovascular events), visual disturbances (34.3%), and GIS irritation findings (15.6%) were found in the patients in the emergency department. However, visual complaints may be in the first place since the visual findings

Table 6. ROC analysis of pH, lactate, anion gap, HCO_3, and base excess values for mortality

	AUC	SD	95% CI	Cut-off	Sensitiviy	Specifity	p
pH	0.937	0.042	0.855-1.000	6.95	0.857	0.909	<0.001
Lactate	0.935	0.042	0.852-1.000	5.27	0.810	0.818	<0.001
Anion gap	0.760	0.093	0.577-0.943	23.2	0.619	0.818	0.017
HCO_3 (mmol/L)	0.818	0.093	0-0.364	5.85	0.810	0.727	0.004
Base excess	0.855	0.068	0.012-0.278	-25.2	0.714	0.818	0.001

AUC: Area under the curve, CI: Confidence interval, HCO_3: Bicarbonate, SD: Standard deviation

could not be evaluated in 46.8% of the patients due to poor general condition. In our study, we could not investigate the effect on the prognosis of the patients because we could not determine the time of arrival to the emergency department as healthy. However, patients present to the emergency department late due to the higher frequency of CNS symptoms.

The basic approach to treating methanol intoxication includes the administration of fomepizole or ethanol to prevent the conversion of methyl alcohol to toxic metabolites, dialysis to remove the formed metabolite and methyl alcohol from the body, or administration of folate, and treatment of severe metabolic acidosis (17). Anion gap>30 mEq^{-1} or base gap<-15 mEq^{-1}, visual disturbances, development of renal failure, and persistent metabolic acidosis (pH<7.25) are indications for emergency hemodialysis after methanol exposure (18). Studies from Turkey have reported that 73% to 100% of patients with methanol intoxication received RRT, 47.7% to 58.1% ethyl alcohol, 48.4% to 64.1% folic acid, and 7.4% fomepizole (3,10,12). Hovda et al. (19) stated that RRT was used in 73% of the patients, and fomepizole was used in 71%. In our study, RRT was applied to 93.7% of the population, ethyl alcohol or fomepizole was applied to 40.6%, and folic acid treatment was applied to 28.1%. The patient's clinical status, the ICU physicians' preferences, and access to the agents used in the treatment were influential in the treatment plan. RRT was not applied to two patients discharged after treatment without severe metabolic acidosis (pH=7.20 and pH=7.23), and ethyl alcohol or fomepizole treatment was applied in addition to supportive treatment. Zakharov et al. (20) applied intermittent hemodialysis and continuous RRT in patients with methanol intoxication and suggested that intermittent hemodialysis is more beneficial than continuous renal replacement therapy. Since we did not have the opportunity to perform intermittent hemodialysis in our ICU, continuous RRT was applied to all patients.

Due to higher tax policies on labeled alcohol products, cheaper methanol has become a cheap and powerful blend of illicit alcohol products. This situation may cause an increase in cases in underdeveloped or developing countries in specific periods. A study from Turkey reported that methanol intoxications are primarily seen in the autumn and winter months. That illegal liquor may have been released via the port at certain times (10). In our study, 87.4% of methanol intoxications were observed in winter and spring.

It has been reported that late admission to the hospital after methyl alcohol intake, seizures, and coma are correlated with mortality (21). In addition, severe metabolic acidosis, severe base deficit, low bicarbonate, hyperglycemia, and respiratory arrest due to unconsciousness indicate a poor prognosis (22). In our study, the effect of early or late admission on mortality could not be evaluated since the time of admission to the emergency department could not be adequately determined. However, considering that the most common findings when patients come to the emergency department are CNS findings and coma, we can say that late admissions are at a high rate, thus worsening the prognosis. In the literature, it has been reported that the GCS score was significantly lower, and the APACHE-2 score was significantly higher in patients who died from methanol intoxication compared to those who survived (12). In our study, the GCS score, which we routinely evaluated during admission to the ICU, was significantly lower, and APACHE-2 scores were significantly higher in the mortality group. However, scoring systems did not find an independent risk factor on mortality. At the same time, considering that the treatment regimens did not differ significantly between the groups, this scoring system at the time of admission to the ICU did not affect the treatment.

Gulen et al. (11) reported that pH<7.07, BE<-31.4, and lactate>2.55 in patients with methanol intoxication were strongly associated with mortality. In our study, very severe metabolic acidosis (pH=6.6) was observed in patients who died, while pH<6.95, BE<-25.2, and lactate>5.27 were found to be strongly associated with mortality. Despite all treatment and efforts, mortality remains high in patients with methanol intoxication. Mortality rates have been reported between 22.2% and 38.8% in the literature (3,10,11,22). In our study, the mortality rate was found to be 65.7%. We think our patients' deep metabolic acidosis and possibly late admission to emergency services may be effective in our high mortality rates.

Study Limitations

The main limitations of our study are its retrospective, single-centered, and low number of cases. Methanol intoxication cases with non-specific diagnoses such as nausea and abdominal pain may have been overlooked. Diagnosis-based searches are done through our hospital's information system and patient files. In addition, the inability to measure methanol levels in our hospital, the fact that it is not known how long after the methanol intake of the patients came to the emergency room and the ICU,

intermittent RRT cannot be performed in our ICU, and the effect of treatment options on the prognosis cannot be investigated due to the lack of specific protocols in the treatment are other limitations of the study.

Conclusion

In our study, high anion gap metabolic acidosis (pH<6.95, BE<-25.2, anion gap>23.2) and high lactate levels (lactate>5.27) were found to be associated with poor outcomes in methanol intoxications, and it is essential to combat metabolic acidosis with aggressive treatment options. Methanol intoxications are an essential public health problem affecting especially the poor in developed and developing countries and require the implementation of effective policies. Despite all advanced treatment methods, high mortality rates can be seen due to late admission to the hospital and delays in diagnosis and treatment. We think that studies on this subject will contribute to the clinical management of patients and improve treatment protocols. Thus sequelae and deaths due to methanol intoxication can be prevented.

Ethics

Ethics Committee Approval: This retrospective cross-sectional study was initiated following the principles of the Declaration of Helsinki after the approval of the Local Ethics Committee of University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital (date: 11.11.2022, number: 211).

Informed Consent: Patients consent form was waived (not required) because the study was a retrospective observational study.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.A., Concept: K.A., A.S.Ş., Design: K.A., A.S.Ş., Data Collection or Processing: K.A., Analysis or Interpretation: K.A., A.S.Ş., Literature Search: K.A., A.S.Ş., Writing: K.A.

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ORIGINAL RESEARCH

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Comparison of the Effectiveness of Ultrasound-guided Transversalis Fascia Plane Block (TFPB) and Transversus Abdominis Plane Block (TAPB) on Postoperative Pain in Caesarean Section: A Prospective Randomized Study

Sezeryan Operasyonlarında Ultrasonografi Eşliğinde Transversalis Fasya Plan Bloğun (TFPB) ve Transversus Abdominis Plan Bloğun (TAPB) Postoperatif Ağrıda Etkinliğinin Karşılaştırılması: Prospektif Randomize Çalışma

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Abstract

Objective: Postoperative peripheral trunk blocks are used for multimodal analgesia in caesarean sections. This trial was planned to compare the efficacy of transversalis fascia plane block (TFPB) and transversus abdominis plane block (TAPB) in postoperative analgesia in patients undergoing caesarean section under spinal anaesthesia.

Method: In this prospective trial, ASA II-III risk group patients between the ages of 20-50 years who were scheduled for elective caesarean section under spinal anaesthesia were evaluated. Demographic data, duration of operation, presence of intraoperative and postoperative nausea & vomiting, pruritus, duration of first analgesia requirement, visual analogue scale (VAS) values for 24 hours postoperatively, paracetamol, diclofenac sodium, the total amount of non-steroidal anti-inflammatory drugs (NSAIDs) used were recorded.

Results: Patients were randomized into two groups: TFPB (75, 50%) and TAPB (75, 50%) groups. There was no significant difference in demographic data, comorbidity, ASA classification and operation times between the two groups (p>0.05). When the duration of the first postoperative analgesia requirement was evaluated, it was higher in the TFPB group (p<0.05). The 24-hour pain scores (VAS 6th hour and

Öz

Amaç: Sezeryanlarda multimodal analjezi amacıyla postoperatif periferik gövde blokları kullanılmaktadır. Bu araştırma spinal anestezi altında sezeryan operasyonu olan hastalarda transversalis fasya plan blok (TFPB) ve transversus abdominis plan bloğunun (TAPB) postoperatif analjezide etkinliğini karşılaştırmak amacıyla planlandı.

Yöntem: Prospektif tasarıma sahip bu araştırmada spinal anestezi altında elektif sezeryan operasyonu planlanan 20-50 yaş aralığında ASA II-III risk grubundaki hastalar değerlendirildi. Demografik verileri, operasyon süreleri, intraoperatif ve postoperatif bulantı & kusma, kaşıntı varlığı, ilk analjezi gereksinim süresi, postoperatif 24 saat boyunca görsel analog ölçeği (VAS) değerleri, parasetamol, diclofenac sodyum, toplam kullanılan Steroid olmayan anti-enflamatuvar ilaçlar (NSAII) miktarı kaydedildi.

Bulgular: Hastalar TFPB (75, %50) ve TAPB (75, %50) grubu olmak üzere iki gruba randomize edildi. İki grup arasında demografik veriler, komorbidite, ASA sınıflaması ve operasyon sürelerinde anlamlı farklılık görülmedi (p>0,05). Hastaların postoperatif ilk analjezi ihtiyaç süreleri değerlendirildiğinde TFPB grubunda daha yüksekti (p<0,05). Yirmi dört saat boyunca ağrı skorları (VAS 6. saat ve vas 12. saat) TFPB grubunda daha düşüktü (p<0,05). Kullanılan parasetamol, diklofenak ve toplam

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Abstract

VAS 12th hour) were lower in the TFPB group (p<0.05). The amounts of paracetamol, diclofenac and total NSAIDs were higher in the TAPB group (p<0.05).

Conclusion: USG-guided bilateral TFPB is more effective than TABP for postoperative analgesia in caesarean sections.

Keywords: Caesarean section, nerve block, obstetrical anesthesia, postoperative pain, spinal anaesthesia

Öz

kullanılan NSAII miktarına bakıldığında ise TAPB grubunda daha fazlaydı (p<0,05).

Sonuç: Sezeryanlarda USG eşliğinde bilateral uygulanan TFPB, postoperatif analjezide TABP'den daha etkindir.

Anahtar kelimeler: Sezaryen, sinir bloğu, spinal anestezi, obstetrik anestezi, postoperatif ağrı

Introduction

Spinal anaesthesia is more frequently preferred in caesareans due to its advantages, such as early postoperative mobilization and pain control. Despite this, patients need postoperative analgesics (1). Pain delays recovery in the mother, may cause depression, disrupts mother-baby bonding, decreases the amount of milk and may even become chronic (2,3). In the enhanced recovery after surgical protocol used for early discharge in caesarean sections, effective pain management is essential and multimodal analgesia is recommended (4). For this purpose, peripheral nerve blocks can be applied to reduce side effects such as constipation, urinary retention, respiratory depression and pruritus due to opioid consumption (5-11). For this purpose, ilioinguinal nerve block after abdominal wall incision, abdominal wall blocks, TFPB, TAPB, quadratus lumborum block, and lumbar erector spinae plane (ESP) block have been tried. Unlike QLB and ESP block, TFPB and TAPB can be applied in the supine position without changing the patient's position. Transversalis fascia plane block (TFPB) and transversus abdominis plane block (TFPB) among peripheral nerve blocks are effective in cesareans. TAPB provides analgesia after caesarean section by targeting the T6-L1 nerve roots involving the anterior abdominal wall and skin (12-14). TFPB blocks the proximal branches of the T12 and L1 nerves between the transversalis abdominal muscle and the transversal fascia (15). Although both blocks block the T12-L1 nerves, TFPB is located more posteriorly than TAPB. That is why we think their activities are different.

In this trial, we aimed to compare the analgesic efficacy of TFPB and TAPB in patients undergoing caesarean section under spinal anaesthesia.

Materials and Methods

This prospective, randomized trial was conducted at University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital by the Declaration of Helsinki. After ethics committee approval (decision no: 2022-74, date: 09.03.2022) and written informed consent was obtained from all patients, the trial was conducted according to consolidated standards of reporting trials guidelines.

Patients aged 20-50 years with ASA II-III and elective caesarean section under spinal anaesthesia were included in the trial. Patients with body mass index (BMI) >40 kg/m^2, bupivacaine allergy, preference for general anaesthesia, coagulopathy and local infection were excluded. Type I error level (alpha level) was set at 0.1, and the number of patients per group was set to at least 70 to achieve 90% statistical power. After accounting for the missing data, a total of 150 patients were divided into two groups using the closed envelope method:

Transversal fascia plane block (TFPB group) and transversus abdominis plane block (TAPB group) (Figure 1). Demographic data (age, weight, height, BMI, comorbidity) and ASA scores were recorded. Patients were taken to the operating room, and routine hemodynamic monitoring with electrocardiography, non-invasive blood pressure

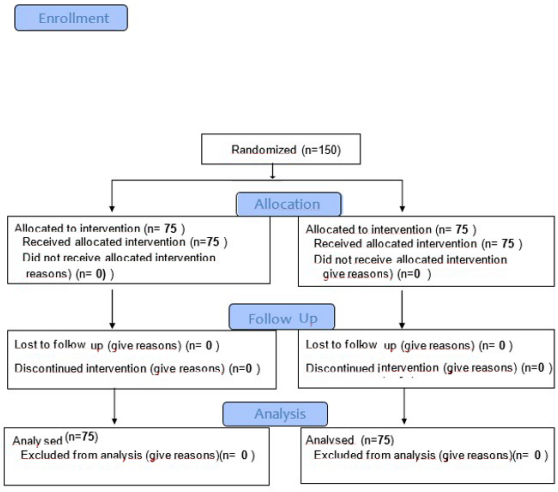

Figure 1. Consort diagram of study

and pulse oximetry (SpO_2) were performed. Peripheral vascular access was established, and intravenous (iv) hydration was initiated. In the sitting position, 10 mg hyperbaric bupivacaine and 20 micrograms fentanyl were administered into the subarachnoid space with a 25 gauge Quincke spinal needle at the L3-L4 or L4-L5 level. The patient was given a supine position with a 15° left inclination. A 20% decrease in systolic blood pressure or less than 90 mmHg was considered hypotension. Patients who developed hypotension received 5-10 mg ephedrine iv, and 250 mL iv bolus crystalloid fluid was given. Those with a peak heart rate below 50/min were considered bradycardic, and 1 mg atropine iv was administered. Ondansetron 4 mg iv for those with nausea and vomiting, increased to 8 mg if necessary. When the sensory block level reached T4 after spinal anaesthesia, surgery was initiated, and the baby was delivered through a horizontal (pfannenstiel) incision just above the pubis. At the end of the surgery, a bilateral block was performed with a 100-120 mm block needle using the in-plane technique under aseptic conditions under USG guidance. 20 mL of 0.25% bupivacaine was applied to the transverse fascia plane between the internal oblique muscle and the transversus abdominis muscle for TAPB and under the fascia where the internal oblique and transversus abdominis muscles meet by visualizing the external-internal oblique and transversus abdominis muscles, quadratus lumborum muscle for TFPB. Sensory block level was evaluated after body blocks. Somatic pain is described as sharp localized Pfannenstiel incision pain. Visceral pain occurs due to uterine contractions, widespread pain is felt in the abdomen.

After the procedure, the patients were followed up for 30 minutes in the recovery unit, and their pain was evaluated with a visual analogue scale (VAS), and VAS was accepted as time 0 (T1). Patients with a modified aldrete score > nine were discharged to the ward. Once on the ward, patients were routinely administered 75 mg diclofenac sodium intramuscularly and 4 mg iv ondansetron in patients with nausea and vomiting. Those with VAS >4 were first given 1 gr paracetamol iv and 75 mg diclofenac sodium iv if the pain did not disappear.

VAS values, time to first analgesic requirement, analgesic requirements, nausea & vomiting and pruritus were evaluated for 24 hours postoperatively [6^{th} hour (T2), 12^{th} hour (T3), 24^{th} hour (T4)].

Statistical Analysis

Analyses were performed using NCSS 11 (Number Cruncher Statistical System, 2017 Statistical Software). In our study, frequency and percentage values were given for the variables. Mean, standard deviation, median, minimum and maximum values were given for continuous variables. The regular distribution test of continuous variables was performed with the Kolmogorov-Smirnov test. Chi-square analysis was used for the relationships between categorical variables. When appropriate, categorical variables were assessed with Fisher's Exact test and Fisher-Freeman-Halton test. An independent sample t-test was used to compare two groups in continuous independent variables with normal distribution. The Mann-Whitney U test was used to compare two independent groups for the variables that did not meet the assumption of normal distribution. For independent variables that did not have a normal distribution, Wilcox's sign-rank test was used to compare the two groups. $P<0.05$ was considered statistically significant.

Results

In the study, a total of 150 patients who underwent caesarean section under spinal anaesthesia were divided into two groups TFPB (75, 50%) and TAPB (75, 50%) (Figure 1). There was no significant difference between the two groups when demographic data, ASA and operation time were evaluated. The mean ages for TFPB and TAPB were (29.2±5.3, and 29.4±5.6) and BMI was (28.5±3.6 29.9±4.2). Comorbidities were similar in both groups ($p>0.05$) (Table 1).

The postoperative VAS values of the patients between the two groups are shown in Figure 2. Since the patients were under spinal anaesthesia, they had no pain at the T1 time point (T1: 0). The median value of VAS at T2 and T3 time points was lower in the TFPB group. 24. VAS values at the hour were similar in both groups (Figure 2).

The duration of the first analgesic requirement was longer in the TFPB group than in the TAPB group (6.67±0.32 hours vs 4.9±0.26 hours, $p<0.01$). When the 24-hour analgesia needs were compared, it was seen that the analgesic need was less in the TFPB group ($p<0.05$). Intraoperative or postoperative nausea & vomiting was similar in both groups (Table 2). No postoperative surgical or block-related complications were observed in any of the patients.

Discussion

The study observed that the initial analgesic requirement duration was longer in the patient group who underwent TFPB for multimodal analgesia in caesarean sections

Table 1. Demographic data, ASA and operation times

	TFPB group	TAPB group	p
Age, year	29.2±5.3	29.4±5.6	0.49
Kilogram, kg	75±10.2	79.4±11.1	0.49
Height, cm	160.8±6.6	161.2±5.6	0.72
BMI	28.5±3.6	29.9±4.2	0.08
Comorbidity			0.29
HT	1 (1.5)	0 (0)	
DM	2 (3)	4 (6)	
Asthma	2 (3)	0 (0)	
Hypothyroid	1 (1.5)	3 (4.5)	
Other	0 (0)	2 (3)	
ASA II/III	72/3	72/3	1
Operation time, minutes	69.5±15.1	82.4±21.8	0.24

p<0.05 shows statistical significance. Categorical variables were shown as numbers (%). Numerical variables with normal distribution were shown as mean § standard deviation.
ASA: American Society of Anaesthesiology, HT: Hypertension, DM: Diabetes mellitus, TFPB: Transversalis fascia plane block, TAPB: Transversus abdominis plane block, BMI: Body mass index

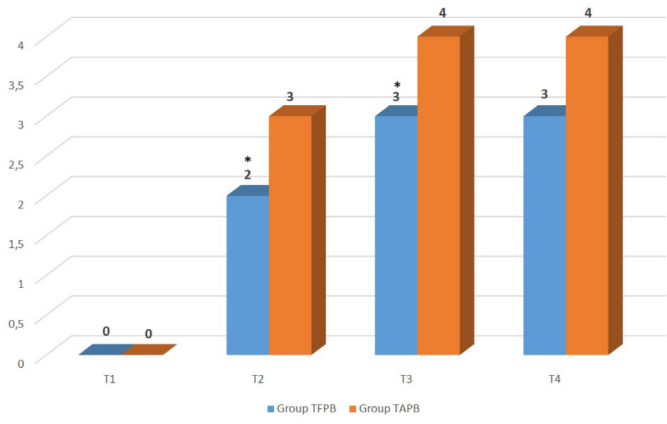

Figure 2. VAS values at different time points

VAS: Visual analogue scale, TFPB: Transversalis fascia plane block, TAPB: Transversus abdominis plane block

compared to TAPB. Patients who underwent TAP block had higher 24-hour VAS values and analgesia needs.

In the caesarean section, postoperative pain due to pfannenstiel incision is caused by somatic and visceral pain involving the peritoneum, uterus and abdominal wall. For this purpose, blockade of the T12 and L1 nerves for somatic pain and non-steroidal analgesics and opioids for visceral pain can be used as part of multimodal analgesia regimens (16,17). Among peripheral body blocks, TFP block is effective in iliac bone graft, caesarean section and inguinal hernia repairs (18-20). Especially in caesarean sections, TFPB application reduces the need for postoperative analgesia (13,21-24). Rahimzadeh et al. (25) also showed that a TAP block performed after a caesarean section decreased morphine consumption and increased patient satisfaction. In another study, TAP block was found to reduce opioid consumption despite inadequate block at T12-L1 after abdominal surgery (24). In a study comparing TAP and TFP block in elective caesarean section, a total

Table 2. Duration of first analgesic requirement and evaluation of analgesics used and side effects

	TFPB group	TAPB group	p
Time of first analgesic requirement, hours	6.67±0.32	4.9±0.26	0.01*
1 g paracetamol need	0.6±0.09	1.5±0.09	0.00*
75 mg diclofenac sodium need	1.3±0.08	1.5±0.06	0.01*
Total number of NSAIs	1.9±0.11	3.1±0.13	0.00*
Nausea & vomiting	2 (2.7)	3 (4)	0.65
Itching	3 (4)	3 (4)	1

*p<0.05 shows statistical significance. Categorical variables were shown as numbers (%). Numerical variables with normal distribution were shown as mean § standard deviation. NSAIs: Non-steroidal anti-inflammatory drugs, TFPB: Transversalis fascia plane block, TAPB: Transversus abdominis plane block

of 15 mL of 0.25% bupivacaine was administered, and postoperative analgesia needs were found to be similar (26).

In this retrospective study by López-González et al. (26), 30 mL of 0.25% bupivacaine was administered for TAP and TFP block in inguinal hernia operations. Postoperative additional analgesia needs were similar in both groups (27). When the literature is reviewed, it is seen that the drugs, doses and volumes administered for TAP and TFP block are different in other studies. Tulgar and Serifsoy (10) applied 20 mL (a mixture of 10 mL bupivacaine 0.5%, 5 mL lidocaine 2% and 5 mL isotonic NaCl) for TFP block in caesarean sections (11). Kanazi et al. (27) administered 20 mL per side containing 0.375% bupivacaine for the TAP block (28). In our study, a total volume of 40 mL was administered as 1 mg/kg bupivacaine. Pain scores were low, and the amount of postoperative analgesia used was less in patients who underwent TFPB compared to TAPB. In both groups, VAS median values were four and below 4 for 24 hours. We think we got better results because of the volume used and the amount of bupivacaine applied.

Postoperative nausea & vomiting was found to be similar in patients who underwent TAP or TFP block in inguinal hernias (27). In the study by Baaj et al. (24), in which TAP block was compared with iv morphine, postoperative nausea & vomiting were observed less in the TAP block group (25). In another study, it was observed that postoperative nausea & vomiting was similar in the patient group treated with intrathecal morphine and the patient group treated with TAP block (29). In our study, the block was applied to avoid opioid consumption for analgesia, and NSAIs were used for analgesia. Therefore, similar results were obtained in both groups.

Study Limitations

Our study has some limitations in addition to its strengths, such as having a prospective design and having the same physician blocking all patients, thus minimizing practice-related differences. These limitations include the single centre, limited time interval for postoperative Evaluation of the patients, application of the block while under the influence of spinal anaesthesia and inability to perform sensory block examination. Although trunk blocks are effective in relieving postoperative pain, their long-term postoperative efficacy is not clear. To increase the power of the results of this block, studies with larger sample sizes, multicenter studies and studies in which continuous analgesia can be provided by catheter placement are needed.

Conclusion

When trunk block was applied for postoperative analgesia in patients undergoing caesarean section, TFPB was more effective on pain than TAPB. In addition, TFPB administration decreased the need for analgesia compared to TAPB. It was observed that both methods were safe in caesarean section operations, and peripheral trunk blocks could be safely preferred for multimodal analgesia, especially for somatic pain. Since only one study in the literature compares the efficacy of TFPB and TAPB in caesarean sections, we think this study will contribute to the literature.

Ethics

Ethics Committee Approval: This prospective, randomized trial was conducted at University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital by the Declaration of Helsinki (decision no: 2022-74, date: 09.03.2022).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: D.A., N.A., F.G.Ö., Design: D.A., N.A., F.G.Ö., Data Collection or Processing: D.A., İ.P., Analysis or Interpretation: D.A., İ.P., Drafting Manuscript: D.A., N.A., F.G.Ö., İ.P., Writing: D.A., N.A., F.G.Ö., İ.P., Critical Revision of Manuscript: D.A., N.A., Final Approval and Accountability: D.A., N.A., F.G.Ö., İ.P., Technical or Material Support: D.A., İ.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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The Role of Hematological Parameters in the Diagnosis of Childhood Allergic Conjunctivitis

Çocukluk Çağında Allerjik Konjunktivitin Tanısında Hematolojik Parametrelerin Rolü

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Abstract

Objective: We aimed to investigate the parameters of complete blood count and the levels of systemic inflammatory biomarkers in children with allergic conjunctivit and to evaluate their role in diagnosis in this study.

Method: We included 71 pediatric patients with allergic conjunctivit diagnosis referred from the ophthalmology outpatient clinics who had sensitivity to at least one allergen and 71 age- and sex-matched healthy controls and compared complete blood count results, immunoglobulin E (IgE), neutrophil/lymphocyte, and platelet/lymphocyte ratios and systemic immune-inflammation index results. We built a multivariate model with correlated results.

Results: Eosinophil counts and serum total IgE values were significantly higher in the patient group compared to the control group (p<0.001). Other parameters were not statistically different. 70.4% (n=50) of the patients had seasonal allergic conjunctivit, and 29.6% (n=21) had perennial allergic conjunctivit. In the skin prick tests performed in the patient group, 60.6% (n=43) of the patients had pollen, 54.9% (n=39) mite, 12.7% (n=9) dander, 11.3% (n=8) cockroach, and 4.2% (n=3) had alternaria sensitivities. In the multivariate analysis, every 100-cell increase in eosinophil count increased the hazard ratio of allergic conjunctivitis 1.3 times (95% confidence interval: 1.1-1.5), and every 100-units increase in total IgE levels increased 1.2 times (95% confidence interval: 1.1-1.5).

Conclusion: We found no significant relationship between neutrophil/lymphocyte and platelet/lymphocyte ratios, and SII with allergic conjunctivit. Increasing eosinophil count and serum total IgE levels increase the hazard ratio for developing allergic conjunctivit. Pollen sensitivity was the most common factor in the skin test in allergic conjunctivit-diagnosed patients.

Keywords: Allergic conjunctivitis, inflammation, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic immune inflammation index

Öz

Amaç: Bu çalışmada allerjik konjonktiviti olan çocuklarda tam kan sayımı parametrelerini ve sistemik enflamatuvar biyobelirteç düzeylerini araştırmayı ve tanıdaki rollerini değerlendirmeyi amaçladık.

Yöntem: Göz polikliniklerinden başvuran ve en az bir alerjene duyarlılığı olan allerjik konjonktivit tanılı 71 çocuk hasta ile yaş ve cinsiyet uyumlu 71 sağlıklı kontrol alındı ve tam kan sayımı sonuçları, immünoglobulin E (IgE), nötrofil/lenfosit ve trombosit/lenfosit oranları ve sistemik immün-enflamasyon indeksi sonuçları karşılaştırıldı. Anlamlı korelasyon saptanan değerlerle çok değişkenli model oluşturuldu.

Bulgular: Hasta grubunda eozinofil sayısı ve serum total IgE değerleri kontrol grubuna göre anlamlı olarak yüksekti (p<0,001). Diğer parametreler açısından istatistiksel olarak anlamlı bir fark saptanmadı. Hastaların %70,4'ünde (n=50) mevsimsel, %29,6'sında (n=21) perennial allerjik konjonktivit vardı. Hasta grubunda yapılan deri delme testlerinde hastaların %60,6'sında (n=43) polen, %54,9'unda (n=39) akar, %12,7'sinde (n=9) kepek, %11,3'ünde (n=8) hamamböceği ve %4,2'sinde (n=3) alternaria duyarlılığı vardı. Multivariate analizde, eozinofil sayısındaki her 100 birim artış, allerjik konjonktivit oranını 1,3 kat (%95 güven aralığı: 1,1-1,5) ve toplam IgE seviyelerindeki her 100 birimlik artış 1,2 kat (%95 güven aralığı: 1,1-1,5) artırdı.

Sonuç: Nötrofil/lenfosit, trombosit/lenfosit oranları ve SII ile alerjik konjonktivit arasında anlamlı bir ilişki bulunamadı. Ancak eozinofil sayısı ve serum total IgE düzeylerindeki yükseklik ile alerjik konjonktivit arasında ilişkili olduğu saptandı. Alerjik konjonktivit tanısı konan hastalarda deri testinde saptanan en yaygın etken polen duyarlılığıydı.

Anahtar kelimeler: Alerjik konjonktivit, enflamasyon, nötrofil/lenfosit oranı, trombosit/lenfosit oranı, sistemik immün-enflamasyon indeksi

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Introduction

Allergic conjunctivitis (AC) progresses with symptoms such as eye itching, watering, redness, and eyelids edema (1). Although AC is a frequently encountered disorder, many ocular diseases with overlapping clinics in their differential diagnosis create difficulties in the diagnosis phase. The classification of different forms of ocular allergy was recently revised by the European Academy of Allergy and Clinical Immunology (2). The conjunctival allergy forms with an immunoglobulin E (IgE)-mediated reaction, including benign seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC), as well as severe vernal keratoconjunctivitis and atopic keratoconjunctivitis involving the cornea (2,3). The most common type is SAC among AC, and PAC is the second most common (1). The frequency of AC has been increasing in recent years. There is no single reason for this increase, but many genetic/environmental factors, such as atopic susceptibility/family history, air pollution, and allergen exposure in early childhood, play a role (4). Although epidemiological studies are limited, it affects up to 25% of European children (3) and 28% of Chinese children (5).

In AC, the clinical picture develops with an IgE-mediated reaction against an allergen (1). As a result of the binding of the allergen to specific IgE, mast cells in the conjunctiva degranulate. In addition to mast cells, eosinophils, and Th2 lymphocytes play an important role in the inflammatory response that occurs in this process (3). In addition, neutrophils and platelets are blood parameters that have important functions in the inflammatory process. The easy accessibility of these blood parameters in today's conditions allows them to be used in diagnosing and following-up on many diseases. Studies have shown that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (TLR), and systemic immune-inflammation index (SII) parameters obtained from complete blood count parameters have prognostic importance in cardiovascular diseases, chronic inflammatory diseases, and various malignancies and can be used as inflammatory markers (6-8).

Studies suggest that hemogram parameters are important in allergic diseases such as asthma, atopic dermatitis, and allergic rhinitis diagnosis and follow-up (9-11); however, studies on the use of these parameters in the diagnosis and follow-up of AC are limited (12,13). We aimed to investigate the parameters of complete blood count and the levels of systemic inflammatory biomarkers in children with AC and to evaluate their role in diagnosis in this study.

Materials and Methods

We included 71 pediatric patients referred to the pediatric allergy clinic from the ophthalmology outpatient clinics with AC diagnosis between March 2022 and May 2023 who had sensitivity to at least one allergen and 71 age- and sex-matched healthy controls. We retrospectively analyzed the complete blood count parameters, serum total IgE levels, and skin prick test results of the cases during active complaints and evaluated neutrophil, lymphocyte, eosinophil, erythrocyte, leukocyte, and platelet counts, and mean platelet volume, and hemoglobin and serum total IgE levels. We calculated NLR and PLR values by dividing the neutrophil and platelet counts by the absolute lymphocyte counts, respectively, and SII using the (neutrophil×platelet)/lymphocyte formula.

Patients whose skin prick tests showed sensitivity and developed symptoms such as itching, watering, burning, redness, and eye rubbing after exposure to these aeroallergens were defined as SAC, and patients with persistent symptoms throughout the year as PAC. Patients who received systemic or ocular/topical treatment for any reason (including AC), had systemic/ocular acute or chronic disease (including vernal keratoconjunctivitis, giant papillary conjunctivitis, allergic rhinitis, asthma, atopic dermatitis) other than AC, and had signs of active infection excluded from the study. We obtained the study approval from University of Health Sciences Turkey, Dr. Lütfi Kırdar City Hospital Ethics Committee (date: 29.03.2023, number: 2023/514/246/22) and conducted the study in adherence to the Helsinki criteria. In the skin prick test, skin reactions of 3 mm or more from the negative control at the 15th minute after application with standardized inhaled allergens were considered positive.

Statistical Analysis

We analyzed the data with JAMOVI 2.3.18 statistical package program. Values are expressed as mean ± standard deviation for presentation. Statistical comparisons were performed using the Student's t-test for parametric continuous variables, the Mann-Whitney U test for non-parametric continuous variables, and the chi-square test for categorical variables. We used a generalized linear model (GLM) for multivariate analysis with skewed data and assessed significant confounding factors ($p<0.01$ considered for significance) with the stepwise method. A type 1 error for $p<0.05$ was considered for statistical significance.

Results

We included 71 AC patients (36 females and 35 males) and 71 healthy controls (37 females and 34 males), and the mean ages of the patient and control groups were 11.3±3.7 years and 10.9±3.9 years, respectively, with no statistical differences either for gender and age (p=0.740, chi-square test, and p=0.396, Mann-Whitney U test, respectively). There was no statistical difference between the patient and control groups by hemoglobin, mean platelet volume and white blood cell, red blood cell, lymphocyte, neutrophil, and thrombocyte counts, and NLR, TLR, and SII values (p>0.05). Eosinophil counts and serum total IgE values were significantly higher in the patient group compared to the control group (p<0.001) (Table 1). A total of 70.4% (n=50) of the patients had SAC, and 29.6% (n=21) had PAC diagnosis. In the skin prick tests performed in the patient group, 60.6% (n=43) of the patients had pollen, 54.9% (n=39) mite, 12.7% (n=9) dander, 11.3% (n=8) cockroach, and 4.2% (n=3) had alternaria sensitivities.

Eosinophil count and total IgE had significant correlations with the patient group but there was no significant correlation by other laboratory parameters (Table 2).

We created a multiple regression model using laboratory parameters (eosinophils and total IgE) as possible confounders. Every 100-cell increase in eosinophil count increased the risk of AC (hazard ratio) 1.3 times (95% confidence interval: 1.1-1.5), and every 100-units increase in total IgE levels increased 1.2 times (95% confidence interval: 1.1-1.5) (GLM, R^2: 0.225). The related graph and the estimated marginal means table are presented below (Figure 1, Table 3).

Table 1. Comparison of laboratory parameters between the patient and the control group

	Control (n=71)	Patients (n=71)	p
White blood cell count (10^3/u L)	9.01±3.0	9.13±2.7	0.527*
Hemoglobin (g/dL)	12.8±1.3	12.6±0.9	0.608*
Red blood cell count (10^6/u L)	4.78±0.38	4.7±0.31	0.443**
Neutrophil count (10^3/u L)	4.8±2.5	4.4±2.2	0.388*
Lymphocyte count (10^3/u L)	3.2±1.2	3.5±1.1	0.056*
Eosinophil count (10^3/u L)	0.22±0.15	0.53±0.65	**<0.001***
Platelet counts (10^3/u L)	359.9±106.9	350.6±67.1	0.652*
Mean platelet volume (fL)	9.7±1.4	9.8±0.8	0.945*
Serum total IgE (kIU/L)	101±260	973±2.049	**<0.001***
Neutrophil/lymphocyte ratio	1.67±0.97	1.41±0.94	0.072*
Platelet/lymphocyte ratio	120±38	113±48	0.073*
Systemic immune-inflammation index	590±378	494±331	0.123*

*Mann-Whitney U test, **Student's t-test, IgE: Immunoglobulin E

Table 2. Laboratory correlations between the patient and the control group

Parameter	Kendall's tau b
White blood cell count (10^3/u L)	0.044
Hemoglobin (g/dL)	0.036
Red blood cell count (10^6/u L)	0.038
Neutrophil count (10^3/u L)	0.060
Lymphocyte count (10^3/u L)	0.133
Eosinophil count (10^3/u L)	0.280***
Platelet counts (10^3/u L)	0.031
Mean platelet volume (fL)	0.005
Serum total IgE (kIU/L)	0.427***
Neutrophil/lymphocyte ratio	0.124
Platelet/lymphocyte ratio	0.124
Systemic immune-inflammation index	0.107

***p<0.001, IgE: Immunoglobulin E

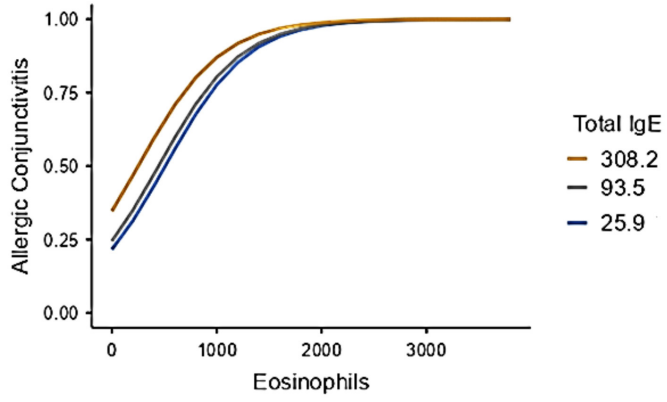

Figure 1. Eosinophil count and total IgE correlations with allergic conjunctivitis

IgE: Immunoglobulin E

Table 3. Estimated marginal means table for eosinophil count and total IgE correlations with allergic conjunctivitis

	Mean allergic conjunktivitis possibility (95%confidence interval)
Eosinophil count	
130/(10^3/u L)	55.5% (33.9-75.2)
230/(10^3/u L)	61.7% (41.9-78.2)
450/(10^3/u L)	73.8% (56.3-86.0)
Total IgE level	
25.9 kIU/L	41.8% (30.4-54.2)
93.5 kIU/L	45.7% (34.8-56.9)
308.2 kIU/L	58.0% (45.8-69.3)

R^2: 0.225, IgE: Immunoglobulin E

Discussion

The incidence of allergic diseases in childhood increases significantly, and AC is one of the most common ocular diseases in clinical practice (14). AC is divided into SAC, where symptoms occur seasonally, and PAC, where symptoms persist throughout the year (15,16). Cellular reactions, mediators, and immunological events that play a role in the pathogenesis of AC have begun to be better understood (17,18). A study stated that eosinophils are the main effective cells in AC, and their interaction between cells through physiologically active substances (for example, histamine and leukotriene), cytokines, and chemokines is influential (15). Also, innate immunity contributes to this reaction with kerato-conjunctival cells, which play a role in the etiology through chemokine production (15).

The relationship between NLR and PLR in childhood and various inflammatory diseases has been shown in many studies (19,20). Studies also emphasized that NLR and PLR can be used as markers of inflammation in many allergic diseases, such as allergic rhinitis, asthma, and atopic dermatitis (9,21,22). Faria et al. (23) showed that NLR is closely related to ocular pathologies such as macular degeneration, glaucoma, and retinal vascular diseases.

A study conducted with 26 patients and 31 healthy control in Turkey compared hemogram parameters and systemic inflammatory markers and did not find a significant difference in results between groups in this study, and high NLR, PLR, and SII levels did not have an association with AC in the pediatric age group, similar to our study (13). Also, Kurtul et al. (12) reported no significant difference between SAC-diagnosed patients and controls in terms of NLR rates. In our study, while eosinophil counts were statistically significantly higher in the patient group than in the control group, the results of other hemogram parameters and systemic inflammatory markers did not differ. We think the low number of patients and mild allergic symptoms in most cases were effective in these results.

Although AC is a clinical diagnosis, laboratory tests support the diagnosis. Cytological examination, skin prick tests, and serum total IgE antibody detection are important in AC diagnosis (24). IgE plays a role in allergic diseases like in many immunological diseases (25,26). In many studies conducted on patients with AC, serum total Ig E levels were elevated, consistent with our results (12,27). In addition, in the multiple regression model, every 100-unit increase in total IgE levels increased the hazard ratio of AC by 1.2 times. Also, studies reported that pollen sensitivity was the most common cause of skin tests in patients with AC, consistent with our result (15,28).

Study Limitations

The limitations of our study were its retrospective and single-centered design and the small number of patients.

Conclusion

We did not find a significant relationship between NLR, PLR, and SII levels between AC and the control group in the pediatric age. Multicenter, prospective and longitudinal studies are needed to evaluate this topic. In addition, increasing eosinophil count and serum total IgE levels increase the hazard ratio of developing AC, and pollen sensitivity was the most common factor in the skin test in AC-diagnosed patients.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital on March 29, 2023 with the decision number 2023/514/246/22.

Informed Consent: Not necessary.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.Ç., M.T.K., Design: F.Ç., M.T.K., Data Collection or Processing: M.T.K., İ.K., Analysis or Interpretation: F.Ç., İ.K., Writing: F.Ç., M.T.K., İ.K., Drafting Manuscript: F.Ç., M.T.K., Critical Revision of Manuscript: F.Ç., M.T.K., İ.K., Final Approval and Accountability: F.Ç., M.T.K., İ.K., Technical or Material Support: F.Ç., M.T.K., Supervision: F.Ç., M.T.K., İ.K.

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ORIGINAL RESEARCH

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The Effect of Early Diuretic Treatment on Clinical Outcomes in Patients with Acute Heart Failure: Door to Diuretic

Akut Kalp Yetmezliği Hastalarında Erken Diüretik Uygulamasının Klinik Sonlanımlara Etkisi: Kapı Diüretik Zamanı

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Abstract

Objective: It was aimed to investigate the effect of early diuretic treatment on hospitalization and short-term mortality in patients with acute heart failure.

Method: Our study was carried out as a retrospective, single-centered, observational study in the department of emergency a tertiary training and research hospital. The study population was the patients presenting with signs and symptoms of acute heart failure. The primary outcome was all-cause 30-day mortality and hospitalization. Univariant tests and ROC analysis were used for analysis.

Results: A total of 325 patients were included. The median age of the patients was 76.0 years (interquartile range 69.0-83.0). The mortality rate of our study population was %14.4 (47). Systolic blood pressure and diastolic blood pressure were significantly higher in the survivor group (p=0.018, 0.033, respectively). Age, troponin-I, and pro-brain natriuretic peptide were significantly higher in the non-survivor group (p<0.001, <0.001, <0.001, respectively). For hospitalization, the area under the curve for the high door to diuretic time was 0.570, the cut-off value was 99 minutes, and the odds ratio was 1.75 (95% confidence interval: 1.09-2.82).

Conclusion: Early initiation of diuretic treatment has no effect on short-term mortality. However, delayed initiation of diuretic treatment may affect hospitalization rates. According to our results, early initiation of diuretic treatment may reduce hospitalization rates.

Keywords: Acute disease, diuretics, emergency service, heart failure, time-to-treatment

Öz

Amaç: Akut kalp yetmezliği hastalarında erken diüretik uygulamasının hastane yatışına ve kısa dönem mortaliteye etkisini araştırmak amaçlanmıştır.

Yöntem: Çalışmamız retrospektif, tek merkezli, gözlemsel çalışma olarak üçüncü basamak eğitim araştırma hastanesinin acil servisinde gerçekleştirildi. Çalışma popülasyonu, akut kalp yetmezliği belirtileri ve semptomları ile başvuran hastalardı. Demografi, yaşamsal parametreler ve laboratuvar parametreleri kaydedildi. Birincil sonlanım tüm nedenler bağlı 30 günlük mortalite ve hastane yatışıydı. Analiz için tek değişkenli testler ve ROC kullanıldı.

Bulgular: Çalışmaya 325 hasta dahil edildi. Hastaların ortanca yaşı 76,0 (çeyrekler arası aralık 69,0-83,0) idi. Çalışma popülasyonumuzun ölüm oranı %12 idi. Sistolik kan basıncı ve diyastolik kan basıncı yaşayanlarda anlamlı yüksekti (p=0,018, 0,033). Yaş, troponin I ve pro-beyin natriüretik peptidi ölenlerde anlamlı yüksekti (p-değeri sırası ile, <0,001 ve <0,001, <0,001). Hastane yatışı için yüksek kapı diüretik zamanı eğri altında kalan alan 0,570, kesme değeri 99 dakika ve olasılık oranı 1,75 (%95 güven aralığı: 1,09-2,82) olarak hesaplandı.

Sonuç: Diüretik tedavinin erken başlanmasının kısa dönem mortaliteye etkisi yoktur. Bununla birlikte geciken diüretik tedavisi hastane yatış oranlarını etkileyebilmektedir. Sonuçlarımıza göre erken diüretik tedavi başlanması hastaneye yatış oranlarını azaltabilir.

Anahtar kelimeler: Acil servis, akut hastalık, diüretikler, kalp yetmezliği, tedaviye kalan süre

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Introduction

Heart failure (HF) is a clinical syndrome that includes complex diseases. Its incidence is expected to increase in the coming years (1). Advanced age is one of the risk factors (2). The most common causes are ischemic heart disease, valvular diseases and hypertension. It is estimated that there are more than 64 million patients with HF worldwide (3). The prognosis of HF is not promising (4). The mortality rate in the first five years approaches 50% (5). Acute heart failure (AHF) is the rapid onset or sudden deterioration of HF symptoms. It is a life-threatening condition with high morbidity and mortality rates. Emergency departments are where the treatment of AHF begins. It is recommended to use international guidelines in the treatment of these patients (6). Effective treatment of symptomatic HF patients also reduces clinical outcomes, quality of life and health expenditures (7).

Despite the development of new medical treatments for many diseases, the management of AHF has not changed significantly for decades. Most drug trials did not show a positive prognostic effect (8). Intravenous (IV) diuretics treatment is the main therapy in the management of AHF. A significant relationship between IV furosemide and in-hospital mortality was demonstrated in studies (9). Door to diuretic treatment in AHF patients is a controversial issue to researchers (10). In this study, it was aimed to evaluate the effect of early diuretic treatment short-term mortality and hospitalization in AHF patients in the emergency department.

Materials and Methods

This was a retrospective, single-centered and observational study. It was carried out in the 655-bed tertiary care Clinic of Emergency University of Health Sciences Turkey, Ümraniye Training and Research Hospital.

Our study population included patients who had signs and symptoms of AHF between January 1, 2019, and January 1, 2020. These symptoms and signs were dyspnea, effort dyspnea, chest pain, fatigue, weakness, edema in the lower extremities, orthopnea, and intra-abdominal ascites. The patients were diagnosed with HF as a result of the evaluation made by the emergency cardiologist or there had been definitive diagnosis of HF within the last 6 months. All patients had a B-type natriuretic peptide higher than normal values. Patients under 18 years of age and those with missing data or unknown mortality status were excluded.

Patient data were scanned from the hospital computer-based data system. Demographic characteristics, comorbidities, laboratory parameters, systolic and diastolic blood pressure, oxygen saturation and pulse values, and hospital stay were recorded. From laboratory parameters; white blood cell count, neutrophil count, lymphocyte count, hemoglobin, hematocrit, platelet count, potassium, mean platelet volume, sodium, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, C-reactive protein/albumin ratio, blood urea nitrogen/albumin ratio, troponin and pro-BNP recorded. All-cause mortality within 30 days of the patients was recorded using the national death notification system.

Approval for the study was obtained from the Local Ethics Committee of University of Health Sciences Turkey, Ümraniye Training and Research Hospital (no: 426, date: 14/01/2021).

Statistical Analysis

The Jamovi (Version 1.6.21.0; The Jamovi Project, 2020; R Core Team, 2019) was used for statistical analyses. The Shapiro-Wilk test was used in the analysis of normality of data. Categorical data were presented as numbers (%) and compared with the chi-square test. Quantitative variables were presented as median and interquartile range (IQR) (25^{th}-75^{th} percentile) values and then compared for normality of distribution for the two groups using the Mann-Whitney U test or Student's t-test. Receiver operating characteristic (ROC) curves were used to determine the predictive power of door diuretic time in predicting hospitalization, and the results were reported as area under the curve (AUC) values. The optimal cut-off value for the parameters with the highest sensitivity and specificity was determined using the Youden index. Odds ratios and 95% confidence intervals of the groups were calculated according to the cut-off value. For p-values, values less than 0.05 were considered statistically significant.

Results

During the study period, a total of 426 patients were recorded in the emergency department with signs and symptoms of AHF. The excluded were 101 patients. As a result, 325 patients were ultimately included.

The median age of the patients was 76.0 (IQR 69.0-83.0). Male were 155 (47.7%). All causes mortality within 30 days were 47 (14.4%). The number of patients who were hospitalized was 138 (42%). The basic characteristics of the survivors and non-survivors are shown in Table 1. Systolic blood

pressure and diastolic blood pressure were significantly higher in the survivor group (p=0.018, 0.033). Age, troponin I, and pro-BNP were significantly higher in non-survivor group (p<0.001, <0.001, <0.001, respectively). There was no significant relationship between door to diuretic treatment and short-term mortality (p=0.539). Hemoglobin and hematocrits values were significantly higher in discharged group (p=0.016, 0.012 respectively). Mortality rate was found to be significantly higher in hospitalized patients 31 (22.5%) (p=0.001). Door to diuretic treatment in hospitalized patients was 62.5 (30.0-149.2) minutes. This value was significantly higher than discharged group 40.0 (22.0-111.0) (p=0.033). The left ventricular ejection fraction (LVEF) was higher in hospitalized than in discharged (p=0.013).

Table 1. Baseline characteristics of the study population and comparison between survivor and non-survivors groups

Parameters	Total n=325	Survivors n=278 (85.6%)	Non- survivors n=47 (14.4%)	p
	n (%)/median (25.-75. percentage)	n (%)/median (25.-75. percentage)	n (%)/median (25.-75. percentage)	
Age	76.0 (69.0-83.0)	76.0 (68.2-82.0)	82.0 (75.5-87.0)	<0.001
<65	52 (16.0)	51 (18.3)	1 (2.1)	0.01
≥65	273 (84.0)	227 (81.7)	46 (97.9)	
Sex				
Female (%)	28 (47.5)	21 (42.9)	7 (70.0)	0.223
Male (%)	31 (52.5)	28 (57.1)	3 (30.0)	
Comorbidities				
Chronic obstructive pulmonary disease (%)	77 (23.7)	67 (24.1)	10 (21.3)	0.814
Hypertension (%)	141 (43.4)	123 (44.2)	18 (38.3)	0.547
Diabetes mellitus (%)	110 (33.8)	97 (34.9)	13 (27.7)	0.422
Coronary artery disease (%)	70 (21.5)	62 (22.3)	8 (17.0)	0.533
Heart failure disease (%)	193 (59.4)	167 (60.1)	26 (55.3)	0.651
Chronic kidney disease (%)	68 (20.9)	59 (21.2)	9 (19.1)	0.897
Malignity (%)	10 (3.1)	8 (2.9)	2 (4.3)	0.961
Diuretic use (%)	151 (46.5)	132 (47.5)	19 (40.4)	0.460
Vital parameters				
Systolic blood pressure (mm/hg)	142.5 (122.0-170.0)	144.0 (124.0-170.0)	131.0 (110.0-150.0)	0.018
Diastolic blood pressure (mm/hg)	80.0 (68.0-95.0)	80.0 (70.0-95.5)	70.0 (65.0-90.0)	0.033
Oxygen saturation (%)	92.0 (85.2-95.0)	92.0 (86.0-95.0)	92.0 (85.0-94.0)	0.543
Laboratory parameters				
White blood cell count (10^3/μL)	9.2 (7.0-12.2)	9.1 (6.9-12.0)	10.1 (7.7-13.6)	0.142
Neutrophil count (10^3/μL)	6.8 (5.0-9.0)	6.7 (4.9-8.8)	7.4 (5.2-10.9)	0.092
Lymphocyte count (10^3/μL)	1.4 (0.9-2.1)	1.4 (1.0-2.1)	1.3 (0.8-2.4)	0.52
Hemoglobin (g/dL)	11.1 (9.8-12.6)	11.1 (9.8-12.6)	11.0 (9.9-12.6)	0.865
Hematocrit (%)	35.5 (31.2-40.0)	35.5 (31.2-40.0)	35.1 (31.1-39.8)	0.83
Mean platelet volume (fL)	88.2 (82.6-92.2)	88.1 (82.6-91.8)	88.5 (82.6-92.8)	0.553
Blood urea nitrogen (mg/dL)	64.2 (47.1-101.1)	62.1 (47.1-94.2)	96.3 (59.9-127.3)	0.001
C-reactive protein (mg/dL)	1.8 (0.5-4.7)	1.6 (0.5-4.4)	3.2 (0.7-9.5)	0.021
Albumin (g/dL)	3.5 (3.2-3.7)	3.5 (3.2-3.7)	3.5 (3.1-3.8)	0.923
Creatinine (mg/dL)	1.3 (1.0-1.9)	1.6 (1.1- 2.5)	1.3 (1.0-2.0)	0.03
Sodium (mEq/L)	138.0 (135.0-140.0)	138.0 (136.0-140.0)	137.5 (135.0-140.0)	0.295
Potassium (mmol/L)	4.8 (4.4-5.3)	4.8 (4.5-5.3)	4.7 (4.3-5.4)	0.756
Troponin I (μg/L)	0.0 (0.0-0.1)	0.0 (0.0-0.1)	0.1 (0.0-0.2)	<0.001
Brain natriuretic peptide (pg/mL)	1170.8 (760.3-2027.5)	1078.2 (732.0-1821.5)	1858.7 (1376.1-2844.6)	<0.001
Left ventricular ejection fraction (%)	45.0 (30.0-55.0)	45.0 (30.0-55.0)	40.0 (30.0-50.0)	0.567
Door to treatment (min.)	46.0 (24.0-120.0)	48.0 (23.0-122.2)	40.0 (27.0-117.5)	0.539

Comparison of all parameters between hospitalized and discharged is given in Table 2. According to the ROC analysis result of door to diuretic treatment predicting hospitalization, AUC was 0.570, cut-off was 99 minutes, Sensitivity was 37.48%, specificity was 74.33%, positive likelihood ratio was 52%, and negative likelihood ratio was 61.78%. Door to diuretic treatment cut-off values and odds ratios of mortality and hospitalization are given in Table 3. A model consisting of door to treatment duration, LVEF, C-reactive protein, creatinine, brain natriuretic peptide and albumin can predict hospitalization with 85% specificity and 54% sensitivity. Logistic regression analysis

Table 2. Comparison of all parameters between hospitalized and discharged patients

Parameters	Discharged n=187 (58%)	Hospitalized n=138 (42%)	p
	n (%)/median (25.-75. percentage)	n (%)/median (25.-75 percentage)	
Age	76.0 (69.0-82.0)	77.0 (69.0-85.0)	0.191
<65	30 (16.0)	22 (15.9)	0.999
≥65	157 (84.0)	116 (84.1)	
Sex			
Female (%)	95 (50.8)	75 (54.3)	0.603
Male (%)	92 (49.2)	63 (45.7)	
Comorbidities			
Chronic obstructive pulmonary disease (%)	48 (25.7)	29 (21.0)	0.399
Hypertension (%)	74 (39.6)	67 (48.6)	0.133
Diabetes mellitus (%)	55 (29.4)	55 (39.9)	0.065
Coronary artery disease (%)	37 (19.8)	33 (23.9)	0.448
Heart failure disease (%)	104 (55.6)	89 (64.5)	0.135
Chronic kidney disease (%)	32 (17.1)	36 (26.1)	0.068
Malignity (%)	6 (3.2)	4 (2.9)	1.000
Vital parameters			
Systolic blood pressure (mm/hg)	140.0 (123.8-164.2)	145.0 (120.0-171.0)	0.502
Diastolic blood pressure (mm/hg)	80.0 (70.0-95.0)	78.0 (65.0-95.2)	0.328
Oxygen saturation (%)	92.0 (87.0-95.0)	90.0 (85.0-95.0)	0.191
Laboratory parameters			
White blood cell count (10^3/μL)	9.0 (7.0-11.3)	9.9 (7.1-13.1)	0.127
Neutrophil count (10^3/μL)	6.7 (4.9-8.5)	7.0 (5.1-9.9)	0.169
Lymphocyte count (10^3/μL)	1.4 (1.0-2.0)	1.4 (0.8-2.3)	0.464
Hemoglobin (g/dL)	11.4 (10.1-12.9)	10.8 (9.4-12.1)	0.016
Hematocrit (%)	36.3 (32.8-40.8)	34.2 (29.8-39.0)	0.012
Mean platelet volume (fL)	87.5 (82.5-91.6)	88.5 (83.5-92.7)	0.277
Blood urea nitrogen (mg/dL)	57.8 (43.9-89.9)	79.2 (53.5-119.8)	<0.001
C-reactive protein (mg/dL)	1.4 (0.5-3.5)	2.3 (0.7-5.9)	0.022
Albumin (g/dL)	3.6 (3.4-3.9)	3.3 (3.1-3.6)	0.002
Creatinine (mg/dL)	1.2 (1.0-1.6)	1.6 (1.1-2.6)	<0.001
Sodium (mEq/L)	138.0 (136.0-141.0)	138.0 (135.0-140.0)	0.112
Potassium (mmol/L)	4.7 (4.3-5.2)	5.0 (4.6-5.5)	0.002
Troponin I (μg/L)	0.0 (0.0-0.1)	0.0 (0.0-0.1)	0.056
Brain natriuretic peptide (pg/mL)	1011.3 (735.8-1779.9)	1484.2 (855.1-2486.3)	0.001
Left ventricular ejection fraction (%)	40.0 (30.0-55.0)	45.0 (35.0-55.0)	0.013
Door to treatment (min)	40.0 (22.0-111.0)	62.5 (30.0-149.2)	0.033
Diuretic use (%)	80 (42.8)	71 (51.4)	0.151
Mortality (%)	16 (8.6)	31 (22.5)	0.001

of independent parameters for predicting hospitalization are presented in Table 4. The ROC curve of parameters and model is shown in Figure 1.

Discussion

We performed this study on 325 HF patients and there was no significant relationship between door to diuretic treatment and short-term mortality. Yet the delay in door to diuretic treatment increased hospitalization rates.

Diuretics is the basis of AHF treatment. Early and rapid treatment in the emergency department is an important step in the management (11). Many studies have confirmed the positive effect of early treatment on the prognosis of patients, and the delay has shown a significant increase in the risk of in-hospital mortality (10). In a retrospective study of more than 700 cases, early IV furosemide treatment was shown to reduce hospital stay (9). A prospective study involving 20 hospitals showed that an increase in door to furosemide treatment time increased the risk of mortality up to the first 100 minutes, and this effect was not seen thereafter. In the same study, early treatment of AHF patients with IV furosemide was independently associated with a reduction in in-hospital mortality (10). On the other hand, by Park et al. (12) concluded that door to diuretic treatment time had no effect on in-hospital, one-month and

Table 3. Door to diuretic treatment cut-off values and odds ratios of mortality and hospitalization

	Cut-off values	Odds ratios	95% confidence intervals	p
Mortality (n=47)	13 min	2.69	1.05-6.89	0.062
Hospitalized (n=138)	99 min	1.75	1.09-2.82	**0.020**

Table 4. Logistic regression analysis of independent parameters for predicting hospitalization.

			95% confidence intervals	
Independent parameters	**p**	**Odds ratio**	**Lower**	**Upper**
Door to treatment time	0.676	1	1	1
Left ventricular ejection fraction	0.022	0.97	0.95	1
C-reactive protein	0.047	0.94	0.88	1
Creatinine	0.003	0.66	0.5	0.87
Brain natriuretic peptide	0.039	1	1	1
Albumin	0.373	1.56	0.59	4.11
Model	**Accuracy**	**Specificity**	**Sensitivity**	**AUC**
	0.74	0.85	0.54	0.800

AUC: Area under the curve

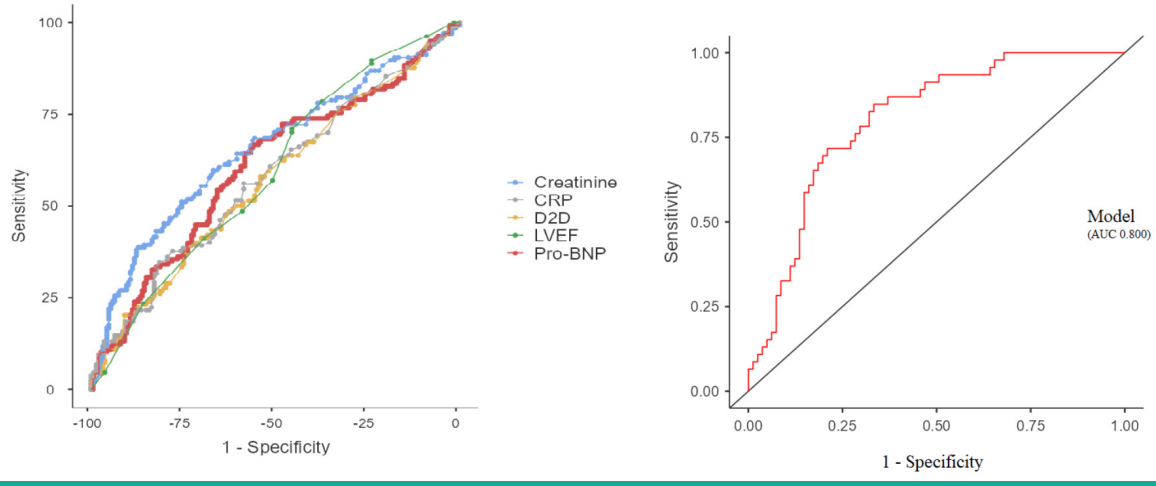

Figure 1. ROC curve of parameters and model

D2d: Door to diuretic treatment, LVEF: Left ventricle ejection fraction, CRP: C-reactive protein, pro-BNP: Pro-B-type natriuretic peptide

one-year mortality. In our study, there was no significant effect on short-term mortality. The biggest reason for this difference may be: AHF has various etiologies and is a syndrome, not a single disease (13). Many reasons, from myocardial infarction to infection, can cause AHF. Diuretic treatment does not give same effect in all HF patients. There are also patients who are diuretic resistant. The inability to fully isolate the patient group who has the same clinical condition and could benefit from diuretic therapy may explain the differences in results in the studies.

HF is one of the leading diseases in hospitalizations worldwide. Since the treatment costs are high, researches have been done to predict hospitalization (14). In our study, we found that the delay in the door to treatment time could predict the need for hospitalization, albeit weakly. There could be many reasons for delay in treatment. One of the reasons is that lung diseases or other cardiac-related diseases that fall into the differential diagnosis of AHF precede the actual diagnosis (15). It can be thought that delayed treatment may cause progression of clinical deterioration and consequently hospitalization.

In our study, left ventricular ejection fraction, C-reactive protein, creatinine, pro-BNP, and albumin were independent predictors. We found that the model formed with these parameters predicted hospitalization more strongly (AUC 0.800). We believe that new models can be developed using these parameters in order to more accurately identify patients who require hospitalization and effectively manage their care.

Study Limitations

There are several important limitations of the study. Most important limitation was that our study had a retrospective design (16). Furthermore, we did not use a classification method, such as the New York Heart Society classification, to group the patients. We did not compare subgroups. Thirdly, we did not evaluate the volume status of the patients. Finally, we could not determine the diuretic resistance of the patients.

Conclusion

According to the results of our study, early diuretic treatment has no effect on short-term mortality. However, the delayed door to treatment may affect hospitalization rates. We recommend early diuretic treatment in AHF patients to use hospital resources efficiently and to reduce hospitalizations. On the other hand, the data of our study should be verified with large multicenter samples.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Local Ethics Committee of University of Health Sciences Turkey, Ümraniye Training and Research Hospital (no: 426, date: 14/01/2021).

Informed Consent: Since this study was retrospective and the data were randomized, informed consent is not required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Design: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Data Collection or Processing: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Analysis or Interpretation: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Writing: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Drafting Manuscript: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Final Approval and Accountability: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Technical or Material Support: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A., Supervision: A.Ö., K.Ö., A.A., A.C., S.Ö., İ.A.

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High Prevalence of Chronic Musculoskeletal Pain and Analgesics Use Habits in the Geriatric Population with Chronic Kidney Disease

Kronik Böbrek Hastalığı Olan Geriyatrik Popülasyonda Kronik Muskuloskeletal Ağrının ve Analjezik Kullanım Alışkanlıklarının Yüksek Prevalansı

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Abstract

Objective: Individuals with chronic kidney disease (CKD) are at a risk of unsuccessful pain management and kidney injury using analgesics inappropriately. In this study, the prevalence of chronic musculoskeletal pain (CMP) and analgesics use habits was investigated in a geriatric population with non-dialysis dependent CKD, as well as the frequency of non-steroidal anti-inflammatory drugs (NSAIDs) and/or paracetamol use.

Method: This single-center cross-sectional study recruited patients over 65 years under follow-up for non-dialysis dependent CKD in nephrology clinic at least 1 year. Frequency of chronic pain was evaluated by Cornell musculoskeletal discomfort questionnaire. Pain was assessed using visual analogue scale (VAS).

Results: A hundred forty-two (52.8%) of 269 CKD patients had CMP. Patients with CMP were older than individuals without CMP (p=0.042). A hundred twenty-nine male patients and 140 female patients were present. Patients with CMP had a substantially higher ratio of females and mean body mass index than patients without CMP (p=0.0001). 9.7% of patients used paracetamol overall, while 42.8% utilized NSAIDs. 10.2% of non-CMP patients and 71.8% of CMP patients were reported to use NSAIDs (p=0.0001). Mean VAS score for patients with CMP was 5.01±2.07, and 48.6% of them reported moderate to severe pain. VAS score and estimated glomerular filtration rate level was similar regardless of analgesic type. Family physicians prescribed NSAIDs in 57.8% of cases, emergency medicine physicians in 9.0%, orthopedist in 17.5%, and others in 15.7% (p<0.0001).

Öz

Amaç: Kronik böbrek hastalığı (KBH) olan bireyler, analjeziklerin uygun olmayan kullanımına bağlı olarak başarısız ağrı yönetimi ve böbrek hasarı riski altındadır. Bu çalışmada diyalize bağımlı olmayan KBH'si olan geriyatrik bir popülasyonda kronik muskuloskeletal ağrı (KMA) prevalansının ve analjezik kullanım alışkanlıklarının yanı sıra steroidal olmayan anti-enflamatuvar ilaçların (NSAİİ) ve/veya parasetamol kullanım sıklığının araştırılması amaçlanmıştır.

Yöntem: Bu tek merkezli kesitsel çalışma, nefroloji kliniğinde en az 1 yıldır diyalize bağımlı olmayan KBH nedeniyle takip edilen 65 yaş üstü hastaları içermektedir. Kronik ağrı, Cornell kas-iskelet rahatsızlık anketi ile değerlendirildi. Ağrı şiddeti, görsel analog skala (VAS) kullanılarak değerlendirildi.

Bulgular: İki yüz altmış dokuz KBH hastasının 142'sinde (%52,8) KMA olduğu belirlendi. KMA olan hastalar, olmayan bireylerden daha yaşlıydı (p=0,042). Yüz yirmi dokuz erkek hasta ve 140 kadın hasta mevcuttu. KMA olan hastalarda kadın oranı ve ortalama vücut kitle indeksi, KMA olmayan hastalara göre önemli ölçüde daha yüksekti (p=0,0001). Hastaların %9,7'si genel olarak parasetamol kullanırken, %42,8'i NSAİİ kullanmıştı. KMA olmayan hastaların %10,2'sinde ve olan hastalarının %71,8'inde NSAİİ kullanımı mevcuttu (p=0,0001). KMA'lı hastalarda ortalama VAS skoru 5,01±2,07 idi ve bunların %48,6'sı orta ila şiddetli ağrı bildirdi. Analjezik tipinden bağımsız olarak VAS skoru ve tahmini glomerüler filtrasyon hızı düzeyi benzerdi. Olguların %57,8'ine aile hekimlerinin, %9,0'ına acil servis hekimlerinin, %17,5'ine ortopedi hekimlerinin ve %15,7'sine başka uzmanların NSAİİ reçete ettiği belirlendi (p<0,0001).

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Abstract

Conclusion: Based on high frequency of CMP, NSAIDs usage and prescriptions in elderly patients with CKD, an accurate risk assessment must be individualized in these patients based on CKD stage, age, comorbid conditions, and concomitant medication use.

Keywords: Analgesics, chronic kidney disease, chronic musculoskeletal pain, geriatric population

Öz

Sonuç: KBH'li yaşlı hastalarda KMA sıklığı, NSAİİ kullanımı ve reçetelenmesinin sıklığının yüksek olmasından ötürü, bu hastalarda doğru bir risk değerlendirmesi KBH evresi, yaş, komorbid durumlar ve eşzamanlı ilaç kullanımına göre bireyselleştirilmelidir.

Anahtar kelimeler: Analjezikler, kronik böbrek hastalığı, kronik muskuloskeletal ağrı, geriyatrik popülasyon

Introduction

The prevalence of chronic kidney disease (CKD), which is age-dependent, is high in the general population (1). Acute and chronic pains are predominant complaints among the adults and geriatric patients (2,3) and drug-related side effects dependent on all analgesic classes place restrictions on the management of disease (4). Due to distorted metabolism and excretion, as well as elevated accumulation of analgesic and their metabolites, the patients with lower glomerular filtration rate (GFR) are more susceptible to drug-related toxicity. As patients proceed to more severe stages of CKD, more medications that have side effects particular to their use in CKD are prescribed (5). Moreover, decreased life quality, a heavy burden of symptoms, and an increased risk of renal disease development, progression, and mortality have all been linked to the pain (6). In order to provide optimal health care for patients with CKD, the pain management is therefore essential (7).

It is well-known that non-steroidal anti-inflammatory drugs (NSAIDs) have been potentially dangerous pharmaceuticals for patients with CKD (8,9). Nephrotoxicity, fluid and electrolyte imbalances, hypertension, and other problems may occur when NSAIDs are used by CKD patients (10-12). To the current knowledge, a limited number of studies have examined the relationship between the analgesics use habits and prescriptions in the geriatric population with CKD, particularly in terms of NSAIDs or paracetamol usage (7,10). The present study investigated the prevalence of chronic musculoskeletal pain (CMP) and analgesics use habits in a Turkish geriatric population with non-dialysis dependent CKD and then aimed to explore factors associated with NSAIDs and/or paracetamol use, as well as short-term outcomes associated with using these analgesics.

Materials and Methods

Patients Selection

This single-center cross-sectional study recruited 320 patients over the age of 65 with a diagnosis of CKD at different stages, who applied to the nephrology clinic of a tertiary hospital between February 2022-May 2022 and who were not yet on hemodialysis. Only the patients who have been under follow-up in the nephrology outpatient clinic for at least 1 year with CKD, who were over 65 years and who want to participate in the survey were selected for the study. The exclusion criteria were to having kidney transplant have a diagnosis of cancer not in remission, not volunteer to participate in the survey, to use of opioid analgesics and not followed up at least one year. According to the exclusion criteria, 51 patients were excluded. The study protocol was approved by the Local Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (number: 2022-40, date: 01/28/2022), in accordance with the Committee on Publication Ethics guidelines and with the Helsinki Declaration of in 2000. Written informed consent was taken from the patients before participating in the study.

Data Collection

All eligible patients (n=269) were carefully interviewed to identify primary disease and current medications. At the time of the visit, the demographic features and the findings of laboratory tests were also recorded. The frequency of chronic pain was evaluated by the Cornell musculoskeletal discomfort questionnaire (CMDQ) in the Turkish language, validated by Erdinc et al. (13). CMDQ involves self-rating of the frequency, severity and work interference of the musculoskeletal discomfort on three scales across 20 body parts. The responses given on the frequency, severity and work interference scales were used in computations as percentages. On the frequency scale, the frequency of experiencing CMP in the past work week is rated across the following anchors: "Never", "1-2 times last week", "3-4 times last week", "Once every day" and "Several times every day" with weights of 0, 1.5, 3.5, 5, and 10, respectively. On the severity scale, the severity of the experienced MSD is rated across the following anchors: "Slightly uncomfortable", "Moderately uncomfortable" and "Very uncomfortable" with weights of 1, 2, and 3, respectively. On the work

interference scale, the interference of the experienced MSD with ability to work is rated across the following anchors: "Not at all", "Slightly interfered" and "Substantially interfered" with weights of 1, 2 and 3, respectively (13).

For patients with chronic pain, the score of pain was assessed using a visual analogue scale (VAS), a scale for pain assessment the pharmacological treatment of musculoskeletal pain proposed by the World Health Organization in 1996 (14). VAS consists of a scale range between 0 mm (no pain) to 100 mm (very painful), after which the patients were examined by a rheumatologist to confirm the information and characterize CMP symptoms. For the calculation of prevalence and for all other analyses, CMP was defined as non-traumatic CMP for over 3 months with a VAS score of >1 (14).

Fasting blood samples were collected from all patients during examination and centrifugated. Whole blood count, blood urea nitrogen, creatinine, uric acid, total protein, albumin, parathormone (PTH), C-reactive protein (CRP), calcium (Ca), phosphorus (P) was analyzed by using a Roche, Cobas 8000 e602 analyzers (Roche Diagnostics, Mannheim, Germany). The levels of urea, urine creatinine, albumin, Ca, P, bicarbonate and hemoglobin were measured by a photometric method while the levels of urine protein and CRP were measured by a turbidimetric method. Electrochemiluminescence assay was used to measure 25(OH)D and PTH.

The demographic features and laboratory data recorded at the time of VAS scoring assessment were compared between groups which were determined according to the presence of chronic pain and to the type of analgesics used and the frequency of analgesic use. The eGFR was calculated according to the equations determined by chronic kidney disease epidemiological collaboration (CKD-EPI) (15,16). CKD was defined as the presence of persistent proteinuria, or a decreased estimated glomerular filtration rate (eGFR) of <90 mL/min per 1.73 m^2 determined by the CKD-EPI creatinine equation, in two separate measurements within an interval of 3 months. The CKD-EPI equation, expressed as a single equation, is GFR =141 × min (Scr/κ, 1) α × max (Scr/κ, 1)-1.209 × 0.993 age × 1.018 (if female), where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κor 1, and max indicates the maximum of Scr/κ or 1. Only eGFR values were compared according to the changes and a decline in eGFR of ≥30% in a 1-year baseline period (17).

NSAIDs usage may cause acute renal impairment but no patient was hospitalized due to this disorder during drug use. In terms of renal diseases, the acute renal changes during NSAIDs usage were analyzed annually. The number and type of analgesics prescribed and the physicians to whom the patients consulted to prescribe these analgesics in the last 1 year with the complaint of pain were screened from the system of national Social Security Agency.

Follow-up

All geriatric patients who were diagnosed with CKD were followed up at 3-month intervals and they were informed not to use NSAIDs regularly in each physical examination.

Statistical Analysis

As a plot study, eGFR levels were measured in patients with and without chronic pain and were found as 47.16±18.21 mL/min/1.73 m^2 in chronic pain group and as 52.49±8.00 mL/min/1.73 m^2 in no chronic pain group. The effect power calculated based on these mean eGFR levels was found to be 0.3789. As a result of the Power analysis performed with the GPower 3.1.9.4 program, the design of the comparison of eGFR levels of two groups with a margin of error of 0.05 gave a power level of 80% in case of minimum of 222 patients included in the study.

All statistical analysis was performed by using SPSS 23 (Statistical Package for the Social Sciences). Continuous quantitative variables were given as mean ± standard deviation or median (minimum-maximum) and categorical variables were given as frequency and percentages. The Kolmogorov-Smirnov test was used to test the normality of continuous variables. The continuous variables of two groups were analyzed by Mann-Whitney U test. The categorical variables were compared by chi-square test and by Fisher's Exact and Fisher-Freeman-Halton test where appropriate. All analysis was tested at 95% confidence interval and p-value <0.05 considered as statistically significant.

Results

A total of 269 patients with a diagnosis of CKD and a mean of age of 72.48±5.88 year was included in the study (Table 1). Of those, 142 patients (52.8%) had a CMP while 127 patients (47.2%) had none. The mean age of patients with a chronic pain was significantly higher than that of patients without pain (71.76±5.74 vs. 73.11±5.96; p=0.042). The ratio of female patients (40.2% vs. 62.7%) and the mean body mass index (BMI) (30.29±4.81 kg/m^2 vs. 32.2±5.46 kg/m^2) were significantly higher in

patients with chronic pain than that in patients without pain (p=0.0001 and 0.007, respectively). There was no significant difference in the distribution of patients according to the education levels, comorbidities and usage of antidepressants between two groups (p>0.05). 71.8% of the patients with chronic pain have used NSAIDs while only 10.2% of patients without pain have used these drugs (p=0.0001).

The mean VAS score of patients with CMP was 5.01±2.07 (median: 4; range: 0-10) (Table 1). The severity of pain was slightly uncomfortable among 37 patients (26.1%), moderate among 69 patients (48.6%) and very uncomfortable among 36 patients (25.4%). Of the patients having CMP, 67 patients declared a knee pain (47.18%), 62 had a lumbar pain (43.66%), 18 had a back pain (12.68%), 4 had a neck pain (2.82%), 12 had a shoulder pain (8.45%), 10 had an arm pain (7.04%), 18 had a hip pain (12.68%). The number of patients who had a pain only at one part of the body was 96 (67.61%), those at two parts was 34 (23.94%), and those at three parts was 7 (4.93%). The number of patients whose pain frequency was 1-2 times for last week

Table 1. Baseline characteristics of patients classified according to the presence of chronic MS pain

Characteristics	Total n=269	No chronic pain n=127	Chronic pain n=142	p-value
Age (y), X ± SD	72.48±5.88	71.76±5.74	73.11±5.96	**0.042**
Gender (n, %)				
Male	129 (52.04)	76 (59.8)	53 (37.3)	**0.0001**
Female	140 (47.96)	51 (40.2)	89 (62.7)	
BMI, kg/m²	31.31±5.25	30.29±4.81	32.2±5.46	**0.007**
Education (n, %)				0.482
Non-literate	74 (27.5)	30 (23.6)	44 (31.0)	
Primary school	155 (57.6)	75 (59.1)	80 (56.4)	
High school	19 (7.1)	10 (7.9)	9 (6.3)	
Undergraduate	21 (7.8)	12 (9.4)	9 (6.3)	
Comorbidities (n, %)				
DM	144 (53.5)	65 (51.8)	79 (55.6)	0.465
HT	261 (97)	121 (95.3)	140 (98.6)	0.154
CHD	55 (20.5)	26 (79.5)	29 (20.4)	0.992
Cancer	21 (7.8)	11 (8.7)	10 (7.0)	0.621
Others	39 (14.5)	22 (17.3)	17 (11.9)	0.213
# ≥3	41 (15.2)	16 (12.6)	25 (17.6)	0.254
NSAIDs (n, %)	115 (42.8)	13 (10.2)	102 (71.8)	0.0001
Paracetamol (n, %)	26 (9.7)	0 (0)	26 (18.3)	
Antidepressants (n, %)	24 (8.9)	10 (7.9)	14 (9.9)	0.569
VAS score, X ± SD	5.01±2.07	-	5.01±2.07	-
Median (range)	4 (0-10)		4 (0-10)	
Severity of pain (n, %)				
Slightly uncomfortable	-	-	37 (26.1)	-
Moderately	-	-	69 (48.6)	-
Very uncomfortable			36 (25.4)	
Pain location (n, %)				
Knee	-	-	67 (47.18)	-
Lumbar	-	-	62 (43.66)	-
Back	-	-	18 (12.68)	-
Neck	-	-	4 (2.82)	-
Shoulder	-	-	12 (8.45)	-
Arm	-	-	10 (7.04)	-
Hip	-	-	18 (12.68)	-
Frequency (n, %)				
1-2 times a week	-	-	50 (35.21)	-
3-4 times a week	-	-	14 (9.86)	-
Each day of 3 weeks	-	-	58 (40.85)	-
More than once in a day	-	-	20 (14.08)	-

X ± SD: Mean ± standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, CHD: Coronary heart disease, NSAIDs: Non-steroidal anti-inflammatory drugs, VAS: Visual analogue scale, MS: Musculoskeletal

was 50 (35.21%), those whose frequency was 3-4 times for last week was 14 (9.86%), those who had pain in each day of three weeks was 58 (40.85%), and those who had pain for more than once in a day was 20 (14.08%) (Table 1). Seventy-three patients (51.41%) stated that the pain they experienced interfered slightly with their ability to work, but 19 patients (13.38%) stated that it interfered substantially.

Comparison of laboratory findings of the patients according to the presence of CMP was presented in Table 2. No significant changes in the laboratory parameters were detected according to the presence of chronic pain (p>0.05) except a significant difference found in the mean hemoglobin level between two groups. The mean hemoglobin level of the patients with chronic pain (12.52±1.6) was significantly lower than that of patients without pain (12.89±1.59) (p=0.04).

Baseline characteristics and laboratory findings of patients classified according to type of analgesics used are presented in Table 3. Overall, 9.7% of all patients (n=26) were using paracetamols and 42.8% (n=115) were using NSAIDs. All these analgesics users had CMP but one of the patients with chronic pain declared not use any analgesic. No significant difference was observed in the distribution of patients according to the age, education, comorbidities, usage of antidepressants, ACE/ARB, and the mean BMI (p>0.05), while the distribution of gender showed a borderline of statistical significance (p=0.052). The most common location of pain was lumbar region in paracetamol group (46.2%) while it was the knee region in NSAIDs group (45.2%). The median VAS score and mean eGFR did not differ significantly according to the type of analgesics used (p>0.05). 18.3% of patients using NSAIDs stated that they used more than 6 boxes of NSAIDs (each box contains 20 tablets) per year. The median VAS score (median: 6; range: 2-10) was significantly higher among patients who used NSAIDs intensively (more than 6 boxes per year) compared to those who did not use NSAIDs intensively (median: 4; range 0-10) (p=0.022).

The number of patients with a decrease in eGFR value over 30% was 4 (36.4%) among the patients using paracetamol and 7 (63.6%) among the patients using NSAIDs (p=0.120) (Table 3). The median eGFR value of the patients using paracetamol was 53.4 (range: 11.3-82) one year ago, while the value at the time of recording VAS score decreased to a median 51.65 mL/min/1.73 m^2 (range: 6-80.2 mL/min/1.73 m^2). The median eGFR value of patients using NSAIDs was 48.7 mL/min/1.73 m^2 (range: 11.6-105 mL/min/1.73 m^2) one year ago, while the current value decreased to a median 48.12 mL/min/1.73 m^2 (range: 9.9-100.7 mL/min/1.73 m^2). The median decrease in eGFR level at the end of one-year follow-up was 2.5 (range: -19.7-20.9) among the patients using NSAIDs while it was 3 (range: -12.9-41.4) among the patients using paracetamol (p=0.801) (Table 3).

The frequency of analgesic use among the patients was compared according to the presence of CMP and CKD stage and presented in Table 4. 16.5%, 66.1% and 17.3% of 127 patients without CMP was at stage 1-2, stage 3 and stage 4 of CKD, respectively. 23.2%, 60.6% and 16.2% of 142 patients with CMP was at stage 1-2, stage 3 and stage 4 of CKD, respectively. No significant difference was found

Table 2. Comparison of laboratory findings of the patients according to the presence of chronic musculoskeletal pain

Parameter	No chronic pain n=127	Chronic pain n=142	p-value
Urea (mg/dL)	48 (21-140)	47.9 (24.6-180)	0.751
eGFR (mL/min/1.73 m^2)	48.22±16.17	49.26±16.64	0.605
Urine P/C ratio (mg/gr)	135 (1-6031)	127 (5-7483)	0.817
Albumin (g/L)	4.49±0.44	4.45±0.31	0.856
Ca (mg/dL)	9.4±0.95	9.44±0.48	0.810
P (mmol/L)	3.76±3.2	3.66±0.63	0.092
Ca × P (mg_2/mL_2)	32.82 (0.37-368.6)	34.78 (22.31-56)	0.092
PTH (ng/L)	55.1 (3.5-244)	55 (9.5-458)	0.630
25(OH)D (µg/L)	19.45 (3-55.7)	20.4 (4.14-99)	0.490
HCO_3^- (mmol/L)	25.7 (18.8-31.1)	26 (17.6-37.5)	0.717
Hb (g/dL)	12.89±1.59	12.52±1.6	**0.04**
CRP (mg/dL)	3.3 (0.1-59.7)	3.62 (0.33-61.4)	0.478

All values are presented as mean ± standard deviation or median (minimum-maximum), P: Phosphorus, PTH: Parathyroid hormone, Hb: Hemoglobin, 25(OH)D: 25 hydroxy vitamin D, HCO_3^-: Bicarbonate, CRP: C-reactive protein, P/C: Protein/creatinine ratio in spot urine, eGFR: Estimated glomerular filtration rate

in distribution of patients according to CKD stages and presence of CMP (p>0.05). Among patients at chronic pain group, 75.8% of 33 patients at stage 1-2, 42.9% of 86 patients at stage 3 and 69.6% of 23 patients at stage 4 were NSAIDs users, all of which were significantly higher than those at no chronic pain group (p<0.0001, p<0.0001 and p=0.0015, respectively). Moreover, the frequency of heavy NSAIDs users (more than 6 boxes per year) was significantly higher in patients with CMP and CKD at stage 3 compared to corresponding patients without CMP (42.9% vs. 5.5%, respectively, p=0.0021). Additionally, the ratio of paracetamol users was significantly higher in patients with CMP and CKD at stage 3 compared to corresponding patients without CMP (11.3% vs. 0%, respectively, p<0.0001). No such significance was found in heavy NSAIDs or paracetamol users among patients at CKD stage 1-2 or stage 4 (p>0.05).

As shown in Figure 1, there was a significant difference between the prescription numbers of NSAIDs by the family physician (57.9%), emergency medicine physicians (9.0%), orthopedists (17.5%), and other physician groups (15.7%) (p<0.0001). As a result of the paired comparisons, it was determined that family physicians prescribed NSAID drugs the most (p<0.0001). There was a significant difference between the prescription numbers of paracetamols by the family physicians (71.4%), emergency medicine physicians (14.3%), orthopedist (5.4%), and other physician groups (8.9%) (p<0.0001). Also, the number of paracetamol prescriptions by the family physicians was higher than those by other physicians (p<0.0001). There was no significant difference between the prescribing numbers of the emergency medicine physicians, orthopedists, and other physician groups (p>0.05).

Table 3. Baseline characteristics and laboratory findings of patients classified according to type of analgesics used

Characteristics	Paracetamol n=26	NSAIDs n=115	p-value
Age (n, %)			0.206
65-75 years	16 (61.5)	85 (73.9)	
≥76 years	10 (38.5)	30 (26.1)	
Gender (n, %)			
Male	7 (26.9)	55 (47.8)	0.052
Female	19 (73.1)	60 (52.2)	
BMI, kg/m² (X ± SD)	32.28±5.34	31.74±5.24	0.730
Education (n, %)			0.959
Non-literate	8 (30.8)	35 (30.4)	
Primary school	15 (57.7)	64 (55.6)	
High school	2 (7.7)	8 (7.0)	
Undergraduate	1 (3.8)	8 (7.0)	
Comorbidities (n, %)			
DM	12 (46.2)	68 (59.1)	0.228
HT	26 (100)	112 (97.4)	0.405
CHD	2 (7.7)	26 (22.6)	0.85
Cancer	3 (11.5)	9 (7.8)	0.540
# ≥3	4 (15.4)	20 (17.4)	0.806
Antidepressants	1 (3.8)	14 (12.2)	0.214
ACE/ARB	19 (73.1)	80 (69.6)	0.724
Pain location			
Knee	9 (34.6)	52 (45.2)	0.324
Lumbar	12 (46.2)	43 (37.4)	0.408
Back	6 (23.1)	10 (8.7)	0.081
Neck	2 (7.7)	2 (1.7)	0.099
Shoulder	1 (3.8)	8 (7.0)	0.558
Arm	2 (7.7)	7 (6.1)	0.762
Hip	2 (7.7)	14 (12.2)	0.515
VAS score			0.782
Median (range)	4 (3-8)	4.5 (0-10)	
eGFR (mL/min/1.73 m²) (X ± SD)	48.62±15.34	49.35±16.82	0.827
Decrease above 30% (n, %)	4 (36.4)	7 (63.6)	0.120

X ± SD: Mean ± standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, CHD: Coronary heart disease, NSAIDs: Non-steroidal anti-inflammatory drugs, ACE: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, VAS: Visual analogue scale, eGFR: Estimated glomerular filtration rate

Discussion

The present study showed that the rate of presence of CMP was 52.8% in the geriatric sample including 269 patients with non-dialysis dependent CKD and the mean age, the ratio of females, the mean BMI and rate of using NSAIDs among the patients with CMP was significantly higher than those without pain. VAS score and eGFR level were comparable between the groups of analgesic type (NSAIDs vs paracetamol). A significant higher ratio of NSAID drugs (57.8%) was prescribed by family physicians compared to other physicians for the patients using NSAIDs. A similar higher ratio was also observed for paracetamol prescriptions by family physicians (71.4%) for patients using paracetamols. Most of patients with CMP were NSAIDs users at all stages 1-4 of CKD but the ratio of heavy NSAIDs users decreased at higher stages. These findings showed that a high frequency of CMP, NSAIDs usage and prescriptions in elderly patients with CKD, suggesting the unnecessary prescriptions and use of analgesics should be avoided in these patients due to the risk of nephropathy emerged by NSAIDs use.

Patients with kidney diseases frequently suffer chronic pain as one of the important symptoms of disease. Pain in patients with early-stage CKD is associated with lower quality of life and CKD has severe impact on quality of life (18). In patients with CKD, chronic pain was reported by more than 70% of patients (7). A study reported that more than 50% of CKD patients but less than 10% of non-CKD patients experienced a chronic pain (19). CMP is the most common type of pain in CKD and a high number of CKD patients have experienced moderate-to-severe pain (20). There are studies claiming that CKD patients with CMP showed independently higher rates of all-cause mortality than those without chronic pain. However, long-term follow-up of CKD patients indicated that patients with CMP had similar risk of CKD progression as those without pain (21). As with the general population, elderly age, female gender, obesity and some comorbid conditions are the best determinants of CMP (22). In the present study, among 269 geriatric patients with non-dialysis dependent CKD, 142 patients (52.8%) had CMP. This relatively high prevalence rates in patients with CKD in its earlier stages may be due to the fact that the burden of comorbidity accounts for a large portion of the pain in CKD. Another reason is that a number

Table 4. Comparison of frequency of analgesic use among the patients according to the presence of chronic musculoskeletal pain and CKD stage

CKD stage		No chronic pain n=127	Chronic pain n=142	p-value
Stage 1-2	Total number, n (%)	21 (16.5)	33 (23.2)	0.223
	NSAIDs user, n (%)	2 (9.5)	25 (75.8)	**<0.0001**
	Heavy NSAIDs user, n (%)	0 (0)	4 (16)	0.261
	Paracetamol, n (%)	0 (0)	5 (20)	0.164
Stage 3	Total number, n (%)	84 (66.1)	86 (60.6)	0.412
	NSAIDs user, n (%)	7 (5.5)	61 (42.9)	**<0.0001**
	Heavy NSAIDs user, n (%)	0 (0)	11 (7.7)	**0.0021**
	Paracetamol, n (%)	0 (0)	16 (11.3)	**<0.0001**
Stage 4	Total number, n (%)	22 (17.3)	23 (16.2)	0.934
	NSAIDs user, n (%)	4 (18.2)	16 (69.6)	**0.0015**
	Heavy NSAIDs user, n (%)	0 (0)	2 (8.7)	0.489
	Paracetamol, n (%)	0 (0)	5 (21.7)	0.065

NSAIDs: Non-steroidal anti-inflammatory drugs, CKD: Chronic kidney disease

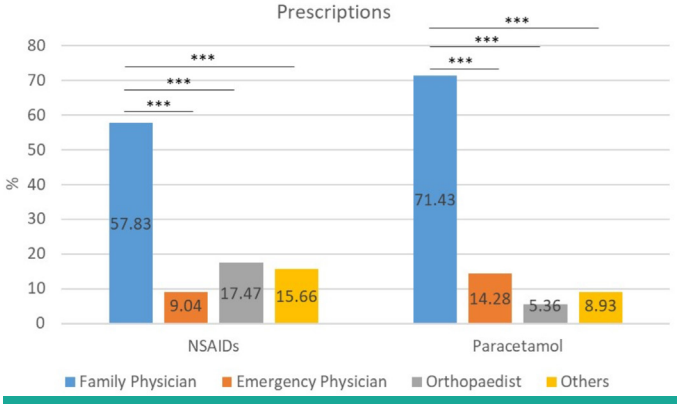

Figure 1. Distribution of prescriptions of non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol among the physicians

of medical professionals lack the knowledge and confidence to pursue appropriate chronic pain treatment options. Some of them are reluctant to administer and supervise analgesics since they believe it is not their obligation to address symptoms that are not specifically linked to CKD. I noticed that the use of analgesics in the patients was mostly due to CMP and mostly as a result of referral to the family physician. In order to reduce the unnecessary use of NSAIDs and limit their prescribing, we recommend that the family physicians be provided with detailed continuous medical education on the damages of NSAIDs use in CKD patients, especially in advance stages.

To manage the CMP in CKD patients, more analgesics have been prescribed especially in the elderlies. The anatomical and physiopathological changes seen with aging alter the responses to neuraxial and peripheral neural blockade and affect the pharmacokinetic and pharmacodynamic properties of the individual agents used. Due to these changes, elderly patients have an increased sensitivity to both therapeutic and adverse effects of many drugs used for pain management (23,24). In this study, the frequency of NSAIDs usage among CKD patients was 42.8% and this frequency increased to 71.8% among CKD patients with CMP. This may be related to lower levels of hemoglobin CKD patients with CMP who may have a gastrointestinal occult bleeding as a complication of NSAIDs usage, although the difference between the groups with and without CMP showed statistically borderline significance. This finding is consistent with the literature suggesting that NSAIDs can cause mucosal injury in the upper, mid- and lower GI tract resulting in bleeding which can be overt (with melaena) or occult (iron deficiency) (25). NSAIDs inhibit platelet cyclooxygenase, thereby blocking the formation of thromboxane A2. These drugs produce a tendency toward systemic bleeding by impairing thromboxane-dependent platelet aggregation and consequently prolonging bleeding time (26). Therefore, a lower level of hemoglobin among CKD patients with CMP is an expected finding.

Female patients tend to use NSAIDs and painkillers more frequently than male patients, which may be due to the fact that women are typically more susceptible to developing chronic and autoimmune diseases and conditions like arthritis (27). In the literature, NSAIDs prescribing and utilization has been associated with the female gender among elderly patients (28). In a study conducted in Italy, the use of NSAIDs was more common in the elderly and women (29). In a study from UK, the rate of NSAIDs usage was 12.3% among female and 9.4% among male patients with CKD (30). The present study showed that the frequencies of NSAIDs usage were more common among female patients with CMP, showing a borderline significance difference with compared to male patients.

The present study revealed that there was no significant difference in the mean eGFR value and the decrease in eGFR over 30% in CKD patients using NSAIDs and paracetamol, which showed that the drug choice did not cause a significant change in kidney function. The use of NSAIDS should be questioned in every patient with a decrease in eGFR, although it is recommended not to use it, over-the-counter use can be seen frequently. The reason for this is the inadequacy of chronic pain management. Epidemiologic studies examining analgesics and kidney failure have revealed controversial findings about the risk of NSAIDs usage (10,31). There are studies reporting no risk of decreased GFR among moderate users of NSAIDs (32,33). On the other hand, several case-control studies found substantial consumption of NSAIDs was associated with an increased risk of kidney failure (34). Prolonged use of NSAIDs was related to reduction of eGFR in CKD patients (31). A study of patients with CKD using opioids and NSAIDs demonstrated that NSAIDs usage was associated with a lower risk of kidney failure with kidney replacement therapy in patients with eGFR <45 mL/min/1.73 m^2 (34). This finding may also be related to the frequency of analgesic use which was restricted to self-report, hence did not necessarily reflect actual use of all prescribed drugs. Opioid use is relatively low in this country compared to other analgesics because there is a restriction on opioid analgesics. It is available with a special prescription. The data of NSAIDs usage was collected by the patient interviews; obviously this approach is prone to recall bias.

Use of prescription analgesics, both paracetamols and NSAID, has been reported to increase in time especially in patients with CKD (10). There are several evidence-based reports suggesting not to prescribe NSAIDs for geriatric patients with CKD due to common comorbidities including cardiovascular or renal diseases, however, it has been demonstrated that the prescription and use of NSAIDs is widespread among these patients (35-38). The use of NSAIDs is associated with increased gastrointestinal and cardiovascular risks and renal function disorders, particularly in elderly patients (37). The use of NSAIDs was reported to be associated with a two-fold increased risk of CKD, especially in patients aged >65 years. In one study, the ratios of individuals with hypertension, heart failure, or CKD used prescribed NSAIDs for musculoskeletal pain

management were between 14.4% and 16.2% (38). Ndlovu et al. (39) reported that 5.7% of people with moderate to severe CKD reported using NSAIDs; however, the majority of these people used over-the-counter drugs, and many of them were not aware that they had CKD. In a large cohort study of primary care visits involving older adults with a musculoskeletal disorder and history of hypertension, heart failure, or CKD, almost 10% of patients were found to prescribed and use NSAIDs despite the high risk for cardiovascular and renal complications. They also reported that widespread prescription of NSAIDs among primary care practices and physicians while the use of prescribed NSAIDs was not associated with significantly higher (or lower) risk of cardiovascular or renal outcomes (35). The present study contributes to these earlier studies by showing that a high frequency of NSAIDs and paracetamols use among the geriatric patients with CKD and high rates of comorbidities, such as hypertension (97%), diabetes mellitus (53.5%), and cardiovascular disease (20.5%).

The variations in analgesic use among different countries that have been documented in the literature may be related to obstacles to receiving medical care and varying cultural views of how to manage pain. In a study conducted in 835 Turkish patients aged over 65 years (mean age 74.2±6.6 years), the mean number of drugs used was 6.8±3.2, total number of inappropriate drugs used was 688 and the number of patients using inappropriate drugs was 431 (51.6%) (37). The reports from Europe declared a NSAIDs prescription rate of 73% and 20% among elderly patients (30,40). A recent population-based study evaluating >9 million Canadian residents found that individuals aged 66 years or older formed the majority (93.4%) of those who had received one or more NSAIDs for ≥14 days (41). We found that 9.7% of all patients were using paracetamols and 42.8% were using NSAIDs. The frequency of NSAIDs usage in older CKD patients with CMP (115 of 142 patients) is also consistent with the literature. In every country, different national regulations of the health systems affect these prescription rates of NSAIDs. For example, in USA, there are mainly over-the-counter drugs but in Turkey, all drugs are sold in pharmacies. Therefore, the non-prescribed drugs are in control of the pharmacists. This can be an additional safety measure.

Several drugs with potential toxicity are prescribed to patients with advanced CKD (42). In fact, NSAIDs are considered a class of drugs that should be avoided in patients with CKD, particularly those with advanced CKD (9). This approach has led to increased opioid administration and use of adjuvant therapies to manage pain. Importantly, opioid use poses many risks and data regarding the safety of even commonly used agents in patients with CKD are markedly limited (43). Baker et al. (44) reported that NSAIDs were safer than opioids in this group of patients (34). In view of this, a tighter approach to CKD stage and other risk-enhancing comorbidities should be used in which the management of pain becomes challenging in advanced CKD stages. In the present study, the patients with CMP continued to use NSAIDs regardless of CKD stage, and the frequency of NSAIDs users was significantly higher compared to patients without CMP for all CKD stages, but the patients at CKD stage 4 avoided heavy NSAIDs use, which was different from the data on the paracetamol users compared according to CKD stage and presence of CMP. This finding shows that patients with advanced CKD stage do not completely stop using NSAIDs, but they try to avoid intensive use and we can say that these patients use NSAIDs a little more consciously or carefully. Therefore, correct use of NSAID in patients with CKD should be on the basis of an individualized examination for the type of pain, expected dose and duration, patient risk profile including stage of CKD, availability of alternative therapies, and care targets.

The present study evaluated the prescriptions of NSAIDs and paracetamols in CKD patients. In a study by Arakawa et al. (45), the prescription of NSAIDs within East Asia was examined by means of a questionnaire survey for physicians and most physicians prescribed nonselective NSAIDs, cyclooxygenase-2 inhibitors or aspirin for more than 5 patients per week. In another study, widespread prescribing of NSAIDs were identified among primary care practices and physicians and prescription NSAIDs usage was not associated with the varied risk of cardiovascular or renal safety-related outcomes (35). In a recent study conducted in Turkey, the most common analgesics ordered by physicians were NSAIDs (n=505, 67.9%) in the emergency departments (ED) and physicians prescribed an analgesic at discharge from the ED in 55.6% of the patients and acute pain was present in 7.5% of the patients (46). Here, the frequency of prescriptions for NSAIDs was highest by the family physicians compared to other physicians. One of the reasons why family physicians prescribed NSAIDs more often to patients with CMP depends on the high rate of application to family physicians in Turkey. At this point, it is understood that physicians should continue medical education. The primary care physician should be well aware of the characteristics of the analgesics to be used as

well as the characteristics of the patient in order to be able to effectively manage pain.

Study Limitations

The present cross-sectional study has the limitations that were related with the design such as information bias. Another limitation of this study that non-prescribed medications was probably missed out due to the collection of data of prescriptions by screening the national social security agency. As another limitation, the present study did not assess the independent effect of CKD and not compare the outcomes with a control group or the patients with other diseases. Also, one cannot rule out the possibility analgesic choice may have change in years by the regulations of health authorities on the prescription of NSAIDs.

Conclusion

Based on the high frequency of CMP, NSAIDs usage and prescriptions in patients with CKD, an accurate risk assessment must be highly individualized based on CKD stage, age, comorbid conditions, and concomitant medication use. It is crucial to educate the physicians to consider potentially life-threatening NSAID-related complications before NSAIDs therapy initiation and to avoid prescriptions of NSAIDs in geriatric patients with CKD. Optimizing pain management in a complex condition such as kidney disease should remain a priority for clinicians and researchers. Given the difficulty in pain management in the elderly population, more evidences are required to support NSAIDs usage in CKD patients by a more detailed strategy considering CKD stage and other risk-promoting comorbidities.

Ethics

Ethics Committee Approval: The study protocol was approved by the Local Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (number: 2022-40, date: 01/28/2022), in accordance with the Committee on Publication Ethics guidelines and with the Helsinki Declaration of in 2000.

Informed Consent: Written informed consent was taken from the patients before participating in the study.

Peer-review: Internally and externally peer-reviewed.

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ORIGINAL RESEARCH

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H3B2 Scoring Validation and Comparing of the Other Scoring Systems in Patients with Upper Gastrointestinal Bleeding: A Retrospective Study

Üst Gastrointestinal Kanaması Olan Hastalarda H3B2 Skorunun Doğrulanması ve Diğer Skorlar ile Karşılaştırılması: Retrospektif Bir Çalışma

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Abstract

Objective: We had validation of H3B2 scoring on Turkish patients in this study. In addition, it was compared with Glasgow-Blatchford and AIMS65 scoring.

Method: This study was conducted retrospectively and single centered. It was continued by scanning of tertial education hospital datum in 07-2021 to 07-2022. Patients were the adults who was made endoscopic intervention during initial 24 hours. Glasgow-Blatchford, AIMS65 and H3B2 scoring were calculated according to initial parameters.

Results: The study included 116 patients. Median age was 60 (45,53) years. H3B2, AIMS65 and Glasgow-Blatchford scoring were significantly higher in non-survivor group than survivor group (p=0.005, <0.001, 0.013. respectively). With the addition of lactate and albumin to H3B2, the area under the curve value reached 0.910 and gained a stronger predictive ability.

Conclusion: H3B2 was successful in predicting short-term mortality in Turkish patients, we recommend adding lactate and albumin to the H3B2 for stronger predictivity.

Keywords: AIMS65, Glasgow-Blatchford, H3B2 scoring, mortality, upper gastrointestinal bleeding

Öz

Amaç: Bu çalışmamızda H3B2 skorunun Türk hastalar üzerinde validasyonunu yaptık. Ek olarak Glasgow-Blatchford skoru ile AIMS65 skorlamalarıyla karşılaştırdık.

Yöntem: Bu çalışma retrospektif ve tek merkezli olarak yürütüldü. 07-2021 ile 07-2022 arasında üçüncü basamak hastane verileri taranarak yapıldı. Hastalar ilk başvurudan sonra 24 saat içinde endoskopi uygulaması yapılmış erişkin hastalardı. Glasgow-Blatchford skoru, AIMS65 ve H3B2 ilk başvuru değerlerine göre hesaplandı.

Bulgular: Çalışmaya 116 hasta dahil edildi. Yaş ortanca değeri 60 (çeyrekler arası 45,53) yıldı. H3B2, AIMS65 ve Glasgow-Blatchford skorlamaları non-survivor grupta survivor gruba göre anlamlı olarak yüksekti (sırası ile p=0,005, <0,001, 0,013). Laktat ve albümin H3B2 skoruna eklendiğinde eğri altındaki alan değeri 0,910 seviyesine ulaştı ve daha güçlü öngörü kabiliyeti kazandı.

Sonuç: H3B2 skoru Türk hastalarda kısa dönem mortaliteyi öngörmede başarılı oldu. Daha güçlü sonuçlar elde etmek için laktat ve albüminin H3B2 skoruna eklenmesini öneriyoruz.

Anahtar kelimeler: AIMS65, Glasgow-Blatchford, H3B2 skoru, mortalite, üst gastrointestinal sistem kanaması

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Introduction

Upper gastrointestinal bleeding (UGIB) is one of the critical issues encountered in emergency departments. Anatomically it's called for bleeding from the upper part of the ligament of Treitz (1). Peptic ulcers, varices, angiodysplasia, esophagitis, gastritis and duodenitis, are the most common etiological causes (2). Aging is one of significant risk factor of mortality in UGIB. It appears in 150 of 100 000 patients every year. Compared to the data from the USA, it might be estimated that almost 64 000 to 120 000 UGIB patients occur in Turkey (3). It has been reported that UGIB short-term mortality is between 5% and 14% (4,5). The diagnosis is easily made by taking a quality history and performing a physical examination. However, determining the need for early intervention and classifying the urgency of patients is not as easy as the diagnosis. For these reasons, various scoring systems have been developed, such as the Glasgow-Blatchford score (GBS) and AIMS65 (6-8). The most important issue to be predicted with these scores is the necessity of an endoscopic procedure for bleeding control in the patient. Additionally, other poor outcomes such as mortality, the need for the intensive care unit, and the length of hospital stay are tried to be anticipated. These scores include patients' hemodynamic parameters, examination findings, and laboratory results. In a recent study on Japanese patients with UGIB, Sasaki et al. (9) suggested the H3B2 score to predict the need for intervention. The H3B2 score is formed by scoring hematemesis, pulse, blood pressure, systolic, hemoglobin, and blood urea nitrogen, with its name consisting of the initials of these parameters. A successful result was obtained in determining the risks of patients and predicting the requirement for urgent hemostatic treatment in 675 patients evaluated between 2015 and 2019. In this study, we validated the H3B2 score in Turkish patients and compared it with GBS and AIMS65.

Materials and Methods

This study was conducted retrospectively and in a single center. University of Health Sciences Turkey, Ümraniye Training and Research Hospital, data between 07-2021 and 07-2022 were scanned. Patients presenting with hematemesis, melena, hematochezia, and coffee grounds vomiting were included. The patients were adult patients who underwent endoscopy within 24 hours after the first admission and were diagnosed with non-variceal UGIB. Patients who did not undergo endoscopic intervention were excluded. The patients were divided into two groups according to their 28-day mortality status. One of the groups was determined as a survivor and the other as a non-survivor. GBS, AIMS65 and H3B2 calculated at the Initial values. At the same time, the initial laboratory and vital parameters of the patients were recorded. Patient age, sex, BUN, albumin values, survival status, comorbidities, white blood cell, hemoglobin, hematocrit, platelet (PT), international normalized ratio (INR), lactate and pH values were recorded. The hospital stays were obtained by scanning the data from the clinical registry office system. AIMS65 score calculated with albumin, PT-INR, disturbance of consciousness, systolic blood pressure and age. GBS was calculated using Initial BUN, systolic blood pressure, melena present, hemoglobin, hepatic disease history, heart rate ≥100, sex, cardiac failure present and recent syncope. The parameters used for the H3B2 score are shown in Table 1.

The study was conducted following the principles of the Declaration of Helsinki, and ethical agreement was provided by the Local Committee of University of Health Sciences Turkey, Ümraniye Training and Research Hospital (no: 277, date: 08/09/2022).

Statistical Analysis

The Jamovi 2.3 version program was used for statistical analysis. The Shapiro-Wilk test was used to assess the normal distribution of the data. According to the results obtained, the data did not follow a normal distribution. Therefore, we used the Mann-Whitney U test when comparing groups for continuous data. We used the chi-square test when comparing the categorical data. Number and percentage for categorical data, median for continuous data, and 25th and 75th percentiles were used when presenting the data. Receiver characteristic operation (ROC) analysis was performed to evaluate the power of the scores in predicting mortality. Differences between the area under the curve (AUC) were evaluated with the deLong test. A binominal logistic regression analysis was performed to evaluate independent producers and propose a stronger model. The upper limit of the p-value was taken as 0.05 in for statistical significance.

Table 1. H3B2 score, parameters, and scores

Parameters	Standard	Score
Hematemesis		1
Heart rate (times/minute)	≧100	1
Blood pressure, systolic (mmHg)	≦100	1
Hemoglobin (g/dL)	≦10	1
Blood urea nitrogen (mg/dL)	≧22.4	2

Results

A total of 225 patients were admitted to the emergency department with the suspicion of UGIB. Sixty-five of them were excluded. Number of patients included was 160 in the study. The median age was 60 [interquartile range (IQR) 45, 53] years. The median age in the mortality group was 73 (IQR 57, 80) years and was significantly higher than those who survived. The number of men in the study population was 79 (68.1%). The most comorbidity was hypertension 48 (41%). In our sample, 15 (13%) all-causes died within a 30-day period. Lactate values were 5.9 mmol/L (IQR 4, 8) in the non-survivor group and were significantly higher than the survivor group. Albumin values were significantly lower in the non-survivor group compared to the survivor group 2.2 g/dL (IQR 1.7, 3.2). The median value of hemoglobin was 9.4 g/dL (IQR 7.6, 11.6) and there was no significant difference between the groups. the mostly complaint was melena 75 (64.7%). Systolic blood pressure was significantly lower in the non-survivor group 101.0 mm/hg (91.5, 111.5). H3B2, AIMS65 and GBS were significantly higher in the non-survivor group than the survivor group (p=0.005, <0.001, 0.013, respectively). Demographic and baseline characteristic data of the groups are shown in Table 2.

Table 2. Baseline characteristics of the enrolled patients and their comparison between the survivor and non-survivor groups

Parameters	Survivor n=101 (87%)	Non-survivor n=15 (13%)	Total n=116 (100%)	p
Age (25^{th}-75^{th} percentiles)	60 (45 to 71)	73 (57 to 80)	60 (45 to 53)	0.04
Female (%)	31 (31%)	6 (40%)	37 (31.9)	0.671
Male (%)	70 (69%)	9 (60%)	79 (68.1)	
Diabetes mellitus (%)	28 (28%)	1 (6.7%)	29 (25%)	0.110
Hypertension (%)	43 (43%)	5 (33%)	48 (41%)	0.500
Coronary artery disease (%)	26 (26%)	6 (40%)	32 (28%)	0.350
Heart disease (%)	7 (6.9%)	1 (6.7%)	8 (6.9%)	>0.99
Chronic obstructive pulmonary disease (%)	8 (7.9%)	1 (6.7%)	9 (7.8%)	>0.990
Chronic kidney disease (%)	8 (7.9%)	1 (6.7%)	9 (7.8%)	>0.990
Cirrhosis (%)	8 (7.9%)	2 (13.3%)	10 (8.6%)	0.838
Laboratory parameters				
Lactate (mg/dL)	2.1 (1.6 to 2.9)	3.7 (2.8 to 7.2)	2.2 (1.7 to 3.2)	<0.001
Hemoglobin (g/dL) (25^{th} to 75^{th} percentiles)	9.9 (7.8 to 11.6)	8.2 (7.0 to 9.4)	9.4 (7.6 to 11.6)	0.057
Hematocrit (%)	30.9 (24.1 to 36.2)	26.6 (22.4 to 29.2)	29.9 (23.5 to 35.6)	0.037
White blood cell count (10^3/μL)	9.6 (7.3 to 13.0)	15.1 (7.6 to 19.7)	9.7 (7.3 to 14.7)	0.149
Platelet count (10^3/μL)	245.0 (195.0 to 330.0)	219.0 (131.5 to 347.5)	244.0 (191.5 to 330.2)	0.573
Albumin (g/dL) (25^{th} to 75^{th} percentiles)	3.6 (3.1 to 4.1)	2.8 (2.4 to 3.2)	3.5 (3.0 to 4.0)	<0.001
International normalized ratio (25^{th} to 75^{th} percentiles)	1.1 (1.0 to 1.4)	1.3 (1.1 to 1.5)	1.2 (1.0 to 1.4)	0.081
Blood urea nitrogen (mg/dL)	59.6 (42.0 to 94.0)	103.0 (67.9 to 130.0)	65.1 (42.5 to 100.5)	0.040
Vital parameters				
Systolic blood pressure (mm/hg) (25^{th} to 75^{th} percentiles)	115.0 (101.0 to 129.0)	101.0 (91.5 to 111.5)	113.0 (98.5 to 128.2)	0.011
Diastolic blood pressure (mm/hg) (25^{th} to 75^{th} percentiles)	67.0 (56.0 to 75.0)	56.0 (51.0 to 60.5)	63.5 (55.0 to 74.2)	0.004
Pulse rate (b/min.)	90.0 (81.0 to 104.0)	101.0 (81.5 to 110.5)	90.0 (81.0 to 105.0)	0.365
Oxygen saturation (%)	98.0 (96.0 to 99.0)	94.0 (86.0 to 96.0)	97.0 (95.0 to 98.2)	<0.001
Respiratory rate (b/min.)	20.0 (18.0 to 22.0)	26.0 (26.0 to 32.0)	20.0 (18.0 to 24.0)	<0.001
Temperature (°C)	36.6 (36.3 to 37.1)	36.7 (36.3 to 37.1)	36.6 (36.3 to 37.1)	0.509
Symptoms				
Hematemesis (%)	42 (41.6)	9 (60.0)	51 (44.0)	0.265
Melena (%)	66 (65.3)	9 (60.0)	75 (64.7)	0.774
Hematochezia (%)	10 (9.9)	2 (13.3)	12 (10.3)	0.653
Syncope (%)	11 (10.9)	1 (6.7)	12 (10.3)	0.990

Table 2. Continued

Parameters	Survivor n=101 (87%)	Non-survivor n=15 (13%)	Total n=116 (100%)	p
Scores				
H3B2 scoring	4.0 (3.0 to 4.0)	5.0 (4.0 to 5.0)	4.0 (3.0 to 4.0)	0.005
AIMS65 scoring (25th to 75th percentiles)	1.0 (0.0 to 1.0)	2.0 (1.0 to 3)	1.0 (0.0 to 2.0)	<.001
Glasgow-Blatchford scoring (25th to 75th percentiles)	10.0 (7.0 to 13.0)	14.0 (11.0 to 15.0)	11.0 (7.8 to 14.0)	0.013

The cut-off value for predicting mortality for H3B2 was 5 and the AUC value was 0.720. AUC, cut point, sensitivity (%), specificity (%), positive predictive value PPV (%) and negative predictive value NPV (%) of scores are given in Table 3. There was no significant difference between AUCs of GBS, AIMS65 and H3B2 (p=0.862 DeLong tests). Among the scores, H3B2 had the highest odds ratio for mortality, 7.74 (95% confidence interval 2.4-24.92). Odds ratios and 95% confidence intervals of the scores are presented in Table 4. When Lactate and albumin values were added to the H3B2 score, the AUC value reached 0.910 and gained stronger predictive ability. Binominal logistic regression analyzes of parameters that are significant for mortality are shown in Table 5. The ROC curve of the scores to predict mortality and the roc curve of the model we proposed by adding lactate and albumin are presented in Figure 1.

Discussion

In this study, we validated the H3B2 score on 116 Turkish patients who presented to the emergency department with the complaint of UGIB. Also, we compared predictability of short-term mortality with GBS and AIMS65. The H3B2 score was able to successfully predict short-term mortality with high specificity (87.13%). It was as successful as the

Table 3. The area under the receiver operating characteristic curve values of scores

	Cut point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
H3B2 scoring	5	53.33%	87.13%	38.10%	92.63%	0.720
AIMS65 scoring	3	66.67%	76.24%	29.41%	93.90%	0.760
Glasgow-Blatchford scoring	10	66.67%	69.31%	24.39%	93.33%	0.700

AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value

Table 4. Odds ratios of the scores and 95% confidence intervals

		95% confidence intervals	
	Value	Lower	Upper
Glasgow-Blatchford scoring	7.74	2.4	24.92
AIMS65 scoring system	4.63	0.99	21.59
H3B2 scoring	2.98	0.81	10.97

Table 5. Logistic regression analysis of the parameters and AUC of the proposed model

Predictor	p	Odds ratio	95% confidence intervals	
			Lower	Upper
Intercept	0.829	0.52	0	184.21
Blood urea nitrogen	0.132	1.01	1	1.01
Hematemesis	0.369	0.48	0.1	2.38
Pulse rate	0.279	1.02	0.99	1.04
Systolic blood pressure	0.795	1	0.96	1.03
Hemoglobin	0.395	1.15	0.83	1.59
Lactate	0.003	1.66	1.19	2.32
Albumin	0.009	0.17	0.05	0.64
	Accuracy	**Specificity**	**Sensitivity**	**AUC**
Model	0.91	0.98	0.47	0.91

AUC: Area under the curve

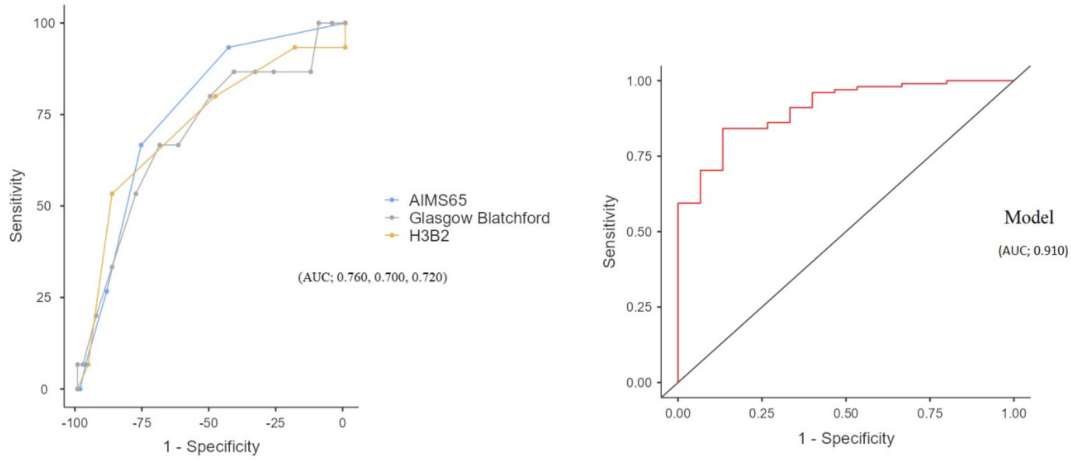

Figure 1. The ROC curve of the scores to predict mortality and the ROC curve of the model we proposed by adding lactate and albumin

ROC: Receiver characteristic operation, AUC: Area under the curve

GBS and AIMS65 scores commonly used in emergency clinics in predicting poor outcome.

It is important to categorize the patients with suspected UGIB for poor outcome as well as the diagnosis. The need for early intervention in high-risk patients and the effect of early intervention on mortality have been shown in many studies (10,11). Early endoscopic intervention associated with lower mortality was reported in a study of more than 900 patients (11). In their study with 240 non-variceal UGIB patients, Güven et al. (12) found that early endoscopic intervention could reduce blood transfusion and reduce health expenditures. These studies showed that the determination of severity and the decision of early endoscopy intervention in patients with UGIB are important for both mortality and quality of treatment. In 1995, Rockall et al. (13) they proposed a new scoring system for the evaluation and management of the UGIB. In 1997, Blatchford et al. (14) associated the mortality of UGIB patients with comorbidity, age, BUN, and hypotension, and then GBS was developed for UGIB. In 2011, Saltzman et al. (15) developed AIMS65 and recommended its application in UGIB patients, highlighting its ease of use. In a retrospective study conducted in Japan in 2022 on 675 patient data, it was shown that the H3B2 score developed was more successful than these scores in predicting hemostatic therapy and mortality (9). This newly developed score includes hemodynamic parameters such as heart rate and systolic blood pressure. Since blood pressure and pulse rate are negatively affected in critically ill patients, it is expected that this score can predict mortality (16). The H3B2 score was as successful as GBS and AIMS65 in our study. We thought that the reason why the scores have the same predictive ability is because the parameters they contain are different but independent predictors. Differently, H3B2 had the best outcome for short-term mortality in the odds ratios than GBS, and AIMS65. For a better outcome, we showed that H3B2 has a higher predictive power for mortality when lactate and albumin were included (AUC 0.910). Albumin is known to be associated with mortality in UGIB (17,18). Albumin was significant for mortality in our study. Liver diseases, chronic diseases or malnutrition in patients with UGIB may be the reasons for the change in albumin levels. Similarly, lactate has been shown to be associated with mortality in UGIB as in many diseases (19). Perfusion failure, which develops as a result of deterioration of hemodynamics in bleeding patients, may be a cause of high lactate (20,21). In addition, albumin and lactate measurements are easily accessible and frequently measured blood values in emergency services. For these reasons, adding lactate and albumin to the H3B2 score will provide stronger results for mortality prediction.

Study Limitations

There are some limitations in our study. It is a retrospective study. Sample size smaller than Sasaki et al. (9). We did not differentiate the patients as those who underwent early endoscopy intervention and those who underwent delayed intervention. Therefore, we could not calculate the predictive power of the scores in early and delayed intervention.

Conclusion

H3B2 was successful in predicting short-term mortality in Turkish patients. This was able to predict as poor outcome as the GBS and AIMS65. We recommend adding lactate and albumin to the H3B2 score for stronger results.

Ethics

Ethics Committee Approval: The study was conducted following the principles of the Declaration of Helsinki, and ethical agreement was provided by the Local Committee of University of Health Sciences Turkey, Ümraniye Training and Research Hospital (no: 277, date: 08/09/2022).

Informed Consent: In keeping with the policies for a retrospective review, informed consent was not required.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: A.Ö., K.Ö., A.A., A.C., Design: A.Ö., K.Ö., A.A., A.C., Data Collection or Processing: A.Ö., K.Ö., A.A., A.C., Analysis or Interpretation: A.Ö., K.Ö., A.A., A.C., Final Approval and Accountability: A.Ö., K.Ö., A.A., A.C., Drafting Manuscript: A.Ö., K.Ö., A.A., A.C., Critical Revision of Manuscript: A.Ö., K.Ö., A.A., A.C., Writing: A.Ö., K.Ö., A.A., A.C.

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ORIGINAL RESEARCH

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Diagnostic Prevalence of Celiac Disease by Routine Duodenum Biopsy in Adult Patients with Iron Deficiency

Demir Eksikliği Olan Erişkin Hastalarda Rutin Duodenum Biyopsi ile Çölyak Hastalığının Tanısal Prevalansı

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Abstract

Objective: Iron deficiency anemia (IDA) frequently emerges as a consequence of Celiac disease (CeD), and in some cases, it can be the sole clinical manifestation of the condition, especially among patients with subclinical or atypical forms. Histological analysis plays a pivotal role in the diagnostic process. Our study aimed to assess the significance of duodenal biopsies in diagnosing CeD among patients with IDA of unknown origin and to determine the prevalence of CeD within the group of patients with unexplained IDA.

Method: Between June 2019 and December 2022, we enrolled 248 consecutive patients aged 18 and above who underwent duodenal biopsies during esophagogastroduodenoscopy procedures for evaluating unexplained IDA in our endoscopy unit. A retrospective analysis of CeD prevalence was performed. Patients with abnormal duodenal histology were tested for anti-endomysium antibody and tissue transglutaminase antibody levels. A positive serological test along with abnormal duodenal histology confirmed the diagnosis of CeD. Histopathological changes were categorized according to the Marsh classification.

Results: A total of 248 patients, including 171 women, meeting the study criteria were included. CeD was identified in 8 (3.2%) patients who underwent duodenum biopsies. The average age of celiac patients was 36±14 years, and the female-to-male ratio was 1.3:1. Histopathology revealed Marsh III in 5 (62.5%) patients, Marsh II in 2 (25%), and Marsh I with lesions in 1 (12.5%) patient. All patients with pathological changes in duodenal biopsies (Marsh I, II & III) tested positive serologically. No significant differences were observed in mean hemoglobin, mean corpuscular volume, and ferritin levels between patients with and without CeD accompanied by IDA.

Öz

Amaç: Çölyak hastalığı (ÇH), demir eksikliği anemisinin (DEA) iyi bilinen bir nedenidir. DEA, özellikle subklinik veya atipik ÇH olan hastalarda, ÇH'nin tek klinik belirtisi olabilir. Histolojik inceleme en önemli tanı aracıdır. Çalışmamızda nedeni bilinmeyen DEA ile başvuran hastalardan alınan duodenal biyopsilerin ÇH tanısındaki rolünü ve nedeni bilinmeyen DEA'lı hastalarda ÇH prevalansını incelemeyi amaçladık.

Yöntem: Haziran 2019-Aralık 2022 tarihleri arasında endoskopi ünitemizde nedeni bilinmeyen DEA'nın değerlendirilmesi kapsamında özofagogastroduodenoskopi işlemi sırasında duodenal biyopsi yapılan 18 yaş üstü ardışık 248 hasta çalışmaya dahil edildi. ÇH prevalansı retrospektif olarak değerlendirildi. Anormal duodenal histolojiye sahip hastaların anti-endomysiyal antikor ve doku transglutaminaz antikor seviyeleri değerlendirildi. ÇH tanısı pozitif serolojik test ve anormal duodenal histoloji ile konuldu. Histopatolojik değişiklikler Marsh sınıflamasına göre değerlendirildi.

Bulgular: Çalışma kriterlerini karşılayan toplam 248 hasta (171 kadın) çalışmaya alındı. Duodenum biyopsisi alınan 8 (%3,2) hastada ÇH saptandı. ÇH'nin yaş ortalaması 36±14 idi. Kadın erkek oranı 1,3:1 olarak bulundu. Histopatoloji 5 hastada (%62,5) Marsh evre III, 2 hastada (%25) Marsh evre II ve 1 hastada (%12,5) Marsh evre I lezyonları gösterdi. Duodenal biyopside (Marsh I, II & III) patolojik değişiklik gösteren tüm hastaların serolojisi pozitifti. ÇH olan ve olmayan DEA olan hastalar arasında ortalama hemoglobin, ortalama alyuvar hacmi ve ferritin düzeylerinde anlamlı fark yoktu.

Sonuç: DEA hastalarının üst endoskopik muayenesi sırasında alınan rutin duodenal biyopsiler ÇH'de tanısal fayda sağlamaktadır. Bu nedenle,

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Abstract

Conclusion: Routine duodenum biopsies performed during upper endoscopic examinations of IDA patients contribute to a diagnostic yield of 3.2% for CeD. Thus, even in cases where the endoscopic appearance of the mucosa seems normal, this procedure should be routinely integrated into the diagnostic evaluation of patients with IDA.

Keywords: Celiac disease, duodenal biopsy, iron deficiency anemia

Öz

bu uygulama, mukozanın endoskopik görünümü normal olsa bile, DEA'lı hastaların tanısal çalışmalarında sistematik olarak yer almalıdır.

Anahtar kelimeler: Çölyak hastalığı, demir eksikliği anemisi, duodenal biyopsi

Introduction

Celiac disease (CeD) is an enteropathy triggered by gluten sensitivity, characterized by small intestine villous atrophy, primarily affecting genetically predisposed individuals. Its global prevalence is estimated to range between 0.5% and 1% (1). While classic malabsorption symptoms such as diarrhea and weight loss are only present in a small fraction of celiac patients, the majority exhibit subclinical or silent forms (2). Early consideration of CeD disease is crucial for accurate diagnosis. Despite the estimated prevalence of CeD in our country being around 0.5-1%, it is believed that asymptomatic or atypical cases are more common. Thus, CeD should be considered in the differential diagnosis, particularly for patients presenting with atypical symptoms.

Anemia frequently accompanies CeD and sometimes can be its sole manifestation. The cause of anemia might stem from deficiencies in vitamin B12 and folic acid absorption. Iron deficiency is the primary cause of anemia in CeD. Iron deficiency anemia (IDA) is a common extraintestinal manifestation of subclinical and silent CeD presentations (3).

The prevalence of IDA in subclinical CeD has been reported to be up to 46% in adults compared to children (4). The IDA observed in CeD arises from impaired iron absorption due to duodenal mucosal villous atrophy and the multifaceted etiology that triggers the mechanism leading to anemia of chronic disease (5).

Guidelines for managing IDA from the American Academy of Family Physicians and the British Society of Gastroenterology recommend considering CeD in the differential diagnosis of patients undergoing anemia investigation (6,7). The prevalence of CeD among adult patients with IDA is estimated to be around 2-3%. Specific serum antibody testing should be conducted for suspected CeD cases. Upper GI endoscopy and small bowel biopsy play a crucial role in diagnosing suspected CeD and are recommended for confirming the diagnosis (6-8). Common serological tests for CeD involve measuring serum endomysium antibodies (EMAs) and antibodies against tissue transglutaminase (tTG). According to studies, anti-tTG immunoglobulin A (IgA) exhibits a sensitivity and specificity of 92.5% and 97.9%, respectively. While the anti-tTG IgA test is less sensitive, the EMA IgA test boasts greater specificity, with sensitivity and specificity of 79.0% and 99.0%, respectively (9). The primary CeD screening test is anti-tTG IgA, while EMA IgA is often utilized for confirmation. The presence of villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis in duodenal mucosal biopsy remains the gold standard for diagnosing CeD. Positive serology specific to CeD among patients with villous atrophy confirms the diagnosis. Although limited population-based screening is performed on specific adult groups in our country, no comprehensive study has been conducted.

Turkey has seen limited studies exploring the prevalence of adult CeD among patients with unexplained IDA. Our study seeks to determine the prevalence of CeD detected through routine duodenum biopsies during endoscopy in patients with unexplained IDA.

Materials and Methods

Patients and Methodology

Conducted between 2019 and 2022 at the Gastroenterology Endoscopy Unit of University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, our study focused on patients over 18 referred to the institute's endoscopy department for IDA evaluation. Ethical approval for this retrospective study was obtained from the University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital Clinical Research Ethics Committee (07/04/2023, no: 166). Informed consent was collected from patients, and anemia was defined as a hemoglobin (Hb) level <13 g/dL for men and <12 g/dL for women (10).

Patients with evident blood loss, such as those with a history of melena, hematochezia, hemoptysis, recurrent epistaxis,

hematuria, trauma, hypermenorrhea (lasting 7 days or more), menometrorrhagia, pregnancy, gastric surgery, severe respiratory or cardiac conditions, known chronic diseases, and hematological diseases were excluded.

Endoscopies were performed by two gastroenterologists (ND, BY) following standard procedures using a fiber optic Olympus gastro-duodenoscope. Patients without sedation received a topical anesthetic of 5% xylocaine for the oropharynx. Sedation (propofol 1 mg/kg, ketamine 0.5 mg/kg, fentanyl 1 µg/kg) was administered at the anesthesiologist's discretion.

Duodenal biopsy was taken from all patients in the study. According to the Marsh categorization method, the patients' histological examination results were categorized (11): Normal mucosa was defined as Marsh 0; Increased intraepithelial lymphocyte count as Marsh I; crypt hyperplasia as Marsh II; Partial or complete villous atrophy as Marsh III; Incomplete development (hypoplasia) of the small intestine as Marsh IV.

CeD has been defined as the presence of elevated levels of Anti-tTG and/or EMA in addition to abnormal duodenal histology (such as Marsh 1, 2, or 3). Anti-tTG Ig A and anti-tTG IgG antibodies were analyzed via Enzyme Linked Immunoabsorbent Assay (ELISA) method using a diagnostic kit (IMMCO42 diagnostics, ImmuLisaTM, Buffalo, NY, USA). Patients with anti-tTG Ig A, anti-tTG IgG, and anti-EMA antibody levels of <10 EU/mL were considered seronegative, of 10-15 EU/mL borderline, and of >15 EU/mL seropositive.

Statistical Analysis

The data obtained from the research were analyzed using the statistical package program SPSS (Statistical Package for Social Sciences) 15.0. The data were expressed as mean and standard deviation. The normal distribution of the measurement parameters was examined by the "Kolmogorov-Smirnov test", and in the comparison of groups, independent groups t-test was used for parametric data. P-value was determined as <0.05 and confidence interval was accepted and evaluated as 95%.

Results

A total of 248 patients, including 171 women and 77 men, who underwent duodenal biopsy due to iron deficiency anemia, were included in the screening. The mean age of the patients was 3±15 years. CeD was detected in 8 of these patients, resulting in an incidence of 3.2%. The mean age of patients with CeD was 36±14 years. The incidence of CeD was higher in women (6F/2M), with a female-to-male ratio of 1.3:1. The demographic characteristics of the study patients are summarized in Table 1.

The mean Hb value, mean corpuscular volume (MCV), and median ferritin level in patients with CeD were 9.89±1.56 g/dL, 72.57±6.22, and 8.13 ng/mL±8.71, respectively. Table 2 compares the mean Hb, MCV, and serum ferritin levels of patients with IDA and CeD with those of patients with IDA but without CeD. For (Hb: 9.89±1.56 versus 10.23±1.63 g/dL), MCV (72.57±6.22 versus 73.76±6.64 fL), and ferritin levels (8.13±8.71 versus 8.93±9.96 ng/mL) between the two groups, there were no statistically significant differences (p>0.05). Histopathology indicated Marsh III lesions in 5 (62.5%) patients, Marsh II lesions in 2 (25%) patients, and Marsh I lesions in 1 (12.5%) patient (Figure 1).

Discussion

In our study, CeD was observed three times more frequently in women than men. Among the 248 patients who underwent duodenal biopsies for unexplained IDA, CeD

Table 1. Patient characteristics

Characteristics	Patients with iron deficiency anemia n (%)	Patients with disease CeD n (%)
Patient no	248	8
Sex (female /male)	171 (69%)/77 (31%)	6 (75%)/2 (25%)
Age (mean ± SD, yr)	39±15	36±14

SD: Standard deviation, CeD: Celiac disease

Table 2. Hematological parameters in IDA patients with and without CeD

Index	IDA patients with coeliac disease	Patients without coeliac disease	p*
Hb (g/dL)	9.89±1.56	10.23±1.63	0.456[t]
MCV (fL)	72.57±6.22	73.76±6.64	0.089[t]
Ferritin (ng/mL)	8.13±8.71	8.93±9.96	0.170[t]

IDA: Iron deficiency anemia, [t]: Student's t-test, *p<0.05 was considered significant, CeD: Celiac disease, MCV: Mean corpuscular volume, Hb: Hemoglobin

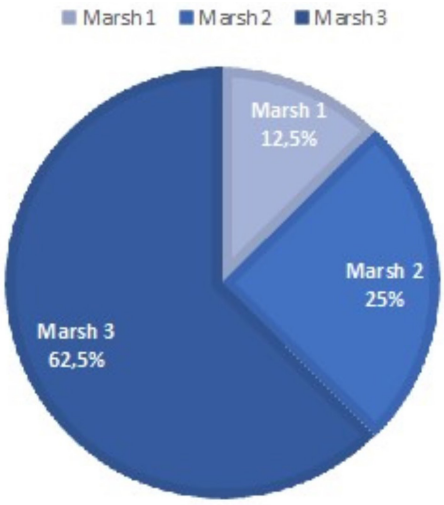

Figure 1. Histopathological examination in patients with disease (Marsh classification)

was identified in 8 (3.2%) cases. However, no significant differences in mean hemoglobin, MCV, and ferritin levels were found between patients with and without CeD accompanied by iron deficiency anemia.

CeD may manifest with various gastrointestinal tract symptoms, extraintestinal findings, or accompanying autoimmune diseases. The etiology of the disease is thought to involve immunological and genetic factors, as well as demographic characteristics such as age, gender, nutritional habits, and the extent of mucosal inflammation (12).

A majority of patients with atypical complaints in our study did not present with gastrointestinal symptoms. While only a small proportion of adult CeD patients exhibit classic symptoms of diarrhea and/or malabsorption, most patients have subclinical or silent forms. IDA is the most common extraintestinal finding in CeD (2). Anemia, especially idiopathic IDA, raises strong suspicion of CeD without any other apparent cause. For many patients, IDA may be the sole reason for presentation (13), with reports indicating that patients with unexplained iron deficiency are more likely to have CeD than adults in the general population (14).

The recommendations of the British Society of Gastroenterology suggest taking duodenal endoscopic biopsies when no obvious cause for iron deficiency is identified (8). In our study cohort, the prevalence of CeD among patients who underwent duodenal biopsies for unexplained IDA was 3.2%, consistent with previous reports of 2-3% in adult IDA patients (8).

A systematic review and meta-analysis by Mahadev et al. (15) in 2018, including 2998 individuals, reported that biopsy-proven CeD is relatively common in patients with IDA, with a prevalence ranging from 2.6% to 3.9% (15).

Studies conducted with children in Turkey (16-20) found an average prevalence of 4.1%. Similarly, Gonen et al. (20) performed duodenal biopsies in adult patients with IDA, revealing a prevalence of 3% for celiac disease.

Similar results in terms of hematological parameters are present in other studies. Our research found no differences in MCV, hemoglobin, or ferritin levels between patients with CeD and those with anemia of unknown origin (Table 2). Zamani et al. (21) did not identify a statistically significant relationship between hemoglobin and ferritin levels in patients with CeD and their histopathological changes. Ganji et al. (22) reported that there was no definitive link between the severity of anemia and intestinal mucosal damage according to the Marsh classification. However, some studies support the hypothesis of a potential relationship between the severity of anemia and the degree of intestinal atrophy in celiac patients (23).

CeD is more prevalent in women (24). In our study, CeD was observed three times more frequently in women than men, consistent with the higher prevalence of CeD in women in our country (25,26). While gender differences are significant in many diseases, autoimmune diseases provide a striking example, with women having a 2-3 times higher risk of developing autoimmune diseases than men. Similar trends are observed in celiac disease.

The retrospective nature of this study, which might introduce inherent referral bias due to the selection of patients referred for endoscopy, is one of its limitations. Additionally, like other observational studies, it is challenging to distinguish between causality and correlation. Selection bias may also be present, as women are more prone to disruptions in iron absorption, either due to iron loss or related conditions.

Conclusion

Given that CeD, the prevalence of which is on the rise, can be managed through a gluten-free diet, early detection is crucial to prevent potential complications and improve patient quality of life. Although IDA is often the initial complaint in cases of non-classical/extraintestinal celiac disease, many physicians rarely screen for CeD as part of their initial assessment. Our findings underscore the importance of identifying anemic patients who may have underlying celiac disease. Recognizing and diagnosing celiac disease, even in cases where IDA is the sole

manifestation, can prevent complications and enhance patient outcomes by enabling timely intervention and dietary management.

Ethics

Ethics Committee Approval: Ethical approval for this retrospective study was obtained from the University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital Clinical Research Ethics Committee (07/04/2023, no: 166).

Informed Consent: We had oral consent of patients.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.D., S.G.B., Concept: N.D., B.Y., Design: N.D., B.Y., E.K., Data Collection or Processing: N.D., B.Y., E.K., S.G.B., Analysis or Interpretation: N.D., E.K., S.G.B., Literature Search: N.D., E.K., Writing: N.D.

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ORIGINAL RESEARCH

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Evaluation of Kinesiophobia, Pain and Functional Status in Adhesive Capsulitis and Rotator Cuff Syndrome

Adeziv Kapsülit ve Rotator Manşon Sendromunda Kinezyofobi, Ağrı ve Fonksiyonel Durumun Değerlendirilmesi

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Abstract

Objective: Kinesiophobia, which is defined as the fear of moving due to the fear of re-injury, impairing the quality of life of the patients, causes various degrees of disability and participation problems, adversely affects the treatment, and may cause the pain to become chronic and may predispose to depression. Severe pain and limitation of movement in a short time are common in muscle, joint and ligament pathologies of the shoulder, which is one of the most common problems of the upper extremity. We aimed to conduct this study in patients with a diagnosis of rotator cuff and adhesive capsulitis, anticipating that the presence and degree of kinesiophobia should be considered when planning treatment for shoulder diseases.

Method: A total of 80 patients, aged 30-75 years, who had shoulder pain complaints for at least 1 month and applied to the outpatient clinic for rehabilitation, diagnosed with rotator cuff syndrome (n=40) and adhesive capsulitis (n=40) were included in the study. Pain degree of the patients, active joint range measurement of the painful shoulder, anxiety and depression, degree of disability and presence of kinesiophobia; it was evaluated with the numerical rating scale (NRS), the arm, shoulder and hand problems questionnaire (DASH), the hospital anxiety depression scale (HAD), and the Tampa kinesiophobia scale. The patients voluntary consent for the study and approval of University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committe with protocol number 2019-421 was obtained on 12.09.2019.

Öz

Amaç: Tekrar yaralanma korkusuna bağlı hareket etme korkusu olarak tanımlanan kinezyofobi, hastaların yaşam kalitesini olumsuz etkileyerek çeşitli derecelerde özür ve katılım problemlerine yol açmakta, tedaviyi olumsuz etkilemekte ve ağrının kronikleşmesine, depresyona yatkınlığa neden olabilmektedir. Sık görülen kas iskelet sistemi problemlerinden olan omuz hastalıklarında ağrı ve kısa sürede gelişen hareket kısıtlılığı önemli bir sorun olarak karşımıza çıkmaktadır. Omuz hastalıklarında tedavi planlanırken kinezyofobinin varlığının ve derecesinin de göz önünde bulundurulması gerektiğini öngörerek rotator manşon ve adeziv kapsülit tanılı hastalarda bu çalışmayı yapmayı amaçladık.

Yöntem: Çalışmaya fiziksel tıp ve rehabilitasyon kliniği ayaktan hasta polikliniğine en az bir aydır olan omuz ağrısı şikayeti nedeniyle başvuran, 30-75 yaş arası, radyolojik ve klinik muayene ile 40 (n=40) rotator manşon sendromu ve 40 (n=40) adeziv kapsülit tanısı konulmuş hastalar dahil edildi. Hastaların ağrı yoğunluğu (hareketle-istirahatte), ağrılı omuz aktif eklem açıklığı ölçümü, psikolojik durum, engellilik ve kinezyofobi varlığı; sayısal değerlendirme ölçeği (NRS), Kol, omuz ve el sorunları anketi (DASH), hastane anksiyete depresyon ölçeği (HAD) ve Tampa kinezyofobi ölçeği ile değerlendirildi. Hastalardan gönüllü onam formu onayı alındı ve Sağlık Bilimleri Üniversitesi, İstanbul Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Etik Kurulu'ndan 12.09.2021 tarihinde 2019-421 protokol numarası ile etik onay alındı.

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Abstract

Results: NRS with movement, at rest and sleep, HAD and TAMPA measurements of the cases did not show any statistically significant difference according to the groups (p>0.05). The DASH score of the cases in the adhesive capsulitis group was found to be statistically significantly higher than that of the cases in the rotator cuff syndrome group (p<0.05). In both groups, a moderate kinesiophobia score was determined according to the Tampa kinesiophobia scale. However, there was no statistically significant difference between the groups.

Conclusion: In this study, kinesiophobia was detected in both patients with rotator cuff syndrome and adhesive capsulitis. It is emphasized that in addition to pain, functional status and psychological factors, the presence of kinesiophobia should be considered in the evaluation, treatment planning and follow-up of patients.

Keywords: Adhesive capsulitis, kinesiophobia, rehabilitation, rotator cuff syndrome, shoulder pain

Öz

Bulgular: Olguların hareketle, istirahat ve uykuda NRS değeri, HAD ve TAMPA ölçümleri istatistiksel olarak gruplar arasında anlamlı farklılık göstermedi (p>0,05). Adeziv kapsülit grubunda ki olguların DASH skoru rotator manşon sendromu grubunda ki olgulardan istatistiksel olarak anlamlı düzeyde yüksek bulundu (p<0,05). Her iki grupta da Tampa kinezyofobi ölçeğine göre orta derece kinezyofobi puanı belirlendi. Fakat gruplar arasında istatistiksel olarak anlamlı bir fark yoktu.

Sonuç: Bu çalışmayla kinezyofobi gerek rotator manşon sendromu tanılı gerekse adeziv kapsülit tanılı omuz ağrılı hastalarda saptanmıştır. Bu hastalarda ağrı, fonksiyonel durum ve psikolojik faktörlerin yanı sıra kinezyofobinin de göz önünde bulundurulması gerektiği vurgulanmaktadır. Tedavinin planlanmasında kinezyofobi varlığı göz önünde bulundurulmalıdır.

Anahtar kelimeler: Adeziv kapsülit, kinezyofobi, omuz ağrısı, rehabilitasyon, rotator manşet sendromu

Introduction

Shoulder pain is one of the important medical, social and economic problems affecting the upper extremity in the society. Shoulder pain is an important cause of morbidity, which ranks third after low back and neck pain in musculoskeletal pain admissions in primary care (1). In a Cochrane study in which all interventions related to shoulder diseases were compiled, it was reported that shoulder pain is seen between 6.9% and 34% in the general population and the treatment of shoulder disorders constitutes 1.2% of all general treatments (2). Pain and limitation of movement that develops in a short time in shoulder diseases appear as an important problem. It has been shown that pain and limitation of movement continued for at least 1 month in 18.6-31% of the patients, and persistent symptoms developed in 22-68% up to 12 months (3). Rotator cuff syndrome is the cause of pain in 0.5-7.4% of patients suffering from shoulder pain, and adhesive capsulitis is the cause of pain in approximately 2-5% (4-6). In recent studies, in addition to the shoulder pain caused primarily by the shoulder joint and surrounding structures; some other factors are reported to be effective in the development and chronicity of pain and limitation. Especially psychological factors (anxiety, depression, fear) are indicated in studies as capable to have an effect on shoulder diseases. Among these factors, fear has an important place; especially trying to protect the painful shoulder of the patient due to fear of movement may increase the limitation of motion and disability of the shoulder (7,8). Kinesiophobia, which is defined as the fear of movement and activity due to the feeling of painful injury or re-injury, negatively affects the rehabilitation of the patients, increases their limitations and causes the pain to become chronic. There are few studies evaluating the effect of kinesophobia on pain and functional status in patients with rotator cuff syndrome and adhesive capsulitis in the literature (2,3). The aim of this study was to investigate the degree of kinesiophobia and its effect on pain and functional status in patients with rotator cuff syndrome and adhesive capsulitis.

Materials and Methods

Patients between the ages of 30 and 75 years, who were diagnosed with rotator cuff syndrome and adhesive capsulitis by radiological (magnetic resonans imaging) and clinical examination, who were admitted to the outpatient clinic of the physical medicine and rehabilitation clinic with complaints of shoulder pain at least for a month, were included in this study. The demographic data of the patients (age, gender, educational status, occupation, etc.) were recorded. In addition, detailed anamnesis, detailed locomotor system examinations and neurological examinations of the patients were carried out by an experienced physical medicine and rehabilitation physician. The shoulder range of motion of the patients were measured and special tests (Hawkins, neer, shoulder painful arc test, Supraspinatus isometric strength tests) were applied for the diagnosis of rotator cuff syndrome and adhesive capsulitis. Patients with a history of systemic disease (diabetes mellitus, heart disease, etc.), rheumatological disease, malignancy, stroke, multiple sclerosis, entrapment neuropathies, etc. neurological conditions, habitual shoulder subluxation, fracture history, previous surgery history, psychosomatic or

major depression and patients with history of a shoulder intraarticular injection for the shoulder pain in the last 3 months were excluded from the study.

One hundred and thirty patients (n=130) who applied to our outpatient clinic with complaints of shoulder pain were evaluated. Reflected pain due to cervical discopathy in 10 patients, previous shoulder surgery in 2 patients, a painful shoulder injection one month ago in 6 patients, a history of additional disease in 13, bicipital tendinitis in 5, calcific tendinitis in 3, 11 of them due to their previous treatment were excluded from the study. A total of 80 people diagnosed with 40 adhesive capsulitis (n=40) and 40 rotator cuff syndrome (n=40) were included in the study. The patients were evaluated in terms of pain intensity (motion-rest), painful active range of motion of shoulder joint, psychological status, disability and kinesophobia. "Zero-ten" numerical rating scale (NRS) was used to evaluate the pain of the patients. The NRS consists of a 10 cm long horizontal line. The sign at the beginning of the line defines "0 cm" painlessness and the sign "10 cm" at the end of the line defines the highest unbearable pain (9). People were asked to put a mark on this horizontal line for the maximum pain they felt during rest, sleep and activity, and the results were recorded in "cm".

Active shoulder range of motion measurement was performed by an experienced physician with goniometer in flexion, extension, abduction, external and internal rotation movements, and the average of 3 measurements was taken.

Shoulder disability and function were evaluated with the disabilities of the arm, shoulder and hand questionnaire (DASH). The DASH questionnaire consists of 21questions are answered according to the 5-point Likert system. It is scored between 0 and 100 (0- no disability, 100- maximum disability). Its Turkish validity and reliability were made in 2006 by Düger et al. (10,11).

Psychological state was evaluated with the hospital anxiety depression scale (HAD). HAD is a scale in which the symptoms of anxiety and depression are screened, completed by the patient and used frequently in the hospital setting (12). Points between 0-7 are considered normal, 8-10 points are considered borderline, and over 11 are considered abnormal. Its Turkish validity and reliability were made by Aydemir et al. (13).

Tampa kinesophobia scale (TKS) was used to evaluate kinesiophobia. The original of TKS was developed by Robert et al. (14). In 1995, the final version of 17 questions was published by Vlaeyen et al. (15). In our country, the validity and reliability of TKS in Turkish in 2011 was made by Tunca Yılmaz et al. (16). The total score between 13-22 is mentioned that the kinesophobia is subclinical, 23-32 mild, 33-42 moderate, and 43-52 severe kinesophobia (17).

The patients' voluntary consent for the study 2019-421 number and 12.09.2019 University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee approval was obtained on.

Statistical Analysis

NCSS (Number Cruncher Statistical System) program was used for statistical analysis. Descriptive statistical analysis (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The suitability of quantitative data to normal distribution was tested by Shapiro-Wilk test and graphical analysis. Student's t-test was used for comparing normally distributed quantitative variables between two groups, and Mann-Whitney U test was used for comparing quantitative variables that did not show normal distribution between two groups. In comparison of qualitative data, Pearson chi-square test, Fisher's Exact test and Fisher-Freeman-Halton exact test were used. Statistical significance was accepted as $p<0.05$.

Results

The study was conducted with a total of 80 cases, 63.7% (n=51) of whom were female and 36.3% (n=29) of whom were male. The ages of the subjects participating in the study ranged from 34 to 75, and the mean age was found to be 54.69±9.85 years. The socio-demographic characteristics of the patients are shown in Table 1.

In the study, age, gender, marital status, education, occupation, dominant hand and painful shoulder distributions did not show statistically significant difference between the groups ($p>0.05$). There was female gender and housewife majority in both groups. The diseased shoulder is the dominant upper extremity side.

The range of motion measurements (flexion, extension, abduction, internal and external rotation), kinesiophobia and quality of life values of the affected shoulder joint in all directions of the groups are shown in Table 2.

Shoulder flexion, extension, abduction, adduction and rotation range of motion measurement values of the cases in the adhesive capsulitis group were found to be significantly lower than the cases in the rotator cuff syndrome group

(p<0.05). Pain NRS (movement, rest and sleep), HAD and TKS measurements of the cases did not show any statistically significant difference according to the groups (p>0.05). The DASH score of the cases in the adhesive capsulitis group was found to be statistically significantly higher than the cases in the rotator cuff syndrome group (p<0.05).

The mean score of kinesiophobia was 40.44, the score was 41.43 in the adhesive capsulitis group and 39.45 in the rotator cuff syndrome group. Moderate kinesiophobia was detected in both groups. However, there was no statistically significant difference between the groups. The correlation of kinesiophobia on shoulder range of motion, disability and pain intensity in both groups is shown in Table 3. There was a weak correlation between kinesiophobia and pain and limitation of joint movement in the group with rotator cuff syndrome.

Discussion

While the symptoms and signs of adhesive capsulitis and rotator cuff syndrome overlap, the patient's complaints often differ. While patients with adhesive capsulitis often have severe pain; there is also reduced active and passive range of motion. (18). Patients with rotator cuff syndrome typically complain of pain with active movement. However, passive range of motion is usually with in normal limits. In acute and chronic pain, a negative vicious circle occurs between avoidance of movement and pain (19). In this study, we investigated the effect of kinesiophobia on pain and functionality in patients with rotator cuff syndrome and adhesive capsulitis. In the study, no superiority was found in pain level between the groups, but shoulder ROM measurements were more limited in the adhesive capsulitis group. However, no significant difference was found between groups, in which we evaluated the degree of kinesiobia, and the pain and ROM measurements.

Kinesiophobia was defined for the first time in 1990 as "a fear of activity that reduces excessive, irrational, and physical movement resulting from a feeling of vulnerability to painful injury or re-injury" [Kori et al. (20)]. When pain is perceived as a non-threatening perception, the people try to participate in daily activities. On the contrary, if the pain is perceived as catastrophic and there is a fear associated with the pain, avoidance of pain and safety-seeking behaviors may occur (20). Recent studies have also shown that kinesiophobia, which is defined as the fear of moving,

Table 1. Evaluation of demographic characteristics of patients with rotator cuff syndrome and adhesive capsulitis

Total		Groups			
		Adeziv capsulit	Rotator cuff syndrome	p	
Age	Min-max (median)	34-75 (54)	38-75 (56.5)	34-70 (52.5)	[a]**0.055**
	Med ± SD	53.64±8.58	55.50±7.83	51.77±8.98	
Gender	**Female**	51 (63.7)	24 (60.0)	27 (67.5)	[b]**0.485**
	Male	29 (36.3)	16 (40.0)	13 (32.5)	
Marital status	**Single**	2 (2.5)	0 (0.0)	2 (5.0)	[c]**0.601**
	Married	68 (85.0)	35 (87.5)	33 (82.5)	
	Divorced	3 (3.8)	1 (2.5)	2 (5.0)	
	Widow	7 (8.8)	4 (10.0)	3 (7.5)	
Education status	**Primary school**	38 (47.5)	20 (50.0)	18 (45.0)	[b]**0.889**
	Middle school	17 (21.3)	9 (22.5)	8 (20.0)	
	High school	15 (18.8)	7 (17.5)	8 (20.0)	
	University	10 (12.5)	4 (10.0)	6 (15.0)	
Occupation	**Housewife**	30 (37.5)	16 (40.0)	14 (35.0)	[c]**0.802**
	Shoulder strain job	15 (18.8)	8 (20.0)	7 (17.5)	
	Retired	26 (32.5)	13 (32.5)	13 (32.5)	
	No-shoulder job	9 (11.3)	3 (7.5)	6 (15.0)	
Dominant hand	**Right**	74 (92.5)	36 (90.0)	38 (95.0)	[d]**0.675**
	Left	6 (7.5)	4 (10.0)	2 (5.0)	
Shulder pain	**Right**	45 (56.3)	22 (55.0)	23 (57.5)	[b]**0.822**
	Left	35 (43.8)	18 (45.0)	17 (42.5)	

[a]Student's t-test, [b]Pearson chi-square test, [c]Fisher-Freeman-Halton test, [d]Fisher's Exact test, SD: Standard deviation

Table 2. Comparison of range of motion, pain, sleep quality, depression, anxiety, functional status and kinesiophobia values in patients with rotator cuff syndrome and adhesive capsulitis

Total		Groups			
		Adeziv capsulitis	Rotator cuff syndrom	p	
Shoulder flexion	Min-max (median)	30-180 (150)	30-170 (110)	90-180 (180)	[e]**0.001****
	Med ± SD	139.81±37.42	110.63±26.56	169±19.59	
Extantion	Min-max (median)	10-60 (42.5)	10-50 (40)	15-60 (45)	[e]**0.001****
	Med ± SD	38.81±12.51	32.75±13.25	44.88±8.12	
Abduction	Min-max (median)	30-180 (110)	30-170 (90)	70-180 (175)	[e]**0.001****
	Med ± SD	125.63±43.63	94.75±27.64	156.5±33.71	
I. rotation	Min-max (median)	10-90 (50)	10-70 (45)	40-90 (70)	[a]**0.001****
	Med ± SD	56.38±18.35	44.75±11.93	68±16.2	
E. rotation	Min-max (median)	10-90 (45)	10-80 (40)	10-90 (70)	[e]**0.001****
	Med ± SD	52.19±22.75	39.63±15.42	64.75±22.07	
Movement NRS	Min-max (median)	0-10 (6)	0-10 (5.5)	0-10 (6.5)	[a]**0.478**
	Med ± SD	6.13±2.81	5.9±2.82	6.35±2.82	
At rest NRS	Min-max (median)	0-10 (8)	0-10 (7.5)	0-10 (8)	[e]**0.301**
	Med ± SD	6.94±2.94	6.75±2.66	7.13±3.21	
Sleep quality	Min-max (median)	0-10 (5)	0-10 (5)	0-10 (5)	[a]**0.496**
	Med ± SD	5.41±3.09	5.65±2.73	5.18±3.43	
HAD	Min-max (median)	0-21 (7)	0-21 (7)	2-17 (7)	[a]**0.424**
	Med ± SD	7.46±4.03	7.83±4.41	7.1±3.62	
TAMPA	Min-max (median)	23-58 (40)	29-58 (40.5)	23-54 (39.5)	[a]**0.185**
	Med ± SD	40.44±6.63	41.43±6.26	39.45±6.92	
DASH	Min-max (median)	5-98.3 (39.55)	13.3-98.3 (43)	5-69.2 (37.5)	[a]**0.005****
	Med ± SD	42.95±20.8	49.42±21.57	36.49±18.04	

[a]Student's t-test, [e]Mann-Whitney U test, **p<0.01, HAD: Hospital anxiety-depression scale, TAMPA: Kinesiophobia rating scale, DASH: Arm, shoulder, hand problems evaluation questionnaire, I. rotation: Internal rotation, E. rotation: External rotation, SD: Standard deviation, NRS: Numerical rating scale

Table 3. Relationship between TAMPA score and other parameters in groups

Adeziv capsulitis		TAMPA score	
		Rotator cuff syndrome	
Shoulder flexion	[g]r	-0.066	**-0.161**
	p	0.687	**0.322**
Extantion	[g]r	0.096	**-0.244**
	p	0.556	**0.129**
Abduction	[g]r	0.160	**-0.081**
	p	0.324	**0.617**
I. rotation	[g]r	-0.084	**-0.197**
	p	0.605	**0.223**
E. rotation	[g]r	0.064	**-0.243**
	p	0.693	**0.130**
Movement NRS	[f]r	-0.016	**0.246**
	p	0.920	**0.125**
At rest NRS	[g]r	0.110	**0.233**
	p	0.499	**0.147**
Sleep quality	[f]r	-0.180	**0.053**
	p	0.267	**0.747**
HAD	[f]r	-0.014	**0.032**
	p	0.932	**0.845**
DASH	[f]r	0.062	**-0.008**
	p	0.704	**0.962**

[g]Spearman's correlation coefficient, [f]Pearson correlation coefficient, DASH: Arm, shoulder, hand problems assessment questionnaire, I. rotation: Internal rotation, E. rotation: External rotation, HAD: Hospital anxiety-depression scale, NRS: Numerical rating scale

is associated with altered motor behaviors that may mask individuals true functional capacities when faced with a stressful action (8).

Kinesiophobia has been found to be a central factor in the pain process that develops from acute pain. The cognitive fear prevention model explains that when a painful experience is interpreted as threatening, the activity can produce disastrous cognitions that will cause further pain and re-injury. As this continues, it can lead to avoidance behavior in the long term causing a patient trapped in a cycle of increased pain, more pain and fear of disability as well as disability, use and depression (21). Supporting this model, studies on patients with chronic low back pain reported that patients with greater pain-related fear had higher pain and disability scores (15,18). In addition, studies on acute low back pain and osteoarthritis in primary care have confirmed the relationship between fear avoidance and disability (18,22). A meta-analysis by Zale et al. (23) showed a strong association between fear of pain and disability in people experiencing acute pain less than 3 months. This finding was consistent with the fear avoidance model of chronic pain, as pain-related fear may predict disability after acute injury and serve to preserve disability. There is also evidence showing that reduced fear of pain is associated with recovery after acute injury (26). In a study by Mintken et al. (24) it has been reported that fear of pain should be taken into account when evaluating patients with shoulder pain.

The main purpose in the treatment of shoulder disorders is to reduce pain and increase range of motion (24). In treatment, kinesiophobia is a barrier to physical activity. In addition, the resulting hypervigilance and avoidance behavior increase pain and disability. In addition, it can be used as a modifiable factor, and it is possible to achieve earlier pain relief and functional recovery (25,26).

Exercise therapy provides significant benefits in individuals with shoulder pain and is usually the first treatment option (8,25). In the follow-up of patients who were recommended exercise therapy in rotator cuff syndrome, it was observed that approximately 50% of them reapplied 6-12 months after the treatment with the complaint of chronic pain (26). This situation led to the need to investigate the underlying causes of shoulder pain (27,28). Symptoms of adhesive capsulitis can last up to several years. It is worrisome that the person restricts shoulder movements regardless of pain and protects the shoulder in daily work. In most studies investigating the relationship between pain and disability in patients who have medical treatment, physical therapy or undergone surgery, it has been stated that kinesiophobia is one of the causes in the chronicity of pain (6,29,30). Luque-Suarez et al. (8) similarly, in a study conducted by kinesiophobia, the effect of kinesiophobia on pain severity and disability was determined in individuals with chronic shoulder pain, and it was stated that it was an important factor in treatment. In contrast, Clausen et al. (31) however, they did not find the effect of kinesiophobia on pain and disability significant (8).

In this study, moderate kinesiophobia was detected in patients with adhesive capsulitis and rotator cuff tendinitis. However, when the two groups were compared, the effect of kinesiophobia on pain and functional status was not statistically significant. It was observed that patients with adhesive capsulitis were more anxious about exercising. We think that this anxiety will decrease with pre-treatment education.

It was thought that the underlying reason for the chronicity of shoulder pain was that the patient did not use her shoulder by trying to protect her shoulder due to pain beliefs and fear. Anxiety, depression, somatization, fear avoidance, kinesiophobia can also cause permanent pain by affecting central pain modulation (26,31). Therefore, the underlying psychological causes of chronic pain should be considered. In a systematic review, psychological factors such as anxiety in 23.2%, depression in 22.8-26.2%, and insomnia in 70.2% of patients with rotator cuff syndrome were reported (32). It has been shown that anxiety and depression have an effect on pain in patients with adhesive capsulitis, and that the severity of pain and functional limitation may be higher in patients with psychological disorders (33). In this study, the HAD scale was used to evaluate the psychological state of both patient groups. However, there was no significant difference between the two groups in terms of the effects of psychological factors on pain and functionality.

Study Limitations

Among the limitations of our study may be the lack of post-treatment evaluation of the patients and the small sample size. The positive side of our study is that it drew attention to the relationship between shoulder pain, which we frequently encounter, and kinesiophobia.

Conclusion

Kinesiophobia is an important factor in the treatment of shoulder pain. In this study, the presence of kinesiophobia was detected in both patients with rotator cuff syndrome and patients with adhesive capsulitis, but it was not found

that kinesiophobia was influencial on pain and quality of life. We suggest that kinesiophobia should be considered while planning the treatment in the rehabilitation of patients with shoulder pain.

Ethics

Ethics Committee Approval: The patients voluntary consent for the study and approval of University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committe with protocol number 2019-421 was obtained on 12.09.2019.

Informed Consent: Informed consent was obtained.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: B.A., M.V., Design: B.A., M.V., Data Collection or Processing: B.A., M.Ç., S.E., Analysis or Interpretation: B.A., M.V., M.Ç., S.E., Drafting Manuscript: B.A., S.E., M.V., Critical Revision of Manuscript: M.V., M.Ç., S.E., Writing: B.A.

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ORIGINAL RESEARCH

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The Effect of Early Rehabilitation on COVID-19: A Prospective, Observational Study

Erken Rehabilitasyonun COVID-19 Üzerine Etkisi: Prospektif, Gözlemsel Çalışma

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Abstract

Objective: The aim of this study was to investigate the effect of early pulmonary rehabilitation (PR) on the course of the disease, respiratory functions, physical activity, fatigue, and discharge time in Coronavirus disease-2019 (COVID-19) patients in the intensive care unit (ICU) setting.

Method: A total of 31 patients (20 females, 11 males) with COVID-19 confirmed by real-time polymerase chain reaction who were admitted to the ICU were included. Demographic, clinical, and laboratory data of the patients were recorded. Physical activity, dyspnea, and fatigue of all patients were evaluated before and after PR program. All patients were evaluated on the day of PR in the ICU, the day of discharge from ICU to the ward, and on the day of discharge from hospital. Functional status was evaluated using the functional disability questionnaire (FDQ), the ambulation status using the functional ambulation classification (FAC), dyspnea using the modified Borg scale (MBS), and fatigue using the fatigue severity scale.

Results: The mean length of ICU and hospital stay was 17.93±11.54 days and 18.29±8.41 days, respectively. The mean number of sessions was 8.87±7.66. The mean time from hospitalization to recovery was 13.00±9.62 days. Median FDQ and MBS scores were significantly higher during the ICU stay than the ward stay and at the time of discharge (p<0.05). Median FAC scores were significantly higher at the time of discharge than the ward and ICU scores (p<0.05). There was a positive and statistically significant correlation between the FDQ scores during the ward stay and C-reactive protein (CRP) values during the ICU stay (r=0.382, p=0.034) and CRP values during the ward stay (r=0.379, p=0.035). There was a

Öz

Amaç: Bu çalışmanın amacı, yoğun bakım ünitesinde (YBÜ) yatan Koronavirüs hastalığı-2019 (COVID-19) hastalarında erken pulmoner rehabilitasyonun (PR) hastalığın seyri, solunum fonksiyonları, fiziksel aktivite, yorgunluk ve taburculuk süresi üzerindeki etkisini araştırmaktır.

Yöntem: Çalışmaya gerçek zamanlı polimeraz zincir reaksiyonu ile doğrulanmış COVID-19 tanılı olup YBÜ'ye yatışı yapılan toplam 31 hasta (20 kadın, 11 erkek) alındı. Hastaların demografik, klinik ve laboratuvar verileri kaydedildi. Tüm hastalarda PR programından önce ve sonra fiziksel aktivite, dispne ve yorgunluk değerlendirildi. Hastalar YBÜ'de PR'nin ilk günü, YBÜ'den servise taburcu edildikleri gün ve hastaneden taburcu edildikleri gün değerlendirildi. Fonksiyonel durum, fonksiyonel yetersizlik ölçeği (FYÖ), ambulasyon durumu fonksiyonel ambulasyon sınıflandırması (FAS), dispne modifiye Borg ölçeği (MBÖ) ve yorgunluk yorgunluk şiddet ölçeği ile değerlendirildi.

Bulgular: YBÜ ve hastanede kalış süresi sırasıyla 17,93±11,54 gün ve 18,29±8,41 gün idi. Ortalama seans sayısı 8,87±7,66 idi. Hastane yatışından iyileşmeye kadar geçen ortalama süre 13,00±9,62 gün idi. Medyan FYÖ ve MBÖ skoru, servis yatışına ve taburculuk esnasına kıyasla YBÜ yatışı sırasında anlamlı düzeyde daha yüksekti (p<0,05). Medyan FAS skoru, servis ve YBÜ skorlarına kıyasla, taburculuk sırasında anlamlı düzeyde daha yüksekti (p<0,05). Servis yatışı sırasında FYÖ skorları ve servis yatışı (r=0,379, p=0,035) ve YBÜ yatışı sırasında (r=0,382, p=0,034) C-reaktif protein (CRP) değerleri arasında pozitif ve istatistiksel olarak anlamlı bir ilişki izlendi. Taburculuk sırasında FYÖ skorları ve YBÜ yatışı sırasında ferritin düzeyleri arasında negatif ve istatistiksel olarak anlamlı bir ilişki

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Abstract

negative and statistically significant correlation between the FDQ scores at the time of discharge and ferritin levels during the ICU stay (r=-0.421, p=0.018). A positive and statistically significant correlation was observed between MBS scores at the time of discharge and CRP values during the ward stay (p=0.418, p=0.019).

Conclusion: Our study suggests that PR is an effective and safe approach with improved physical and functional results and COVID-19 survivors should undergo a PR program in an individualized manner using a multidisciplinary approach to improve short- and long-term outcomes.

Keywords: COVID-19, early rehabilitation, pulmonary rehabilitation, intensive care unit

Öz

görüldü (r=-0,421, p=0,018). Taburculuk sırasında MBÖ skorları ve servis yatışı sırasında CRP düzeyleri arasında pozitif ve istatistiksel olarak anlamlı bir ilişki tespit edildi (p=0.418, p=0,019).

Sonuç: Çalışmamız PR'nin fiziksel ve fonksiyonel sonuçlarda iyileşme sağlayan etkili ve güvenli bir yaklaşım olduğunu göstermektedir. COVID-19 geçiren hastalar, kısa ve uzun dönem sonuçlarda iyileşme elde etmek için multidisipliner bir yaklaşım ile bireysel olarak PR programına alınmalıdır.

Anahtar kelimeler: COVID-19, erken rehabilitasyon, pulmoner rehabilitasyon, yoğun bakım ünitesi

Introduction

On December 31st, 2019, pneumonia cases of unknown etiology in the city of Wuhan, Hubei province, China were reported by the China Office of the World Health Organization. On January 7th, 2020, the causative agent was defined as a new coronavirus which was not identified in human before and it was named novel Coronavirus disease-2019 (COVID-19), due to its close resemblance to severe acute respiratory disease-coronavirus-2 (SARS-CoV-2) (1,2). The first COVID-19 case in Turkey was reported in March 11th, 2020 (3). The virus dramatically affected all over the world and the number of infected individuals increased rapidly. By the end of August 2022, a total of 1,629,517 confirmed cases were reported with 99,678 deaths.

The SARS-CoV-2 infection may be asymptomatic or it may cause a wide spectrum of symptoms, such as mild symptoms of upper respiratory tract infection and life-threatening sepsis (4). It can damage multiple systems such as cardiovascular, gastrointestinal, nervous and musculoskeletal systems (5). According to the Turkish national guidelines, pneumonia and severe pneumonia are the criteria for admission to the intensive care unit (ICU) (6).

The main goal of pulmonary rehabilitation (PR) is to reduce disability in patients with lung disease and improve their quality of life, thereby reducing the burden on the healthcare system (7,8). In COVID-19, PR principles have been defined for acute, subacute, and post-COVID-19 rehabilitation (9). Early rehabilitation has been shown to have a positive effect on the recovery of patients with COVID-19 (10,11).

In the present study, we aimed to investigate the effect of early PR on the course of the disease, respiratory functions, physical activity, fatigue, and discharge time in COVID-19 patients in the ICU setting.

Materials and Methods

Study Design and Study Population

This single-center, prospective, observational study was conducted at the Department of Physical Medicine and Rehabilitation (PMR) of University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, between March 2021 and April 2022. A written informed consent was obtained from all participants. The study was approved by the institutional Ethics Committee and the Republic of Turkey, Ministry of Health and conducted in accordance with the principles of the Declaration of Helsinki.

Patients infected with COVID-19 as confirmed by real-time polymerase chain reaction who were admitted to the ICU were included. All patients who were eligible for PR program were evaluated by a PMR specialist. Inclusion criteria were as follows: A fraction of inspired oxygen (FiO_2) of <60% (0.6); oxygen saturation (SpO_2) of >90%; respiratory rate of ≤40 breaths/min; positive end-expiration pressure of ≤10 cmH_2O; systolic blood pressure of ≥90 to ≤180 mmHg; mean arterial pressure of ≥65 to ≤110 mmHg; and heart rate of ≥40 to ≤120 bpm. All patients were extubated before inclusion in the PR program. Exclusion criteria were as follows: Fever (≥38.5 °C); >50% disease progression within 24 to 48 hours on radiological imaging of the lungs; severe cardiac problems such as heart failure, arrhythmia, bundle branch block, and cardiac involvement; renal or hepatic failure with progressive deterioration of the renal or hepatic functions; congenital musculoskeletal deformities which prevent mobilization; malignancies; rheumatic diseases; psychological disorders; resting blood pressure of <90/60

or >140/90 mmHg; receiving mechanical ventilation (MV) support; having shock evidence (lactic acid ≥4 mmol/L); new-onset unstable deep vein thrombosis and pulmonary embolism; a suspicion of aortic stenosis. Finally, a total of 44 patients who met the inclusion criteria were included.

Data Collection

Demographic data such as age and sex, clinical data, and laboratory data of the patients such as hemoglobin, hematocrit, white blood cell count, platelet count, C-reactive protein (CRP), lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase (AST), D-dimer, fibrinogen, procalcitonin, ferritin, cortisol, urea, creatinine, partial pressure of oxygen (pO_2), and SpO_2 were recorded. Physical activity, dyspnea, and fatigue of all patients were evaluated before and after PR program. The PR was applied to the patients during the entire hospital stay by experienced physiotherapists. All patients were evaluated on the day of PR in the ICU, on the day of discharge from ICU to the ward, and on the day of discharge from hospital.

PR Protocol

The PR protocol was applied for a week with varying durations based on the performance of each individual patient. The protocol consisted of breathing exercises (10 reps every 2 hours daily), postural drainage, percussion, and vibration (three times daily), secretion excretion and coughing (three times daily), respiratory muscle training (Triflo) (10 reps every 2 hours), positioning, in-bed mobilization (5 reps three times daily), bedside mobilization (5 reps three times daily), and postural exercises (5 reps three times daily). All patients were given a home-based PR program after discharge including postural exercises, lifestyle modifications, and walking exercises.

Assessment

Physical activity, dyspnea, and fatigue of all patients were evaluated before and after the PR program. Functional status was evaluated using the functional disability questionnaire (FDQ). The ambulation status was assessed using the functional ambulation classification (FAC) (12), dyspnea was assessed using the modified Borg scale (MBS) (13), and fatigue was assessed using the fatigue severity scale (FSS) (14).

Statistical Analysis

Statistical analysis was performed using the SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation, median and interquartile range or number and frequency, where applicable. The normality of distribution of variables was checked using the Kolmogorov-Smirnov test. The Wilcoxon test was used to analyze non-parametric variables. The Spearman correlation analysis was performed to identify the correlation between the variables. A p-value of <0.05 was considered statistically significant.

Results

A total of 31 patients were included in the study. Of these patients, 20 were females and 11 were males. Six patients received high-flow nasal oxygen therapy, 13 received non-invasive ventilation, and 12 patients underwent endotracheal intubation. The mean length of ICU and hospital stay was 17.93±11.54 days and 18.29±8.41 days, respectively. The mean number of sessions was 8.87±7.66. The mean time from hospitalization to recovery was 13.00±9.62 days. Twenty-eight patients were able to breath room air during discharge, while two patients were discharged with non-invasive nasal mask and one with non-invasive mask with ventilation support (Table 1).

Biochemistry test results and FDQ, FAC, MBS, and FSS scores during ICU and ward stay and at the time of discharge are shown in Table 2.

As shown in Table 3, there was a statistically significant difference in the FDQ scores between the measurements during the ward and ICU stay ($p<0.001$), during the ward stay and at the time of discharge ($p<0.001$), and during the ICU stay and at the time of discharge ($p<0.001$). The median FDQ scores were significantly higher during the ICU stay than during the ward stay and at the time of discharge and significantly higher during the ward stay than the measurements at the time of discharge. In addition, there was a statistically significant difference in the median MBS scores between the measurements during the ward and ICU stay ($p<0.001$), between the ICU stay and at the time of discharge ($p<0.001$), and during the ward stay and at the time of discharge ($p<0.001$). The median MBS scores were significantly higher during the ICU stay than the ward and discharge scores and significantly higher during the ward stay than the scores at the time of discharge. Also, there was a statistically significant difference in the median FAC scores between the measurements during the ward and ICU stay ($p<0.001$), between the ICU stay and at the time of discharge ($p<0.001$), and between the ward stay and at the time of discharge ($p<0.001$). The median FAC scores were significantly higher at the time of discharge than the ward and ICU scores and significantly higher during the ward stay than the ICU scores.

Table 1. Demographic and clinical characteristics of patients

Variable		n	%
Sex	Male	20	64.5
	Female	11	35.5
Age	≤50 years	9	29.0
	51-60 years	10	32.3
	≥61 years	12	38.7
Alcohol use	Yes	4	12.9
	No	27	87.1
Smoking	Yes	5	16.1
	No	26	83.9
BMI	Underweight	1	3.2
	Normal	8	25.8
	Overweight	19	61.3
	Obesity	3	9.7
Intubation status	HFNO	6	19.4
	Niv mask	13	41.9
	Trx	12	38.7
Respiratory support ICU (n=34)	HFNO	27	79.4
	Niv mask	3	8.8
	Niv nasal	4	11.8
Respiratory support ward (n=35)	Niv mask	16	45.7
	Niv nasal	15	42.9
	Room air	4	11.4
Respiratory support discharge	Niv mask	1	3.2
	Niv nasal	2	6.5
	Room air	28	90.3
Comorbidities (n=44)	None	13	29.5
	CVD	6	13.6
	CKD	2	4.5
	Diabetes	7	15.9
	Hypertension	11	25.0
	Asthma	2	4.5
	Thyroid disease	3	6.8
Mean ± SD			
Age, year			58.80±13.68
BMI, kg/m²			26.04±3.73
LOS in ICU, day			17.93±11.54
PR session in ICU, n			8.87±7.66
LOS in ward, day			18.29±8.41
Time to mobilization, day			13.00±9.62
PR session in ward, n			12.25±6.55
Total PR session, n			21.12±10.42

BMI: Body mass index, HFNO: High-flow nasal oxygen, Niv: Non-invasive, trx: Tracheostomy, CVD: Cardiovascular disease, CKD: Chronic kidney disease, LOS: Length of stay, ICU: Intensive care unit, PR: Pulmonary rehabilitation, SD: Standard deviation

Table 2. Biochemistry test results and FDQ, FAC, MBS, and FSS scores during ICU and ward stay and at the time of discharge

	ICU Mean ± SD	Ward Mean ± SD	Discharge Mean ± SD
FDQ	**57.87±5.60**	52.51±9.01	32.80±10.39
MBS	1.74±1.34	0.79±0.75	0.29±0.33
FAC	0.19±0.47	0.70±1.07	4.29±0.78
CRP, mg/dL	104.30±74.98	43.82±44.17	13.62±16.73
Lymphocyte count, x109/L	0.86±1.05	1.80±2.92	2.34±1.28
Neutrophil count, x109/L	12.89±4.52	10.50±12.74	5.97±2.62
Eosinophil count, x109/L	0.01±0.03	0.24±0.30	0.15±0.14
Ferritin, mL/ng	1240.10±1212.48	651.02±412.27	417.96±271.25
Procalcitonin, ng/mL	0.65±0.92	0.33±0.98	0.09±0.06
D-dimer, µg/mL	1.60±1.54	1.92±1.24	0.95±1.02

FDQ: Functional disability questionnaire, MBS: Modified Borg scale, FAC: Functional ambulation classification, FSS: Fatigue severity scale, ICU: Intensive care unit, SD: Standard deviation, CRP: C-reactive protein

Table 3. Comparison of FDQ, MBS, FAC scores during the ICU and ward stay and at the time of discharge

Variable	n	Median (IQR)	p-value*
FDQ-ICU	31	60.00 (8.00)	**<0.001**
FDQ-ward	31	55.00 (10.00)	
FDQ-ICU	31	60.00 (8.00)	**<0.001**
FDQ-discharge	31	30.00 (14.00)	
FDQ-discharge	31	30.00 (14.00)	**<0.001**
FDQ-ward	31	55.00 (14.00)	
MBS-ICU	31	2.00 (1.00)	**<0.001**
MBS-ward	31	0.50 (1.00)	
MBS-ICU	31	2.00 (1.00)	**<0.001**
MBS-discharge	31	0.00 (0.50)	
MBS-discharge	31	0.00 (0.50)	**<0.001**
MBS-ward	31	0.50 (1.00)	
FAC-ICU	31	0.00 (0.00)	**0.001**
FAC-ward	31	0.00 (1.00)	
FAC-ICU	31	0.00 (0.00)	**<0.001**
FAC-discharge	31	4.00 (1.00)	
FAC-discharge	31	4.00 (1.00)	**<0.001**
FAC-ward	31	0.00 (1.00)	

*Wilcoxon test. p<0.05 indicates statistical significance.
IQR: Interquartile range, FDQ: Functional disability questionnaire, MBS: Modified Borg scale, FAC: Functional ambulation classification, ICU: Intensive care unit

The correlation analysis results of FDQ, MBS, FAC, CRP, and ferritin are shown in Table 4. Accordingly, there was a positive and statistically significant correlation between the FDQ scores during the ward stay and CRP values during the ICU stay (r=0.382, p=0.034) and CRP values during the ward stay (r=0.379, p=0.035). In addition, there was a positive and statistically significant correlation between the FDQ scores at the time of discharge and CRP during the ward stay (r=0.383, p=0.034) and a negative and statistically significant correlation between the FDQ scores at the time of discharge and ferritin levels during the ICU stay (r=-0.421, p=0.018). Furthermore, a positive and statistically significant correlation was observed between the MBS scores at the time of discharge and CRP values during the ward stay (p=0.418, p=0.019).

The correlation analysis results of FDQ, MBS, FAC, lymphocyte, neutrophil, and eosinophil counts are given in Table 5. Accordingly, there was a positive and statistically significant correlation between the FDQ scores at the time of discharge and eosinophil count during the ward stay (r=0.399, p=0.026). In addition, a negative and statistically significant correlation was observed between the FAC during the ward stay and eosinophil count during the ward stay (r=-0.423, p=0.018).

There was a negative and statistically significant correlation between the FDQ scores during the ward stay and procalcitonin levels at the time of discharge (r=-0.411, p=0.22). In addition, there was a negative and statistically significant correlation between FAC during the ICU stay and D-dimer values during the ward stay (r=-0.368, p=0.041) and at the time of discharge (r=-0.469, p=0.008) (Table 6).

Discussion

In the present study, we investigated the effect of early PR on the course of the disease, respiratory functions, physical activity, fatigue, and discharge time in COVID-19 patients in the ICU setting. Our study results showed that early PR could improve physiological and functional results of COVID-19 patients.

Previous studies have shown that many patients infected with COVID-19 suffer from limited physical functions, as well as respiratory and psychological dysfunctions (15). Nearly 5% of COVID-19 patients are severe cases requiring ICU care and 71% are critically ill patients with acute respiratory distress syndrome or sepsis requiring MV support (16,17). Pulmonary injuries are major complications of COVID-19 (18). In particular, prolonged MV is associated with secondary lung damage (19,20). Nearly half of patients suffer from obstructive pulmonary patterns and develop restrictive pulmonary disease following hospitalization (21,22). All these effects have been shown to be linked to decreased functional capacity and impaired quality of life.

Early rehabilitation refers to rehabilitation interventions that are initiated immediately after stabilization (23). It has been shown that early rehabilitation and mobilization can improve respiratory muscle strength, decrease functional impairments, and yield more satisfactory outcomes (24,25). In the current study, we applied the early PR protocol for a week with varying durations based on the performance of each individual patient. The protocol consisted of breathing exercises, postural drainage, percussion, and

Table 4. Correlation analysis results of FDQ, MBS, FAC scores, CRP, and ferritin levels

		FDQ/ ICU	FDQ/ ward	FDQ/discharge	MBS/ ICU	MBS/ ward	MBS/ discharge	FAC/ ICU	FAC/ward	FAC/discharge
CRP-ICU	r	0.151	0.382*	0.128	0.053	-0.037	0.286	-0.218	0.017	-0.086
	p	0.417	**0.034**	0.492	0.777	0.844	0.119	0.239	0.926	0.646
CRP-ward	r	0.061	0.379*	0.383*	0.104	0.147	0.418*	-0.435*	-0.169	-0.325
	p	0.746	**0.035**	**0.034**	0.578	**0.429**	**0.019**	**0.014**	0.364	0.074
CRP-discharge	r	0.018	0.084	0.332	-0.161	-0.121	0.071	-0.351	-0.137	-0.332
	p	0.922	0.652	0.068	0.385	0.515	0.704	0.053	0.463	0.068
Ferritin-ICU	r	0.188	0.068	-0.421*	0.001	0.170	-0.064	-0.117	-0.200	0.335
	p	0.312	0.717	**0.018**	0.996	0.360	0.731	0.532	0.282	0.065
Ferritin-ward	r	-0.055	-0.124	-0.246	-0.194	-0.114	-0.079	0.185	0.101	0.339
	p	0.771	0.507	0.182	0.297	0.542	0.674	0.320	0.589	0.062
Ferritin-discharge	r	-0.024	-0.249	-0.321	-0.029	-0.040	-0.038	0.317	0.184	0.220
	p	0.899	0.178	0.079	0.875	0.832	0.840	0.082	0.323	0.234

*Significant at p<0.05 (Spearman correlation analysis), FDQ: Functional disability questionnaire, MBS: Modified Borg scale, FAC: Functional ambulation classification, ICU: Intensive care unit, CRP: C-reactive protein

Table 5. Correlation analysis results of FDQ, MBS, FAC scores, lymphocyte, neutrophil, and eosinophil counts

		FDQ/ ICU	FDQ/ ward	FDQ/ discharge	MBS/ ICU	MBS/ ward	MBS/ discharge	FAC/ ICU	FAC/ ward	FAC/ discharge
Lymphocyte-ICU	r	0.012	0.108	0.040	0.324	0.107	0.076	-0.047	-0.095	0.065
	p	0.948	0.562	0.830	0.075	0.568	0.684	0.800	0.610	0.729
Lymphocyte-ward	r	0.084	0.345	0.268	0.259	0.291	0.142	0.014	-0.011	0.116
	p	0.654	0.057	0.146	0.160	0.112	0.445	0.940	0.953	0.533
Lymphocyte-discharge	r	0.233	0.190	-0.041	0.489**	0.305	0.219	0.106	-0.112	0.069
	p	0.207	0.305	0.826	**0.005**	0.095	0.237	0.571	0.547	0.711
Neutrophil-ICU	r	-0.137	-0.125	0.121	-0.105	-0.269	-0.183	0.218	0.250	0.084
	p	0.461	0.504	0.515	0.574	0.143	0.326	0.239	0.175	0.652
Neutrophil-ward	r	-0.112	0.185	-0.252	-0.071	-0.001	-0.063	-0.065	-0.162	0.300
	p	0.549	0.319	0.172	0.706	0.995	0.735	0.726	0.384	0.101
Neutrophil-discharge	r	-0.254	-0.020	0.165	-0.002	0.038	0.019	-0.016	0.170	-0.036
	p	0.168	0.914	0.374	0.993	0.839	0.921	0.933	0.362	0.846
Eosinophil-ICU	r	0.059	0.105	0.032	0.403*	0.403*	0.147	0.071	-0.262	-0.180
	p	0.751	0.573	0.865	**0.024**	**0.025**	0.431	0.704	0.155	0.332
Eosinophil-ward	r	0.309	0.132	0.399*	0.325	0.379*	0.379*	-0.381*	-0.423*	-0.371*
	p	0.091	0.480	**0.026**	0.074	**0.036**	**0.035**	**0.034**	**0.018**	**0.040**
Eosinophil-discharge	r	0.076	-0.272	-0.078	-0.037	-0.155	-0.168	-0.156	-0.043	-0.027
	p	0.686	0.138	0.676	0.842	0.406	0.367	0.401	0.820	0.884

*Significant at p<0.05 (Spearman correlation analysis), **Significant at p<0.01 (Spearman correlation analysis): FDQ: Functional disability questionnaire, MBS: Modified Borg scale, FAC: Functional ambulation classification, ICU: Intensive care unit

Table 6. Correlation analysis results of FDQ, MBS, FAC scores, procalcitonin and D-dimer levels

		FDQ/ ICU	FDQ/ ward	FDQ/discharge	MBS/ ICU	MBS/ward	MBS/ discharge	FAC/ ICU	FAC/ward	FAC/discharge
Procalcitonin-ICU	r	-0.120	-0.025	-0.058	-0.270	-0.111	-0.133	-0.129	-0.134	-0.013
	p	0.520	0.894	0.757	0.142	0.553	0.475	0.488	0.473	0.943
Procalcitonin-ward	r	0.181	0.209	0.182	-0.014	-0.039	0.060	-0.244	-0.198	-0.284
	p	0.329	0.259	0.328	0.940	0.835	0.748	0.186	0.285	0.122
Procalcitonin-discharge	r	-0.214	-0.411*	0.183	-0.057	-0.076	-0.128	0.141	0.089	-0.349
	p	0.247	0.022	0.325	0.762	0.686	0.491	0.450	0.635	0.054
D-dimer-ICU	r	0.176	0.083	0.124	0.167	0.229	0.057	-0.219	-0.237	-0.259
	p	0.344	0.657	0.505	0.369	0.216	0.759	0.236	0.200	0.159
D-dimer-ward	r	-0.107	-0.055	0.350	0.024	0.077	0.049	-0.368*	-0.105	-0.287
	p	0.566	0.771	0.054	0.896	0.682	0.794	**0.041**	0.575	0.117
D-dimer-discharge	r	0.196	0.117	0.248	0.092	0.087	-0.017	-0.469**	-0.358*	-0.319
	p	0.292	0.532	0.178	0.623	0.642	0.929	**0.008**	**0.048**	0.081

*Significant at p<0.05 (Spearman correlation analysis), **Significant at p<0.01 (Spearman correlation analysis): FDQ: Functional disability questionnaire, MBS: Modified Borg scale, FAC: Functional ambulation classification, ICU: Intensive care unit

vibration, secretion excretion and coughing, respiratory muscle training, positioning, in-bed mobilization, bedside mobilization, and postural exercises. Also, all patients were given a home-based PR program after discharge including postural exercises, lifestyle modifications, and walking exercises. We evaluated physical activity, dyspnea, and fatigue of all patients before and after the PR program. Our study results showed that the median FDQ scores were significantly higher during the ICU stay than the ward stay and at the time of discharge and significantly higher during the ward stay than the discharge scores. In addition, the median MBS scores were significantly higher during the ICU stay than the ward and discharge scores and significantly higher during the ward stay than the discharge scores. Also, the median FAC scores were significantly higher at the time of discharge than the ward and ICU scores and significantly higher during the ward stay than the ICU scores. These findings are consistent with previous study findings suggesting that early rehabilitation after COVID-19 is effective with significant improvements in functional outcomes (26,27).

Several studies have shown the benefit of early inpatient rehabilitation after ICU admission among COVID-19 survivors (28,29). In a retrospective study, physical and occupational therapy was found to be feasible in the ICU setting for COVID-19 patients (30). In another study, early mobilization effectively shortened the time to extubation and length of hospital stay with improved quality of life (31). Despite concerns about the rehabilitation of severe COVID-19 pneumonia cases, a consensus has been established recently including PR (32). As increased spontaneous breathing is associated with decreased intrathoracic pressure and pulmonary edema (33), the main goal of PR is to protect the lungs in severe COVID-19 cases (34).

In previous studies, D-dimer, CRP, and serum ferritin levels have been shown to be linked to COVID-19 severity and mortality (35,36). In a study, decreased diffusing capacity of the lungs for carbon monoxide (DLCO) was found to be most prevalent respiratory function impairment and ferritin level was found to be a significant clinical factor (37). Similarly, in our study, we found a negative and statistically significant correlation between the FDQ scores at the time of discharge and ferritin levels during the ICU stay. In addition, we observed a negative and statistically significant correlation between the FAC during the ICU stay and D-dimer values during the ward stay and at the time of discharge. We also found a positive and statistically significant correlation between the FDQ scores during the ward stay and CRP values during the ICU and ward stay.

Study Limitations

Nonetheless, there are some limitations to this study. First, it has a single-center study with a relatively small sample size and, therefore, the results should be cautiously interpreted. Second, there is no control group which precludes evaluating the rehabilitation effect on clinical outcomes. Third, long-term functional outcomes were unable to be assessed. Further multi-center, large-scale studies are needed to draw more reliable conclusions on this subject.

Conclusion

COVID-19 survivors should undergo PR in an individualized manner during the hospitalization to minimize the adverse outcomes of the disease. Based on our study findings, PR is an effective and safe approach with improved physical and functional results. Therefore, it seems to be a promising intervention for patients with COVID-19. However, we recommend a multidisciplinary approach to improve short- and long-term outcomes. Further large-scale prospective studies are warranted to elucidate which PR protocol is more effective in this group of patients.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, between March 2021 and April 2022. The study was approved by the institutional Ethics Committee and the Republic of Turkey, Ministry of Health and conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: A written informed consent was obtained from all participants.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: I.Ü., M.V., S.Ç., İ.D.A., G.O.H., Design: I.Ü., M.V., S.Ç., İ.D.A., G.O.H., Data Collection or Processing: İ.D.A., S.B., T.A., E.K., F.A., Analysis or Interpretation: F.A., İ.D.A, I.Ü., Drafting Manuscript: I.Ü., M.V., S.Ç., G.O.H., Critical Revision of Manuscript: İ.D.A, T.A., S.B., E.K., F.A., Final Approval and Accountability: I.Ü., M.V., S.Ç., G.O.H., T.A., İ.D.A., E.K, S.B., F.A., Technical or Material Support: T.A., S.B., İ.D.A., E.K., S.B., F.A., Supervision: I.Ü., M.V., S.Ç., G.O.H., Writing: I.Ü., M.V., S.Ç., G.O.H., T.A., İ.D.A., E.K, S.B., F.A.

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ORIGINAL RESEARCH

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The Effect of the COVID-19 Pandemic in Adult Vaccination in Turkey

COVID-19 Pandemisinin Türkiye'deki Yetişkin Aşılamaya Etkisi

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Abstract

Objective: This study aimed to evaluate the impact of the Coronavirus disease-2019 (COVID-19) pandemic on adult vaccination rates in Turkey.

Method: This retrospective descriptive study included individuals aged 18 and over who sought adult vaccination at the Education Family Health Centers of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital between 11.03.2019 and 11.03.2021. The data were analyzed for one year before and one year after 11.03.2020, which marked the first COVID-19 case in Turkey. Vaccination information was obtained from the family medicine information system, and data analysis was performed using the IBM SPSS program.

Results: A total of 1.139 participants were included in the study, with a mean age of 57.27±17.74 years (min: 18, max: 96). Among the participants, 60.8% were female and 39.2% were male. The total number of vaccine doses administered between 11.03.2019-11.03.2020 (pre-pandemic) was 310, while the total number of vaccine doses administered between 11.03.2020-11.03.2021 (post-pandemic) was 829. Before the pandemic, the most commonly administered vaccines were hepatitis B (54.8%), conjugated pneumococcal (50.7%), and seasonal influenza vaccines (11%). The mean age of those vaccinated before the pandemic was 58.41±15.63 years. Following the pandemic, there was a significant increase in adult vaccination rates among the participants, particularly in females ($p<0.05$). The vaccination status did not show a significant change with age ($p=0.781$).

Conclusion: The utilization of adult vaccination services has significantly increased since the onset of the COVID-19 pandemic.

Keywords: COVID-19, pandemics, primary care, vaccination

Öz

Amaç: Bu çalışma, Koronavirüs hastalığı-2019 (COVID-19) pandemisinin Türkiye'deki yetişkin aşılama oranları üzerindeki etkisini değerlendirmeyi amaçlamıştır.

Yöntem: Retrospektif tanımlayıcı nitelikteki bu çalışmaya 11.03.2019-11.03.2021 tarihleri arasında Sağlık Bilimleri Üniversitesi, Prof. Dr. Cemil Taşcıoğlu Şehir Hastanesi'nin Eğitim Aile Sağlığı Merkezleri'nde erişkin aşısı olmak isteyen 18 yaş ve üzeri bireyler dahil edildi. Veriler, Türkiye'deki ilk COVID-19 olgusu olan 11.03.2020 tarihinden bir yıl öncesi ve bir yıl sonrası için analiz edildi. Aşı bilgileri aile hekimliği bilgi sisteminden elde edildi ve veri analizi IBM SPSS programı kullanılarak yapıldı.

Bulgular: Çalışmaya yaş ortalaması 57,27±17,74 (min: 18, maks: 96) olan toplam 1,139 katılımcı dahil edildi. Katılımcıların %60,8'i kadın, %39,2'si erkektir. 11.03.2019-11.03.2020 (pandemi öncesi) tarihleri arasında uygulanan toplam aşı dozu sayısı 310 iken, 11.03.2020-11.03.2021 (pandemi sonrası) tarihleri arasında uygulanan toplam aşı dozu sayısı 829 oldu. Pandemi öncesi en sık uygulanan aşılar hepatit B (%54,8), konjuge pnömokok (%50,7) ve mevsimsel grip aşıları (%11) idi. Pandemi öncesi aşı olanların yaş ortalaması 58,41±15,63 yıldı. Pandeminin ardından, katılımcılar arasında, özellikle kadınlarda yetişkin aşılama oranlarında önemli bir artış oldu ($p<0,05$). Aşılanma durumu yaşla birlikte önemli bir değişiklik göstermedi ($p=0,781$).

Sonuç: Yetişkin aşılama hizmetlerinin kullanımı, COVID-19 pandemisinin başlangıcından bu yana önemli ölçüde artmıştır.

Anahtar kelimeler: Aşılama, birinci basamak, COVID-19, pandemi

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Introduction

In the realm of safeguarding public health against infectious diseases, a multifaceted strategy encompassing fundamental preventive measures (such as personal hygiene, access to clean drinking water, and effective waste management) intertwined with the power of immunization, whether through active or passive means, emerges as pivotal (1,2). Vaccination stands out as the most effective and cost-efficient method for preventing infectious diseases. Its primary objectives are to mitigate the risks of disease, disability, and death, thereby promoting overall health (3). The widespread implementation of vaccinations in the 20th century led to a significant reduction in the incidence of most vaccine-preventable diseases, with some, like smallpox, being completely eradicated (4). Vaccines are possibly among the most crucial and impactful interventions in public health history, contributing significantly to saving lives (5).

Vaccinations, considered an integral part of children's health, are often neglected in adults (5,6). Vaccination in adulthood is also necessary because the protective effect of some childhood vaccines ends in adulthood (e.g., tetanus, diphtheria, pertussis) and exposure to vaccine-preventable diseases in work and social life must be considered. While childhood vaccinations are closely monitored by health authorities worldwide, the same monitoring does not exist for adult vaccinations (3,6). In contrast to the remarkable success observed in pediatric immunizations, vaccine-preventable diseases like influenza, pneumococcal disease, and hepatitis B lead to an annual death toll of approximately 40,000 to 80,000 adults in the USA. This results in a substantial strain on healthcare resources, with numerous hospitalizations and associated costs. Neglecting adult immunization leaves individuals with chronic conditions vulnerable, such as heart disease and diabetes, heightening the risk of severe complications from vaccine-preventable illnesses. Regrettably, high-risk adults, in the United States, remain inadequately immunized, with vaccination rates as low as 20 percent for pneumococcal disease and 28.6 percent for hepatitis B among certain groups. This leads to complex and expensive care for infected individuals. Unlike the pediatric population, where immunization coverage disparities have been reduced through programs like Vaccines for Children, significant disparities persist among adults (5)

The Coronavirus disease-2019 (COVID-19) pandemic has caused health resources to be redirected from regular primary care. It has greatly affected global healthcare, putting a lot of pressure on healthcare systems. Measures such as curfews and quarantine protocols, implemented to slow the transmission of the virus, have hindered access to healthcare services (7,8). Routine health screenings, childhood vaccinations, and adult immunization programs have been disrupted or entirely halted in many countries during certain periods (9-14). However, in Turkey, immunization services for both children and adults have continued uninterrupted throughout the pandemic, with individuals still able to access vaccinations even during quarantine periods (15).

While existing literature predominantly focuses on the impact of the pandemic on childhood vaccinations, no similar studies have been identified in Turkey when considering adult vaccination through searches conducted in databases such as Google Scholar, PubMed, Web of Science, Scopus, and ULAKBIM. Therefore, this study represents the first original research article examining the effect of the COVID-19 pandemic on adult vaccinations in Turkey.

The aim of this study is to assess the impact of the COVID-19 pandemic on adult vaccination rates carried out by primary care services (family health care centers) in Turkey by analyzing the changes in vaccination patterns before and after the pandemic's onset.

Materials and Methods

Ethic

Ethics committee permission for the study was obtained with the decision number 47 of the meeting held on 28.02.2022 at the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital.

Study Design

This is a descriptive and cross-sectional study. The sample size was calculated as 530 people by taking the total number of patients registered to our primary care outpatient clinic as 4314 on the Open-Epi site, predicting an adult immunisation rate of 35.5% based on the study conducted by Mutlu et al. (16) in 2018, taking a margin of error of 5% and taking the design effect 1 in the 99% confidence interval. Patient data were analyzed retrospectively, one year before and one year after 11.03.2020, when the first COVID-19 case was seen in Turkey. The pre-pandemic period between 11.03.2019-11.03.2020 is defined as pre-pandemic period, the period between 11.03.2020-11.03.2021 is defined as pandemic period The patient data utilized for this study were acquired from the Family

Health Care Center Information System and the patient files of designated family health units. The Family Medicine Information System is a specialized software infrastructure that enables family physicians to comprehensively document the healthcare services rendered to citizens in an electronic format. This recorded information is then systematically transmitted to a centralized database, adhering to standardized data structures stipulated by the Ministry of Health. Within this system, family physicians possess the capability to administer vaccinations to both adult and pediatric patients, even if these patients are not formally registered with them. This flexibility allows for the timely and appropriate administration of vaccinations in accordance with established schedules. Subsequently, these vaccination records are meticulously logged into the system, capturing critical details such as age, gender, presence of chronic diseases, medications administered, vaccination type, and date of vaccination. In our study, we specifically focused on the adult patient demographic seeking immunization at our family health care units. A total of 1.193 adults presented themselves to the family health center for vaccination during the predefined date ranges. To ensure the integrity of the data, 54 patients were excluded from the study due to incomplete or inaccurate information within their respective personal files. A total of 1.139 adult patients included in our study. During the data collection process, instances of redundant vaccine entries were identified. In these cases, where the same vaccination was recorded multiple times, we meticulously curated the dataset to include only a single instance of each vaccination. This meticulous approach helped maintain the precision and reliability of our study's findings, as we aimed to avoid duplication and ensure that each vaccination entry was uniquely accounted for.

Statistical Analysis

The SPSS 25.0 package program was used for statistical analysis. (IBM Corp. 2011. IBM SPSS Statistics for Windows, version 25.0. Armonk, NY: IBM Corp.) The distribution of interval data was analyzed using the Kolmogorov-Smirnov or Shapiro-Wilk test. Data were expressed as mean ± standard deviation and median. The normality of numerical variables was assessed using the Kolmogorov-Smirnov test. The comparison of proportions in independent groups was performed using the chi-square test. Since the numerical variables satisfied the assumption of normal distribution, independent two-group analyses were conducted using the Independent Samples t-test. $p<0.05$ was considered statistically significant.

Results

The mean age of the participants was 57.27±17.74 years (min: 18, max: 96). While 60.8% of the participants were female, 39.2% were male. The total number of vaccine doses between 11.03.2019 and 11.03.2020 (pre-pandemic period) was 310, and the total number of vaccine doses between 11.03.2020-11.03.2021 (pandemic period) was 829. 5.8% of the participants had diabetes mellitus, 11.6% had essential hypertension, 2.4% had hyperlipidemia, 2.4% hypothyroidism, 2.6% chronic ischemic heart disease, 1.4% COPD, 0.8% osteoporosis was diagnosed. While the mean age of those vaccinated before the pandemic was 54.03±22.15 years, the mean age of those vaccinated after the onset of the pandemic was 58.41±15.63 years (Table 1).

After the pandemic, the rate of adult vaccination of our participants increased significantly ($p=0.000$), while the rate of vaccination in female gender increased significantly ($p<0.05$), the vaccination status did not change with age ($p=0.781$).

Of the vaccines administered before the pandemic, 54.8% were hepatitis B, 50.7% were conjugated pneumococci, and 1% were seasonal influenza vaccines. Of the vaccines administered after the onset of the pandemic, 11.3% were hepatitis B, 75.5% conjugated pneumococci, and 13.1% seasonal influenza (Figure 1, Table 2).

Table 1. Patients' age, gender and chronical diseases and vaccination status according to pandemic

		Vaccination before pandemic		Vaccination after pandemic		
		Median + SD	**Min, max**	**Median + SD**	**Min, max**	**p-value***
Age (year)		54.03±22.15	18-96 (min, max)	58.41±15.63	18-95 (min, max)	0.781
		Number	**Percentage**	**Number**	**Percentage**	**p-value****
Female		166	23.9%	526	76.1%	0.03
Male		120	26.9%	327	73.1%	
Chronical diseases	Yes	126	45.4%	152	54.6%	0.08
	No	258	29.9%	603	70.1%	

*Independent t-test, **chi-square, SD: Standard deviation

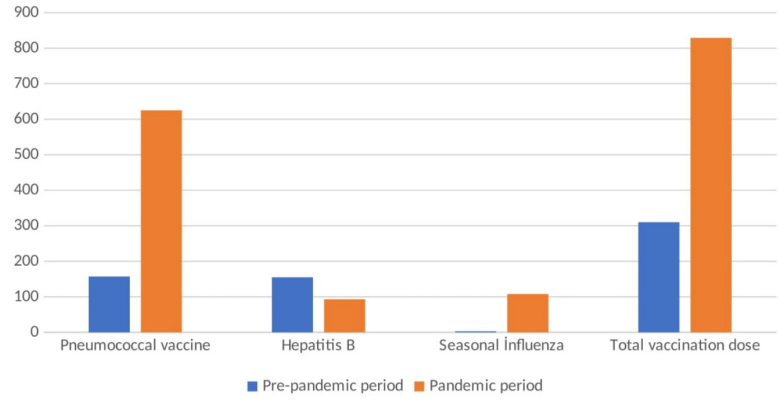

Figure 1. Adult vaccination rates in pre-pandemic and pandemic period

Table 2. Vaccination status at pre-pandemic and pandemic period

	Pre-pandemic period	Pandemic period	p-value*
Pneumococcal vaccine	157	625	p=0.00
Hepatitis B	155	93	p=0.67
Seasonal influenza	1	108	p=0.00
Total	327	826	p=0.00

*chi-square test

Upon analyzing the timeline of adult vaccinations, it becomes evident that there was a substantial surge in demand for adult immunization immediately following the onset of the pandemic. When vaccines administered from March 2020 onwards were examined, a significant increase in adult immunization rates during the months of September, October, and November compared to the remaining months was observed (p=0.019). However, as time progressed, this heightened demand has gradually declined (Figure 2).

Discussion

As a result of our study, within a year after 11.03.2020, when the first COVID-19 case was seen in Turkey, adult immunization applications increased significantly (p<0.05). Vaccination in the adult population is applied to certain patient groups in many countries around the world, and it is not at the targeted level in most countries. However, adult vaccination is very beneficial for the individual, family, society and country in terms of medical, social and economic benefits. Considering that life expectancy is increasing in most countries, protection

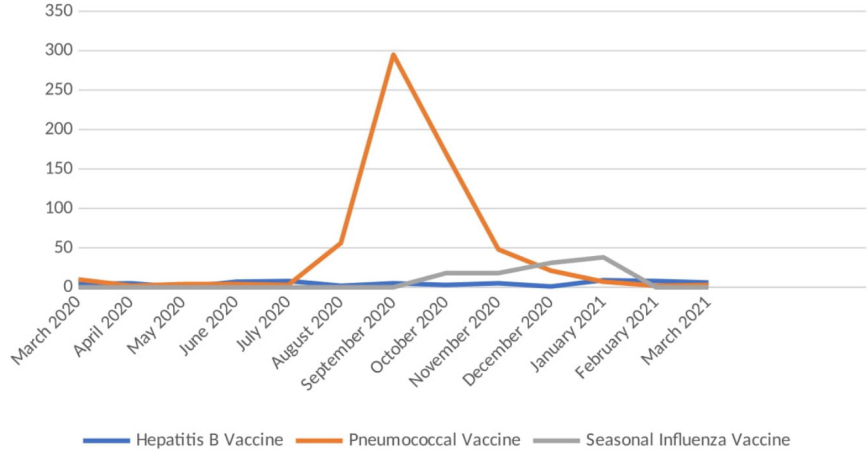

Figure 2. Adult vaccination rates between March 2023-March 2021

from vaccine-preventable diseases is of great importance, and individuals and healthcare practitioners should be prioritized (3). The COVID-19 pandemic has created health anxiety in the adult population, especially in vulnerable people with chronic diseases, immune supressed people, pregnant women; and has increased preventive health measures such as hand washing, healthy eating, and hygienic behaviors (2,17,18). In addition, it has brought adult routine vaccinations to the agenda. In our study, the vaccination rate increased significantly at the pandemic period compared to pre-pandemic period. The most significant increase in our country was observed during the months of September, October, and November, particularly in pneumococcal vaccination. The reason for this could be attributed to the absence of a definite treatment or preventive method for COVID-19 during that period. Individuals may have turned to vaccination as a means to protect themselves. The subsequent decrease in adult vaccination after these months could be attributed to the initiation of COVID-19 vaccination, leading individuals to prioritize that vaccine.

In our study, the mean age of the participants was 57.27 years, 60,8% were female, and the rate of vaccination in females was significantly higher. 23.1% of the vaccines were hepatitis B, 68.7% of them were conjugated pneumococci, and 9.8% were influenza vaccines. In a study evaluating the vaccination of people over 65 years old between June 2020 and June 2021 in Turkey, the most frequently administered vaccine was conjugated pneumococcus (76.72%), and the least administered vaccine was influenza vaccination (7.03%) (19).

In a study examining the effect of covid-19 on vaccination using September 2019 and July 2020 data in Pakistan, it was found that there was a 52.2% decrease in all childhood vaccinations (10). In a study conducted with 232 Pediatricians in Tuscany during the first quarantine period in Italy (March 11-May 4, 2020), 7% of pediatricians stopped vaccination altogether. Of those who continue to be vaccinated, 31.7% are in the compulsory hexavalent vaccine (diphtheria, tetanus, pertussis, polio, h. influenza type and hepatitis B) and MMRV (measles, mumps, Rubella, varicella) vaccines, 42.3% reported a decrease in non-essential vaccinations (11).

It has been reported that a decrease in childhood vaccination doses was observed 1 week after 8 March 2020 (the date of the New York index case). In the weeks following the index case, the vaccination rate decreased by 62% in children aged 0-24 months and by 96% in children aged 2-18 years, and vaccination campaigns were started at the end of March 2020. As of May-June 2020, the severity of the decrease in vaccination decreased, but at the end of June, vaccination was still lower than the 2019 June data. Similarly, after the measles epidemic in New York in 2018-2019, there was a decrease in childhood vaccinations (12).

In a study conducted in Canada, it was observed that childhood vaccinations and adult population vaccinations were adversely affected, with school immunization studies being the most prominent between March and April 2020. After the first quarantine period (March-April 2020), childhood vaccinations, school follow-ups, maternal/prenatal follow-ups were revised and continued in accordance with the COVID-19 pandemic conditions, while adult vaccinations were partially suspended (13).

In a study conducted in Nigeria evaluating pre- and post-index immunization rates, BCG vaccination decreased from 85.8% to 82.1% before the index case, and HBV vaccination decreased from 63.5% to 60%. Penta 3 decreased from 76.1% to 72%, Oral polia vaccine decreased from 75.4% to 72%, PCV decreased from 75.1% to 71.4%, and IPV from 73.5% to 71.9%. Average coverage rates for yellow fever and measles fell sharply from 77.0% and 74.5% and 64.6% and 58.6%, respectively (14).

Study Limitations

In the study, the data were examined for a period of 2 years, longer-term studies can be made. Five family medicine units were examined in the study, studies can be done with a larger sample.

Conclusion

This study shows an increase in adult vaccination status in the study sample after the COVID-19 pandemic. The findings highlight a significant shift in vaccination rates among participants in the post-pandemic period. This post-pandemic increase in vaccination rates, particularly evident among women, suggests a paradigm shift in public health priorities and awareness.

The data show a significant increase in the total number of vaccine doses administered in the post-pandemic period, indicating a growing awareness of the importance of adult immunisation.

The profound disruptions that the pandemic has brought to routine health care delivery and access are undeniable,

but the post-pandemic increase in vaccination rates is indicative of the health system's continued resilience and people's willing engagement in self-protection and efforts to protect their health in the face of unique challenges.

As the global community moves on in the wake of the pandemic, these insights on shifting vaccine trends can inform targeted interventions and strategies to increase adult immunisation rates.

Ethics

Ethics Committee Approval: Ethics committee permission for the study was obtained with the decision number 47 of the meeting held on 28.02.2022 at the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital.

Informed Consent: In accordance with the retrospective nature of our study, informed consent from individual patients was not required as the analysis involved anonymized data collected as part of routine medical practice.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: F.E., Design: F.E., Data Collection or Processing: F.E., N.Ç.A., M.M., Analysis or Interpretation: F.E., N.Ç.A., M.M., Drafting Manuscript: F.E., S.A., Final Approval and Accountability: S.A., Technical or Material Support: M.M., Supervision: S.A., Writing: F.E., N.Ç.A., M.M., S.A.

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ORIGINAL RESEARCH

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Morphometric Comparison of Interbody Fusion with Cage and Autograft at L4-L5 Levels versus Autograft Alone for Fusion

L4-L5 Seviyesinde Kafes ve Otogreftle Yapılan İnterbody Füzyonunun Tek Başına Otogreftle Yapılan Füzyonla Morfometrik Karşılaştırılması

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Abstract

Objective: Lumbar interbody fusion (LIF) entails the placement of a bone graft within the intervertebral space, with or without the use of a cage, subsequent to discectomy. While numerous studies have explored caged LIF methods within the literature, limited attention has been given to direct comparisons between caged and cageless LIF techniques. This study aims to scrutinize the delayed outcomes of interbody fusion involving peek-caged and cageless laminar autografts. The investigation was specifically carried out at the L4-5 level.

Method: This retrospective comparative study was conducted on patients who underwent surgical procedures at our institution's neurosurgery clinic between 2011 and 2018, with the sanction of the ethics committee from the same institution. The study group (Group 1, n=27) comprised patients who underwent L4-5 single-level lumbar instrumentation and transforaminal LIF using a banana cage alongside autograft for the purpose of fusion. The control group (Group 2, n=31) consisted solely of cases that underwent posterior LIF operations with the utilization of autografts. Corticocancellous bone fragments sourced from posterior structures during decompression were utilized as autografts. The study parameters encompassed fusion rates, segmental and lumbar lordosis angles, disc height, ipsilateral and contralateral foramen heights, as well as slip distance.

Results: Within our study, the late-stage fusion rates were determined to be 96.3% in the caged group and 96.7% in the cageless autograft group. No alterations were identified in segmental and lumbar lordosis angles across both groups. Notably, the caged group exhibited a propensity for late-stage cage embedding, while graft migration was the most prevalent complication within the autograft group.

Öz

Amaç: Lomber interbody füzyon (LIF), diskektomi yapıldıktan sonra intervertebral boşluğa bir kafesle veya kafes olmaksızın kemik greft yerleştirilmesi işlemidir. Literatürde kafesli LIF yöntemlerini karşılaştıran birçok çalışma vardır. Buna rağmen kafesli ve kafessiz LIF yöntemlerini karşılaştıran çalışma çok azdır. Bu çalışmada peek kafesli ve kafessiz laminar otogreft kullanılarak yapılan interbody füzyonun geç dönem sonuçlarının karşılaştırılması amaçlanmıştır. Çalışma spesifik olarak L4-5 seviyesinde yapılmıştır.

Yöntem: Bu retrospektif karşılaştırmalı çalışma 2011-2018 yılları arasında kurumumuz nöroşirurji kliniğinde opere edilen hastalar üzerinde aynı kurumdan etik kurul onayı alınarak yapılmıştır. L4-5 tek seviyeli lomber enstrümantasyon uygulanıp füzyon amacıyla otogreftle birlikte muz kafes kullanılarak transforaminal LIF operasyonu yapılan hastalar çalışma grubunu (Grup 1, n=27), sadece otogreft ile arka LIF operasyonu yapılan olgular kontrol grubunu oluşturdu (Grup 2, n=31). Otogreft olarak dekompresyon esnasında posterior yapılardan elde edilen kortikokanselloz kemik parçaları kullanıldı. Füzyon oranları, segmental ve lomber lordoz açısı, disk yüksekliği, ipsilateral ve kontralateral foramen yüksekliği ve kayma mesafesi ölçüldü.

Bulgular: Yaptığımız çalışmada kafesli ve kafessiz gruplarda geç dönem füzyon oranları sırasıyla %96,3 ve %96,7 olarak bulundu. Segmental ve lomber lordozda iki grupta da değişiklik olmadı. Kafesli grupta geç dönem kafes gömülmesi, kafessiz grupta ise greft göçü en sık komplikasyonlardı.

Sonuç: Hem kafesli hem de kafessiz LIF yüksek füzyon oranları olan cerrahi tekniklerdir. Füzyon açısından otogreft grubu, dizilim açısından ise kafesli grubun sınırlı bazı avantajları vardır. Kafessiz otogreftle LIF basit,

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Abstract

Conclusion: Both caged and cageless LIF methodologies are associated with elevated fusion rates. The autograft group demonstrates certain limited advantages in terms of fusion, whereas the caged group exhibits some benefits primarily related to alignment. The implementation of cageless autograft LIF, marked by its straightforwardness, simplicity, and cost-effectiveness, appears to be an underappreciated surgical technique within the current context.

Keywords: Autograft, cage, interbody fusion, peek cage

Öz

sade ve düşük maliyet gibi özellikleriyle yeterince takdir edilmeyen bir cerrahi teknik olarak görünmektedir.

Anahtar kelimeler: Gözetleme kafesi, kafes, otogreft, vücutlar arası füzyon

Introduction

Lumbar interbody fusion (LIF) is a surgical procedure involving the placement of a bone graft within the intervertebral space, often accompanied by the use of a cage, subsequent to a discectomy. In contemporary practice, LIF is approached through five primary surgical techniques: Posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF or MI-TLIF), oblique lumbar interbody fusion/anterior psoas (OLIF/ATP), anterior lumbar interbody fusion (ALIF), and lateral lumbar interbody fusion (LLIF). While a discernible array of advantages and disadvantages have been documented for each of these modalities, it remains noteworthy that extant literature does not yet furnish definitive evidence substantiating the unequivocal superiority of any single approach over the others (1). The related literature is replete with numerous investigations that meticulously juxtapose the divergent dimensions of caged LIF techniques (2-8). It is, however, discernible that a paucity of comprehensive studies exists in relation to the comparative evaluation between caged and cageless LIF methodologies (9-12). This emerging trend underscores the progressive propensity towards the integration of intervertebral cages as a de facto standard within the LIF procedure.

The utilization of autografts for LIF has conventionally entailed their extraction from either the iliac crest or the posterior osseous structures during decompression procedures. Iliac crest grafts manifest optimal graft attributes owing to their corticocancellous architecture; nevertheless, they are concomitantly linked to pronounced wound morbidity (13). Conversely, grafts acquired from the lamina and spinous processes during decompression, while susceptible to challenges in sustaining structural integrity, obviate the necessity for supplementary surgical interventions and proffer inherent cost-related benefits. The deployment of autograft material confers an advantageous edge in fusion dynamics when juxtaposed with allograft and synthetic alternatives, primarily attributed to its heightened tissue compatibility.

Interbody cages exhibit a diverse array of structural profiles and configurations, commonly crafted from titanium or polyetheretherketone (PEEK) materials. The osteoconductive attributes of titanium cages are prominently evident, accentuating their capacity to foster optimal bone integration. However, it is noteworthy that the inherent rigidity of titanium constructs may engender an elevated susceptibility to implant embedding, which is a recognized concern (5). In contrast, PEEK lattice architectures offer a distinctive advantage characterized by a closer approximation to the mechanical elasticity of osseous tissue. Nevertheless, the advantageous mechanical harmony offered by PEEK structures is counterbalanced by certain challenges, such as their inherently smooth and hydrophobic surfaces, which may, in turn, impede the process of fusion (5).

In this study, it was aimed a comprehensive comparative analysis of long-term outcomes of interbody fusion employing PEEK cages versus cageless laminar autografts. Potential advantages and disadvantages of two methods were evaluated by meticulous assessment of demographic attributes, radiological metrics, and clinical presentations. The investigation was meticulously circumscribed to a patient cohort exclusively encompassing those who underwent only single-level L4-L5 interbody fusion. This methodological constraint was carefully instituted to confer precision and specificity to the study outcomes, enabling a more incisive examination of the parameters under consideration.

Materials and Methods

This retrospective comparative study was undertaken within the purview of the neurosurgery clinic at our esteemed institution, spanning the duration encompassing 2011 to 2018. The study was executed subsequent to

obtaining the requisite endorsement from the ethics committee affiliated with the same institution. Consent was obtained from all participants. The study cohort, herein referred to as Group I, was composed of patients who underwent TLIF procedures. This involved the application of single-level lumbar instrumentation at the L4-5 level, accompanied by the utilization of a banana-shaped cage housing autograft material. The control group, denoted as Group II, exclusively encompassed cases subjected to PLIF interventions. The autograft was derived from corticocancellous bone fragments sourced from posterior osseous structures during the process of decompression in both groups. The patients were randomly divided into two groups.

The investigation encompassed an extensive review of the hospital registry system and patient records. During this process, meticulous attention was directed towards capturing pivotal demographic attributes, encompassing elements such as operation duration, intraoperative hemorrhage volume, body mass index (BMI), comorbid conditions, as well as postoperative complications. The clinical parameters of interest were supported by the inclusion of preoperative metrics, including visual analog scale (VAS) scores and Oswestry disability index (ODI) assessments.

At distinct time intervals, a comprehensive evaluation of patient outcomes was conducted. This entailed administering questionnaires at the 3-month juncture postoperatively, followed by a subsequent assessment extending beyond the span of 2 years post-surgery. For the sake of methodological rigor, participants who were deceased or rendered uncontactable were judiciously excluded from the analytical framework, thereby fortifying the integrity of the study cohort.

Inclusion Criteria

Individuals who had undergone surgical intervention involving L4-L5 pedicle screw instrumentation in conjunction with interbody fusion were enrolled into the study. This procedural selection was contingent upon a diagnostic framework characterized by degenerative grade 1 listhesis, accompanied by demonstrable clinical and radiological indicators of instability. Furthermore, a key criterion necessitated that these patients had exhausted conservative therapeutic modalities, thus warranting surgical intervention as a subsequent step in their clinical management.

Exclusion Criteria

Exclusion criteria encompassed cases involving procedures beyond the confines of the L4-L5 spinal segment, as well as instances involving multi-level operations. Moreover, patients with a documented history of prior instrumentation, those subjected to either solitary or supplementary posterolateral fusion procedures, and individuals afflicted by malignancy, traumatic injuries, or severe osteoporosis, were methodologically precluded from participation. Additionally, participants meeting the unfortunate outcome of deceased status or deemed non-compliant with the requisite follow-up protocol were excluded from the study. Furthermore, a stipulation was imposed mandating the availability of postoperative lumbar imaging records for a minimum duration of two years subsequent to the surgical intervention. Patients for whom lumbar computerized tomography (CT) and radiographic data were unavailable within the hospital's radiological record system were systematically excluded from the cohort under consideration.

Radiological Investigations

The radiological investigations constituted an integral facet of this study, engaging a comprehensive array of parameters to discern and quantify pertinent anatomical variables. The timeline of measurement encompassed preoperative, early postoperative, and late postoperative stages, extending over a minimum of two years. These assessments were meticulously executed employing both CT imaging and standing X-ray examinations.

Noteworthy metrics subject to meticulous quantification included segmental and lumbar lordosis angles, disc height dimensions, ipsilateral and contralateral foramen heights, as well as slip distances. The determination of segmental lordosis (SL) was methodologically anchored in the calculation of angular deviation from the lower L4 and upper L5 endplates. In parallel, the computation of lumbar lordosis was derived from lines tangentially projected from the upper L1 to S1 endplates.

Concurrently, disc heights were ascertained through meticulous measurement along the anterior, middle, and posterior planes tangential to the respective endplates. The computation of the mean disc height necessitated the division of the cumulative measurements by a factor of three. Correspondingly, foramen heights were discerned through the measurement of distances between lines spanning from the inferior aspect of the L4 pedicle to the superior region of the L5 pedicle (Figure 1).

The framework established by Lee et al., as adapted for this context, constituted the basis for evaluating the fusion status (14). This framework discerns the presence or absence of bridging bony trabeculae, graft-to-bone space, and dynamic motion (≥3°) as evident in radiographs acquired during dynamic movements. The meticulous examination of dynamic radiographs for motion, as indicated in Table 1, underpinned the fusion evaluation.

Ensuring methodological rigor, measurements were conducted by two independent neurosurgeons, with their findings subjected to subsequent averaging. Instances of interpretational discrepancies concerning fusion assessments were judiciously arbitrated through a consensus-driven resolution process (Figure 2).

Surgical Technique

All procedural interventions were undertaken by the co-authors of this study. Employing a posterior midline approach, the surgical field encompassed exposure of the distal facet of L3-4, the entire facet of L4-5, and the initial region of the transverse process. Predominantly, pedicle screws were deployed, save for specific cases involving advanced stenosis where alternative measures were considered. Following this, decompression procedures were administered either unilaterally or bilaterally contingent upon the direction of pressure. In scenarios necessitating unilateral decompression, an extended approach was favored to ensure optimal bone graft capacity.

Post-discectomy and thorough endplate preparation, the implantation of a banana cage was executed at a height commensurate with physiological norms, thereby avoiding encroachment upon the posterior one-third of the intervertebral disc space. It is germane to note that facet osteotomy was executed with judicious precision, calibrated to facilitate the placement of the banana cage. This strategic choice was underscored by the imperative to mitigate the risk of potential instability in prospective revision scenarios. This surgical modality, in essence, mirrors an adapted version of the TLIF technique. Conspicuously, the strategy deployed forgoes complete L4 total laminectomy, a decision rooted in the intention to preclude the exacerbation of superior adjacent segment disease. Instead, an approach characterized by laminectomy of a scope adequate to accommodate microdiscectomy and the subsequent introduction of the cage is employed. Prior to the final placement of rods, meticulous maneuvering of the operating table is undertaken to optimize lumbar lordosis. Importantly, the procedural execution refrains from aggressive compression, as the potential for foraminal stenosis dictates caution.

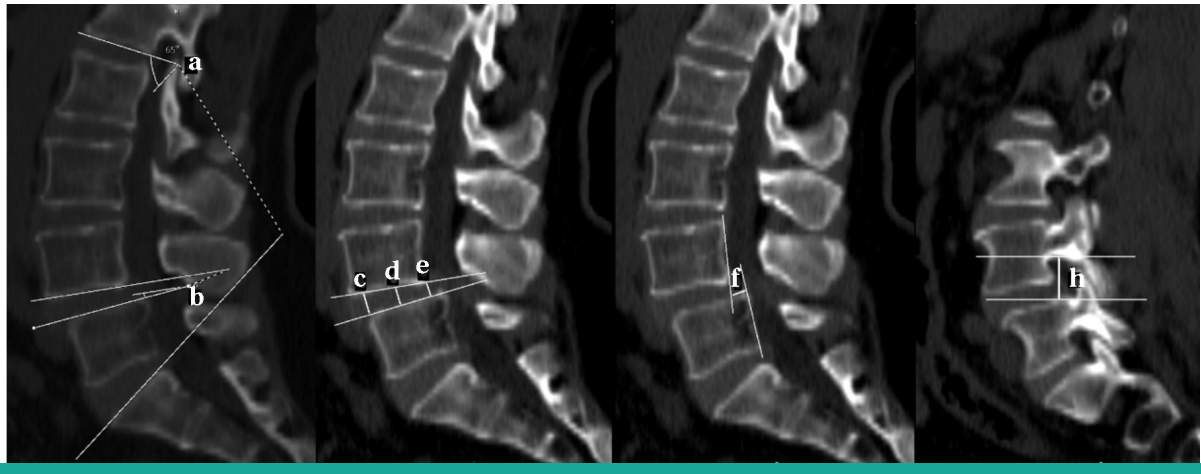

Figure 1. a (lumbar lordosis), **b** (segmental lordosis), **c** (anterior disc height), **d** (middle disc height), **e** (posterior disc height), **f** (shift distance), **h** (foramen height) measurement

Table 1. Modified Lee et al. classification

	Presence of bridging trabecular bone	Gap between corpus and graft	Motion in dynamic radiograph
Fusion	+	-	-
Possible fusion	-	-	-
Possible non-fusion	-	+	-
Non-fusion	-	+	+

In instances where the only autograft technique is embraced, an allocation of 20 to 30 bone fragments, varying in size, is thoughtfully inserted. Conversely, the cage group encompasses the utilization of approximately 10 bone graft pieces, with half of the allocation seamlessly integrated within the confines of the cage apparatus.

Statistical Analysis

Descriptive statistical measures encompassing mean, standard deviation, median, minimum, maximum, frequency, and ratio were employed to elucidate the inherent characteristics of the dataset. The distributional properties of the variables were assessed via the Kolmogorov-Smirnov test. To expound upon the analysis of quantitative independent data, both the Independent Sample t-test and the Mann-Whitney U test were judiciously administered. In parallel, the scrutiny of dependent quantitative data entailed the application of the Paired-Sample t-test and the Wilcoxon test, aptly tailored to accommodate the investigative context. Qualitative independent data underwent rigorous evaluation through the application of the chi-square test, thereby affording insights into the interrelationships within this stratum of variables. All statistical analyses were conducted utilizing the SPSS version 28.0 software.

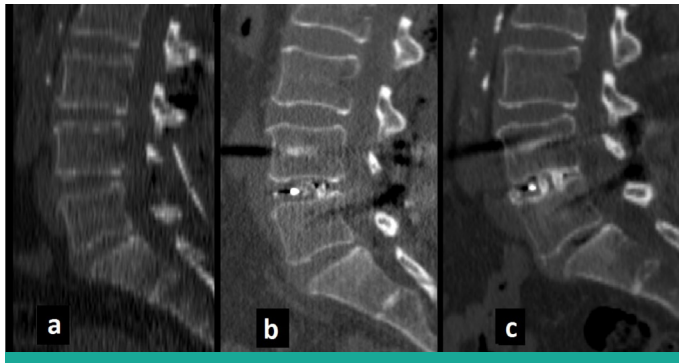

Figure 2. In the case of interbody cage; **a** (preoperative), **b** (early postoperative), **c** (late postoperative) sagittal CT reconstruction

CT: Computerized tomography

Results

The distribution of patients' age, gender, blood loss amount, operation time, and follow-up period demonstrated no significant disparities between Groups I and II ($p<0.05$), as evidenced through the BMI distribution. Similarly, no substantial variation in fusion values was observed between two groups ($p<0.05$) (Table 2).

Disc Height

The preoperative mean disc height (DH) value revealed no substantial distinction ($p>0.05$) between Group I and Group II. Notably, early and late postoperative mean DH values in Group II were significantly diminished relative to those in Group I ($p<0.05$). Conversely, Group I exhibited a noteworthy increase in early and late postoperative mean DH values compared to the preoperative values ($p<0.05$). Meanwhile, Group II experienced a significant

Table 2. Comparison of demographic data and fusion

		Group I		Group II		p	
		Mean ± SD/n-%	Median	Mean ± SD/n-%	Median		
Age		58.3±9.0	57.0	56.6±8.6	56.0	0.473	t
Gender	Female	20, 74.1%		25, 80.6%		0.549	X^2
	Male	7, 25.9%		6, 19.4%			
Weight		82.0±12.3	85.0	76.5±10.4	80.0	0.071	t
Height		161.9±7.2	160.0	161.3±6.8	160.0	0.820	m
BMI		31.4±5.4	30.0	29.6±4.9	29.4	0.179	t
Loss of blood		481.5±170.1	450.0	427.4±183.0	400.0	0.226	m
Duration of surgery		174.1±30.3	170.0	167.4±26.8	160.0	0.446	m
Follow of period		34.7±12.8	28.0	31.9±10.9	29.0	0.638	m
Fusion							
Fusion		17, 63.0%		25, 80.6%		1.000	X^2
Possible fusion		9, 33.3%		5, 16.1%			
Possible non-fusion		1, 3.7%		0, 0.0%			
Non-fusion		0, 0.0%		1, 3.2%			

[t]t-test, [m]Mann-Whitney U test, [X^2]chi-square test, SD: Standard deviation, BMI: Body mass index

increase in early postoperative mean DH value compared to the preoperative baseline (p<0.05), while the late postoperative mean DH value in Group II exhibited no significant difference from the preoperative metric (p>0.05). Within Group II, the preoperative/early postoperative and preoperative/late postoperative mean DH increments were significantly lower in comparison to Group I (p<0.05) (Table 3).

Lumbar Lordosis

No substantial disparity emerged in preoperative, early postoperative, and late postoperative lumbar lordosis (LL) values between Group I and Group II (p>0.05). Furthermore, early postoperative and late postoperative LL values exhibited no significant differentiation in either Group I or Group II relative to their preoperative values (p>0.05) (Table 4).

SL

Preoperative, early postoperative, and late postoperative SL values demonstrated no notable discrepancies between Group I and Group II (p>0.05). However, in both groups, the early postoperative SL value exhibited no significant deviation from the preoperative benchmark (p>0.05), while

Table 3. Comparison of disc height between and within groups

	Group I		Group II		p	
	Mean ± SD	Median	Mean ± SD	Median		
Avg DH						
Preop	7.0±2.1	6.5	6.6±1.8	6.8	0.516	t
Early postop	9.1±1.8	8.8	7.6±1.7	7.6	**0.003**	t
Late postop	7.8±2.1	7.5	6.5±1.9	6.8	**0.015**	t
Change according to preop						
Preop/early postop	2.1±1.6	1.8	1.0±1.1	0.9	**0.004**	t
Intra-group change p	**0.000**	E	**0.011**	E		
Preop/late postop	0.8±1.6	0.4	-0.1±1.3	-0.4	**0.012**	t
Intra-group change p	**0.000**	E	0.561	E		

E Paired sample t-test, t Independent sample t-test, SD: Standard deviation, DH: Disc height

Table 4. Comparison of lordosis and foramen heights between and within groups

	Group I		Group II		p	
	Mean ± SD	Median	Mean ± SD	Median		
LL						
Preop	52.0±11.1	53.0	52.7±11.1	55.0	0.827	m
Early postop	53.3±8.8	52.0	51.5±9.8	54.0	0.679	m
Late postop	52.6±10.0	53.0	51.7±10.9	52.0	0.623	m
Change according to preop						
Preop/early postop	1.3±7.4	1.0	-1.2±4.2	-1.0	0.211	m
Intra-group change p	0.526	w	0.161	w		
Preop/late postop	0.6±7.7	1.0	-1.0±3.6	-1.0	0.352	m
Intra-group change p	0.656	w	0.137	w		
SL						
Preop	5.9±3.3	5.0	6.6±3.6	6.0	0.461	m
Early postop	6.3±2.3	6.0	6.2±3.2	6.0	0.771	m
Late postop	4.6±2.1	4.0	4.9±3.1	5.0	0.813	m
Change according to preop						
Preop/early postop	0.4±2.5	1.0	-0.4±3.5	-1.0	0.165	m
Intra-group change p	0.263	w	0.531	w		
Preop/late postop	-1.2±2.8	-1.0	-1.7±3.0	-1.0	0.551	m
Intra-group change p	**0.046**	w	**0.003**	w		

Table 4. Continued

	Group I		Group II		p	
	Mean ± SD	Median	Mean ± SD	Median		
FH						
Preop	15.4±2.4	15.5	14.5±3.1	14.4	0.091	m
Early postop	17.7±2.4	17.8	16.2±2.4	15.9	**0.035**	m
Late postop	16.2±2.5	15.7	15.0±2.4	14.8	0.097	m
Change according to preop						
Preop/early postop	2.2±1.5	2.1	1.8±2.5	1.8	0.177	m
Intra-group change p	**0.000**	w	**0.000**	w		
Preop/late postop	0.8±2.1	0.4	0.5±2.7	0.4	0.507	m
Intra-group change p	0.096	w	0.428	w		
CLFH						
Preop	15.9±1.9	16.2	15.6±2.1	15.1	0.454	m
Early postop	17.7±2.1	17.8	16.4±2.4	16.5	**0.015**	m
Late postop	16.0±2.3	16.9	15.1±1.9	14.7	0.098	m
Change according to preop						
Preop/early postop	1.7±1.6	1.7	0.7±1.2	0.5	**0.023**	m
Intra-group change p	**0.000**	w	**0.002**	w		
Preop/late postop	0.1±1.9	0.4	-0.6±1.3	-0.5	0.062	m
Intra-group change p	0.501	w	**0.028**	w		

SD: Standard deviation, [m]Mann-Whitney U test, [w]Wilcoxon test, LL: Lumbar lordosis, SL: Segmental lordosis, FH: Foraminal height, CLFH: Controlateral foraminal height

the late postoperative SL value underwent a significant reduction ($p<0.05$) (Table 4).

Foraminal Height (FH)

Preoperative and late postoperative FH values yielded no considerable distinction between Group I and Group II ($p>0.05$). However, the early postoperative FH value in Group II was significantly lower compared to Group I ($p<0.05$). In both groups, the early postoperative FH values significantly increased in comparison to the preoperative measures ($p<0.05$), while the late postoperative FH values returned to the preoperative values ($p>0.05$). The preoperative/early postoperative and preoperative/late postoperative FH changes exhibited no substantial differences between Group I and Group II ($p>0.05$) (Table 4). Contralateral and ipsilateral foramen height yielded analogous statistical results, as indicated in Table 4.

Slip Measurements

The preoperative, early postoperative, and late postoperative slip values displayed no discernible differentiation between Group I and Group II ($p>0.05$). In Group I, both early postoperative and late postoperative deviation values exhibited a significant decrease in contrast to the preoperative values ($p<0.05$). Parallelly, Group II showcased a similar pattern ($p<0.05$). The preoperative/early postoperative and preoperative/late postoperative slip reduction, however, was markedly lower in Group II ($p<0.05$) compared to Group I (Table 5).

Functional Outcomes

No noteworthy differences emerged in preoperative, early postoperative, and late postoperative ODI values between Group I and Group II ($p>0.05$). In both groups, both early postoperative and late postoperative values displayed a significant decline compared to the preoperative measures ($p<0.05$). The preoperative/early postoperative and preoperative/late postoperative ODI changes presented a similar trend across both groups ($p>0.05$) (Table 5).

Analogous patterns were observed in the assessment of leg VAS scores. Specifically, preoperative, early postoperative, and late postoperative leg VAS scores exhibited no substantial differentiation between Group I and Group II ($p>0.05$). In both groups, both early postoperative and late postoperative leg VAS scores registered a significant reduction compared to the preoperative values ($p<0.05$). The preoperative/early postoperative and preoperative/late postoperative leg VAS score reductions were analogous between Group I and Group II ($p>0.05$) (Table 6). Analogously, the back VAS score results echoed the trends observed in leg VAS scores across both groups (Table 6).

Table 5. Intergroup and intragroup comparison of slippage distance and ODI changes

	Group I		Group II		p	
	Mean ± SD	Median		Median		
Slippage						
Preop	3.7±3.0	4.0	3.4±2.9	2.0	0.906	m
Early postop	1.3±1.5	1.0	2.4±2.3	2.0	0.072	m
Late postop	1.3±1.5	1.0	2.3±2.3	2.0	0.113	m
Change according to preop						
Preop/early postop	-2.4±2.3	-2.0	-1.0±1.5	0.0	**0.011**	m
Intra-group change p	**0.000**	w	**0.001**	w		
Preop/late postop	-2.4±2.3	-2.0	-1.1±1.5	0.0	**0.024**	m
Intra-group change p	**0.000**	w	**0.001**	w		
ODI						
Preop	56.5±12.4	58.0	54.2±12.8	56.0	0.826	m
Early postop	29.4±12.9	26.0	29.2±8.7	30.0	0.536	m
Late postop	27.3±15.2	24.0	26.6±12.9	22.0	0.833	m
Change according to preop						
Preop/early postop	-27.1±9.3	-26.0	-24.9±13.4	-26.0	0.579	m
Intra-group change p	**0.000**	w	**0.000**	w		
Preop/late postop	-29.3±10.3	-30.0	-27.5±14.8	-30.0	0.628	m
Intra-group change p	**0.000**	w	**0.000**	w		

[m] Mann-Whitney U test, [w]Wilcoxon test, SD: Standard deviation, ODI: Oswestry disability index

Table 6. Comparison of VAS waist and VAS leg changes between and within groups

	Group I		Group II		p	
	Mean ± SD	Median	Mean ± SD	Median		
VAS score-leg						
Preop	7.6±1.3	8.0	7.7±1.6	8.0	0.574	m
Early postop	2.7±1.6	2.0	2.9±1.4	2.0	0.351	m
Late postop	2.6±1.6	2.0	2.8±1.7	2.0	0.602	m
Change according to preop						
Preop/early postop	-4.9±1.5	-5.0	-4.7±1.8	-5.0	0.545	m
Intra-group change p	**0.000**	w	**0.000**	w		
Preop/late postop	-5.0±1.5	-5.0	-4.9±2.0	-5.0	0.633	m
Intra-group change p	**0.000**	w	**0.000**	w		
VAS score-waist						
Preop	7.1±1.4	7.0	7.2±1.7	8.0	0.512	m
Early postop	3.4±1.1	3.0	3.2±1.0	3.0	0.636	m
Late postop	3.0±1.4	3.0	2.9±1.5	3.0	0.652	m
Change according to preop						
Preop/early postop	-3.8±1.5	-4.0	-4.0±1.6	-4.0	0.540	m
Intra-group change p	**0.000**	w	**0.000**	w		
Preop/late postop	-4.1±1.6	-4.0	-4.3±1.9	-5.0	0.496	m
Intra-group change p	**0.000**	w	**0.000**	w		

[m]Mann-Whitney U test, [w]Wilcoxon test, SD: Standard deviation, VAS: Visual analog scale

Complications

A total of 23 complications were seen within the caged group (Group I) with 11 cases of cage embedding, while 14 complications with 4 cases of graft displacement were noted in the cageless cohort. No substantial intergroup disparities emerged concerning dural injury, new-onset loss of strength, reoperation, or the incidence of adjacent segment disease.

Discussion

The central impetus behind employing interbody cages or grafts in lumbar degenerative disease surgeries is to augment fusion rates. Notably, the literature has consistently demonstrated that PLIF and TLIF yield higher fusion rates and superior clinical outcomes when juxtaposed with posterolateral fusion (PLF) approaches (15,16). This trend has culminated in the integration of PLIF and TLIF methodologies as near-standard practices, with interbody cage utilization becoming an inherent component of any posterolateral interbody fusion (PIF) intervention. Contemporary studies, in lieu of pitting against PLF, are now inclined to contrast PLIF and TLIF with innovative minimally invasive modalities such as ALIF, LLIF, and OLIF (17).

Despite the pervasive prevalence of PIF procedures and the amplification of the data corpus in scientific literature, studies on only interbody fusion employing autografts remain underrepresented. Autografts sourced from patients possess an array of merits, devoid of immunological complications and characterized by elevated fusion rates. The application of iliac crest grafts as a graft source in PIF has also been explored (18). Regrettably, despite the benefits, this ideal graft comes with the associated burdens of pain, bleeding, and infection due to secondary incisions, which has led surgeons to seek more minimally invasive alternatives, such as avoiding the utilization of iliac crest grafts.

Bone decompression stands as a necessity in the majority of surgeries related to degenerative spondylolisthesis. Even in cases where minimally invasive methods like ipsilateral contralateral decompression are pursued, ample bone fragments can be sourced to facilitate fusion over a single disc distance. This prompts the inquiry: Can these naturally obtained bone fragments be judiciously placed within the discectomy space, effectively fostering fusion? Does the prevailing attention granted to interbody cages align with their true significance?

Within our study, late fusion rates were observed to reach 96.3% in the caged group and 96.7% in the cage-free autograft group, concordant with existing literature. This echoes findings in independent studies that employed laminar bone fragments, where fusion outcomes correlated with our results. However, divergences in evaluation timeframe and criteria necessitate caution when drawing direct comparisons (9,10).

Although notable fusion rates exhibited by both groups in this study, more definitive evidence of fusion was observed in the autograft group (Group II). In the caged group (Group I), the device appeared to constrict the fusion area, engendering a hypodense space between the device and bone. Fusion was realized through autografts positioned anteriorly and posteriorly to the cage, rather than within the cage itself. These hypodense regions between the cage and end plates might potentially show a disadvantage for PEEK material in terms of fusion. Noteworthy, certain studies have reported the superiority of titanium cages over PEEK cages in terms of fusion efficacy (19).

Furthermore, even though posterolateral fusion was not a primary objective in both groups, significant fusion was observed within the facets, hinting at how PIF methodologies indirectly foster posterior fusion via the rigid construct formed anteriorly. While results pertaining to fusion alignment in both groups were comparable, the autograft group (Group II) exhibited a relative advantage due to its simplicity and cost-effectiveness. Additionally, the diminished facetectomy requirements associated with autograft interbody fusion mitigate the risk of potential instability upon instrument removal. Following the preliminary outcomes of this study, cageless autograft interbody fusion has evolved into the standard modality in our clinical setting for cases focused solely on achieving fusion.

These findings collectively underscore the significance of exploring alternative avenues for achieving successful interbody fusion, with a particular emphasis on harnessing autografts and simplifying procedural approaches, while maintaining an eye on long-term stability and cost-effectiveness.

An integral motivation underlying the adoption of interbody cages is the mitigation of root compression stemming from potential foramen stenosis, accomplished through the preservation of disc and foramen height. Related literature underscores the utility of employing solid interbody cages to sustain disc height (20).

Conversely, another study reported a reduction in disc height when autografts were utilized (21). In the current study, significant early postoperative augmentation in mean disc height within the caged group failed to persist in the long-term. In other words, although late-phase mean disc height exhibited superiority within the caged group, noteworthy collapse ensued in both caged and cage-free groups, deviating from anticipated findings. The incapacity to maintain early postoperative mean disc height increment within the caged group could potentially be attributed to the predominantly elderly female patient cohort, where probable osteoporosis was a contributing factor. The majority of cases avoided complete excision of both ipsilateral and contralateral facets, opting instead for a physiological-sized device. The lack of supraphysiological devices might explain the failure to sustain late-phase disc height, despite prior literature suggesting that such devices are more intrinsically integrated (22,23).

In the realm of lumbar PIF procedures, the paramount objective of employing interbody devices pertains to the rectification of lordosis angles and the achievement of optimal alignment. A systematic review investigating lumbar angle enhancements following PIF revealed mean corrections of 4.67, 4.47, and 3.89 degrees for ALIF, LLIF, and TLIF, respectively (24). In our investigation, no substantive enhancements in lumbar or SL emerged in preoperative, early postoperative, and late postoperative phases within or between both study groups. Notably, even the autograft group (Group II) exhibited a significant decline in late postoperative periods. This divergence from existing literature could stem from a multitude of factors such as a homogeneous patient population without kyphotic deformity, midline device placement rather than anterior placement, usage of interbody cages without angles, not to be performed ipsilateral and contralateral facetectomy, as well as not to be performed compression during rod insertion to avoid foraminal stenosis. Furthermore, the studies reporting some values that should be performed for lordosis correction were usually the studies evaluating operations of diverse levels and multi-level lumbar interbody fusions (LIF), whereas our study exclusively enrolled single-level fusion cases. These findings underscore the pivotal role of procedural application in effecting lumbar lordosis correction, transcending the choice of interbody fusion method. Consequently, our study has prompted an inclination toward the preferential use of interbody cages for lumbar lordosis correction, predominantly employing angled and supraphysiological dimensions. This entails ipsilateral and contralateral facet osteotomies, coupled with enforced compression to facilitate lordotic correction.

Evaluation of slip distances in our statistical analyses revealed a substantial decline in both groups during the early and late postoperative phases. Notably, intergroup scrutiny underscored superior deviation correction within the device group compared to its counterpart. This effect can be attributed to a more aggressive discectomy approach in the device group, coupled with the corrective influence exerted by distraction during cage insertion on the slippage.

Past studies have accentuated the connection between successful fusion and clinical contentment. Moreover, it is postulated that the preservation and enhancement of disc height could theoretically correlate with the amelioration of leg pain (25). In line with this notion, both groups within our study demonstrated notable improvement in VAS and ODI values during early and late postoperative stages, displaying remarkable congruence. While foramen heights were relatively better preserved in the caged group, no significant divergence in leg VAS values was observed. This observation aligns with existing literature (9-11). However, we posit that a larger prospective study would be indispensable to reveal any discernible disparity.

In summary, our findings underscore the multifaceted nature of lumbar PIF interventions, particularly in relation to the deployment of interbody cages. The interplay between patient characteristics, procedural nuances, and device attributes collectively shapes clinical outcomes, thereby advocating for a comprehensive approach that integrates existing evidence with nuanced clinical judgment.

This elevated frequency of cage embedding potentially correlates with the high prevalence of female patients possibly afflicted with osteoporosis, mirroring the diminished maintenance of disc height. However, the challenge of comparing this complication across existing literature persists due to disparities in mean age and gender distribution. A second salient complication manifested in the cageless autograft group, characterized by four instances of graft displacement. This outcome underscores the possibility that solitary reliance on autografts may not invariably yield structurally robust outcomes. A potential remedy lies in modulating the surgical approach, necessitating the creation of a more conservative window within the posterior longitudinal ligament for cageless PIF scenarios. Additionally, judicious placement of grafts posterior to the disc space involves the utilization of substantial bone fragments, preferentially deposited in the anterior and middle regions of the disc space.

Noteworthy, no substantial intergroup disparities emerged concerning dural injury, new-onset loss of strength, reoperation, or the incidence of adjacent segment disease. Anticipating the contours of prospective inquiries, the investigation of larger cohorts emerges as a beneficial avenue, particularly concerning the intricacies of adjacent segment disease. In summary, the intricacies of complications within both interbody cage and cageless autograft scenarios reinforce the necessity of context-sensitive approaches, adeptly reconciling patient-specific attributes, procedural intricacies, and prior scholarly findings.

Study Limitations

The study is constrained by its relatively modest sample size and its retrospective design, which collectively curtail its robustness. The retrospective acquisition of clinical data, encompassing metrics like ODI and VAS at distinct time points, introduces certain vulnerabilities in terms of data comprehensiveness and reliability.

Study Strengths

In contrast to akin investigations in the literature, the distinctive attribute of our study rests in its meticulous focus on cases pertaining exclusively to a single fusion level (L4-5). Moreover, the anatomical dimensions of segmental and lordosis angles were meticulously gauged from standing radiographs, while the evaluation of fusion was grounded in comprehensive CT scans. We posit that the fusion assessment conducted through CT scans yields results of greater significance. The multifaceted nature of parameters inherent to PIF procedures, including factors like cage height, angle, osteotomy configuration, and rod positioning involving compression or distraction, imparts complexity to the interpretative realm. The insight garnered from our study holds potential to serve as a guiding compass for fledgling surgeons, elucidating the nuances behind the dearth of lumbar lordosis enhancement within our study cohort.

Conclusion

Both the caged and cageless autograft LIF cohorts evinced comparably elevated fusion rates, paired with commendable clinical outcomes. Upon juxtaposition, the cageless contingent exhibited certain modest advantages in terms of fusion outcomes, while the caged group showcased superior alignment attributes. The method of autograft only LIF surfaces as an unheralded surgical modality, marked by its streamlined, uncomplicated, and cost-effective attributes.

Ethics

Ethics Committee Approval: Ethical authorization for this study was granted by the University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Clinical Research Ethics Committee on 18.12.2020, under the auspices of decision number: 2020.12.2.05.

Informed Consent: Consent was obtained from all participants.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.T., F.K.G., A.A., Concept: A.T., F.K.G., A.A., Design: A.T., F.K.G., A.A., Data Collection or Processing: A.T., A.A., Analysis or Interpretation: A.T., F.K.G., A.A., Literature Search: A.T., F.K.G., A.A., Writing: A.T., F.K.G.

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ORIGINAL RESEARCH

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Relationship Between Gestational Diabetes and Thyroid Hormones in Pregnant Women

Gebelerde Gestasyonel Diyabet ve Tiroid Hormonları Arasındaki İlişki

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Abstract

Objective: Gestational diabetes and thyroid disorders are common disorders during pregnancy. This study investigated the relationship between gestational diabetes and thyroid hormone levels in pregnant women.

Method: This single-center study was conducted by analyzing retrospectively 190 pregnant women who admitted to the private internal medicine clinic between March 2019 and December 2022. Ninety pregnant women diagnosed with gestational diabetes mellitus (GDM) and one hundred pregnant women without GDM diagnosis were included in the study. The relationship between thyroid markers [thyroid-stimulating hormone (TSH) and free thyroxine hormone 4 (fT4)] and gestational diabetes was examined.

Results: Results did not show a statistically significant association between case and control regarding age and body mass index (p-value >0.05). There was a statistically significant difference between groups regarding TSH (p-value <0.05). Also, results did not find a statistically significant association between the case and healthy pregnant women regarding fT4 (p-value >0.05). There was a statistically meaningful association between healthy women and women with GDM in terms of subclinical hypothyroidism frequency (p-value <0.05).

Conclusion: TSH levels, fasting blood glucose and hypothyroidism are among the risk factors for the development of the gestational diabetes.

Keywords: Diabetes, hypothyroidism, gestational diabetes mellitus, pregnancy, thyroid disorders

Öz

Amaç: Gestasyonel diyabet ve tiroid bozuklukları gebelikte sık görülen bozukluklardır. Bu çalışma, gebe kadınlarda gestasyonel diyabet ile tiroid hormon düzeyleri arasındaki ilişkiyi araştırmak için yapıldı.

Yöntem: Bu tek merkezli çalışma, Mart 2019-Aralık 2022 tarihleri arasında özel dahiliye polikliniğine başvuran 190 gebenin retrospektif olarak incelenmesiyle yapılmıştır. Gestasyonel diabetes mellitus (GDM) tanısı alan 90 ve GDM tanısı almamış 100 gebe çalışmaya dahil edilmiştir. Çalışmada tiroid belirteçleri olan tiroid uyarıcı hormon (TSH) ve serbest tiroksin hormonu (fT4) ile gebelik diyabeti arasındaki ilişki incelenmiştir.

Bulgular: Yaş ve vücut kitle indeksi açısından olgu ve kontrol arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (p-değeri >0,05). Gruplar arasında TSH açısından istatistiksel olarak anlamlı fark vardı (p-değeri <0,05). Ayrıca sonuçlarda, olgu ve sağlıklı gebeler arasında fT4 açısından istatistiksel olarak anlamlı bir ilişki bulunmadı (p-değeri >0,05). Sağlıklı gebe kadınlar ile GDM'li kadınlar arasında subklinik hipotiroidizm sıklığı açısından istatistiksel olarak anlamlı bir ilişki vardı (p-değeri <0,05).

Sonuç: TSH düzeyleri, açlık kan şekeri ve hipotiroidizm gestasyonel diyabet gelişimi için risk faktörleri arasındadır.

Anahtar kelimeler: Diyabet, gebelik, gestasyonel diabetes mellitus, hipotiroidizm, tiroid bozuklukları

Introduction

Thyroid disorders and diabetes are among the most common endocrine diseases worldwide (1). The prevalence of gestational diabetes mellitus (GDM) is increasing in parallel with the increase in the prevalence of obesity and diabetes in the world (2). GDM is also increasing in Turkey; according to Turkish Statistical Institute data, in 2017, 16.2% of pregnant women suffered from GDM (3). Obesity, nutrition, and genetic factors play a vital role in the occurrence of GDM, which can be prevented by changing

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the dietary pattern and lifestyle (4). Gestational diabetes is a common disorder during pregnancy, called a degree of plasma glucose intolerance, caused by the inability of the pancreas to secrete insulin and a decrease in insulin sensitivity during pregnancy (5,6). Pregnant women whose pancreatic function during pregnancy is insufficient to overcome insulin resistance are diagnosed with gestational diabetes. Failure to control GDM increases the risk of premature birth, fetal macrosomia and hypocalcemia, and congenital abnormalities in the fetus (7-9).

Thyroid disorders are more common in women than in men and are divided into hyperthyroidism and hypothyroidism based on thyroid stimulating hormone (TSH) and free thyroxine (fT4) and free triiodothyronine (fT3) serum levels (10). The thyroid gland's impaired functionality causes a decline in the production of thyroid hormones, leading to hypothyroidism, an endocrine condition. The categorization of hypothyroidism into overt and subclinical types is based on the specific biochemical abnormalities observed (11). The effect of diabetes on thyroid function is known, and thyroid hormones also have a reciprocal effect on carbohydrate metabolism and pancreas function (12). Some researchers have reported a higher prevalence of thyroid disorders in diabetic patients (13).

Pregnancy has a significant impact on thyroid function. An increase in protein binding to thyroxine, an increase in the production of thyroid hormones, and stimulation of the thyroid by gonadotropin occur in pregnancy (14). The role of thyroid dysfunction in the occurrence of GDM can be investigated according to the role of thyroid hormones in glucose metabolism and homeostasis (12).

The primary goal of this research is to examine the association between thyroid disorders and gestational diabetes. In previous studies, conflicting results have been reported by scholars. Some studies have reported a relationship between hypothyroidism and the risk of GDM (15). On the other hand, no significant relationship has been reported in some studies (16). Identifying the relationship between thyroid disorders and GDM is crucial in timely diagnosis and providing more effective treatments. Considering the adverse effects of thyroid disorders on the health of the fetus and the prevalence of these disorders in Turkish women, in this study, comprehensive research was conducted to investigate the relationship between gestational diabetes and thyroid hormone.

Materials and Methods

This retrospective case-control study includes 190 pregnant women referred to the clinic of Centermed Plus between March 2019- December 2022. In this case-control study, 190 pregnant women aged 20 to 35 years, who underwent 75 g the orale glucose tolerantie test (OGTT) between 24 and 28 weeks of gestation and were diagnosed with gestational diabetes, were randomly selected from archive scanning. Ethics Committee Approval of the research was obtained from University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Hospital (date: 07.08.2023, decision no: 2023-15) and written inform consent were taken from all patients.

In this study, the total number of participants were divided in two groups including case (women with gestational diabetes; n=90) and control (healthy women; n=100) groups. Gestational diabetes was diagnosed by performing a fasting blood sugar test in the 24th to 28th week of pregnancy. If blood sugar was less than or equal to 92 mg/dL was considered healthy, 92-125 mg/dL was considered prediabetes, and more than 126 mg/dL was considered diabetic. The OGTT test was performed for pregnant women in prediabetes and diabetic groups. In this test, after consuming 75 grams of glucose, plasma glucose level was measured in three stages: before the drink, "1-hour post-prandial blood sugar (mg/dL)"and "2-hour post-prandial blood sugar (mg/dL)". If the fasting plasma glucose level was more than 92 mg/dL, one hour later more than 180 mg/dL, and two hours later more than 153 mg/dL, it was identified as gestational diabetes. With the retrospective screening method of the pregnant women's files, the blood results of the patients in the first trimester (between the first 6 and 20 weeks), TSH, free T4, fasting blood glucose values recorded in our dataset. Diagnosis of hypothyroidism was made by the TSH value. The subclinical hypothyroidism was defined as having a high TSH level (> 4.0 µIU/mL) and a low or normal fT4.

Statistical Analysis

The Kolmogorov-Smirnov test was performed to test the normality of variables. Mean and standard deviations (SD) were measured to check each continuous variable, including age, body mass index (BMI), fasting blood sugar (FBS), TSH, and FT4. The Mann-Whitney U test was accomplished to investigate the difference between healthy women and women with gestational diabetes in all variables. For categorical data, the number of data (n) and percentage (%) was used to describe the data. The chi-square tests were employed to compare groups with categorical variables.

For statistically significant, it is considered not significant as p>0.05. SPSS v.26 was utilized for statistical analyses.

G-Power v.3.1 was used to calculate the sample size, and two groups' total mean and standard deviations were measured based on the non-parametric test with a power of 95%, 0.05 type 1 error, and effect size of 50% for at least 176 (88 patients for each group) (17).

Results

A total of 190 age-matched (27.01±3.54) and BMI-matched (26.95±4.55) pregnant women participated in this study.

Table 1 shows explanatory details of investigation variables. The mean and median age of the pregnant women was 27.01 and 28 years (SD =3.54). The mean and median BMI of the pregnant women was 26.95 and 27.3 kg/m² (SD = 4.55). The mean and median FT4 of the women was 1.24 and 1.12 ng/dL (SD =0.38). The mean and median TSH of the participants was 2.27 and 2.01 µIU/mL (SD =1.2). The mean and median FBS of the participants were 9.94 and 90 mg/dL (SD =1.2).

Table 2 shows study parameters of healthy women and women with gestational diabetes included in the research.

Table 1. Explanatory details of investigation variables in pregnant women (n=190)

Investigation variables	Median (range) mean ± SD
Age (years)	28 (20-35) 27.01±3.54
BMI (kg/m²)	27.3 (18.7-35) 26.95±4.55
fT4 (ng/dL)	1.12 (0.95-4.01) 1.24±0.38
TSH (µIU/mL)	2.01 (0.46-7.98) 2.27±1.2
FBS (mg/dL)	90 (62-142) 93.49±15.65

SD: Standard deviation. BMI: Body mass index, fT4: Free thyroxine 4, TSH: Thyroid stimulating hormone, FBS: Fasting blood sugar

Table 2. The comparison of healthy women and women with gestational diabetes in study parameters

Study parameters	Case (women with gestational diabetes) (n=90) M ± SD	Control (healthy women) (n=100) M ± SD	p-value
Age (years)	27.01±3.6	27.1±3.51	0.874*
BMI (kg/m²)	26.84±4.73	27.06±4.40	0.846*
fT4 (ng/dL)	1.23±0.33	1.25±0.42	0.947*
TSH (µIU/mL)	2.81±1.48	1.77±0.51	**<0.001***
FBS (mg/dL)	103.17±16.55	84.78±7.72	**<0.001***

M: Mean, N: Number of subjects, BMI: Body mass index, FBS: Fasting blood sugar, TSH: Thyroid-stimulating hormone, FT4: Free thyroxine, *Mann-Whitney U test, SD: Standard deviation

A Mann-Whitney U test did not find statistically meaningful difference between women with gestational diabetes and control in terms of fT4 (p-value >0.05).

As can be seen from the Table 2, there was a statistically significant association between women with GDM and controls regarding TSH and FBS (p-value <0.001). The TSH values in case group (2.81±1.48) was higher than controls (1.77±0.51). The FBS values in case group (103.17±16.55) was higher than controls (84.78±7.72).

There was a statistically meaningful association between healthy women and women with GDM in terms of subclinical hypothyroidism frequency (p-value <0.05). As stated in Table 3, the women with gestational diabetes had 26.6% (n=24) hypothyroidism. The healthy women had a 11% (n=11).

Figure 1 shows the comparison of healthy women and GDM in TSH. As can be seen from the Figure 1, the frequency of hypothyroidism in female cases is twice as high as in the control group.

Discussion

In this study, thyroids hormone values and the subclinical hypothyroidism frequency of women with GDM were compared with the control group. According to the results,

Table 3. The significant relationship between case and control groups and hypothyroidism frequency

Variable		Case (n=90) n (%)	Control (n=100) n (%)	p-value
Hypothyroidism	Yes	24 (26.6)	11 (11)	0.006*
	No	66 (57.4)	89 (89)	

*chi-square test

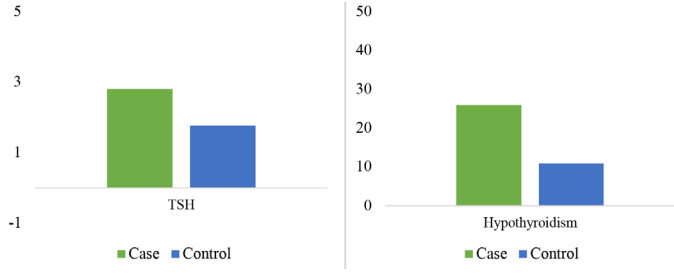

Figure 1. The comparison of healthy women and women with gestational diabetes in TSH and FBS

TSH: Thyroid-stimulating hormone, FBS: Fasting blood sugar

women with gestational diabetes show a significant difference in thyroid disorders compared to healthy pregnant women, consistent with previous studies (15,18-22). Elevated first-trimester TSH levels in pregnant women with normal fT4 levels are associated with an increased risk of GDM. Also, the presence of hypothyroidism in women with GDM is associated with an approximately two times greater likelihood in healthy pregnant women.

In a similar study, Fernández Alba et al. (15), identified the higher first trimester TSH level as a risk factor for GDM by examining the data of 6775 Spanish pregnant women. Demiral Sezer and Topaloglu (21), tested the relationship between thyroid hormones and GDM on 160 Turkish women with multicenter data. High TSH levels had a significant relationship with gestational diabetes. Kent et al. (22), showed that TSH in women with GDM was significantly higher than control group in a meta-analysis. Chen et al. (16), reported no significant relationship between higher TSH level and risk of GDM by investigating the data of 2.849 Chinese pregnant women. Although conflicting results have been reported regarding the significant relationship between higher TSH levels and GDM, it can be concluded that a level of TSH higher than (>4.0 μIU/mL) can be considered a risk factor in pregnant women for GDM.

The prevalence of subclinical hypothyroidism in this study was 26.6% in women with GDM. Which was significantly higher than healthy pregnant women, consistent with previous studies (18-20). Imdad and Shylaja (18) reported 27 cases of hypothyroidism in 100 women with gestational diabetes. The frequency of hypothyroidism was higher in diabetic women. Latifah et al. (19), reported 12-15% for prevalence of hypothyroidism in women with GDM. Reviewing every study in this field is impossible, and meta-analyses and survey articles can be used to compare the results. In a comprehensive review, Dincgez et al. (20), studied hundreds of articles on the relationship between maternal subclinical hypothyroidism and GDM. In their conclusion, they emphasized the effectiveness of maternal subclinical hypothyroidism in increasing the risk of GDM. No significant relationship between two was reported in others meta-analyses, which examined a much smaller number of articles (23,24). The finding of the current studies shows that hypothyroidism in pregnant women has a more increased risk for GDM than healthy pregnant women overall. Hypothyroidism has an adverse impact on glucose homeostasis by causing insulin resistance. Pregnant women with hypothyroidism increase insulin resistance and in this condition the risk of GDM increases (25,26).

In this study, age-matched and BMI-matched pregnant women participated so that age and obesity did not affect the results. Previous studies have shown that the risk of gestational diabetes increases with increasing BMI and maternal age (21,27). The frequency of this disease is higher in women older than 25 and BMI ≥25.0 kg/m^2 (28).

Study Limitations

The number of participants in the paper is relatively small, and it is suggested to conduct research with a higher number of participants. Gestational diabetes and thyroid disorders may be affected by geographical and racial factors. One of the limitations of this study is that the patients' data from a single center, and it is suggested to use patients' data in several centers in future studies. Examining the effect of demographic information such as education, income level, and hereditary history of diabetes and thyroid failure in mothers can add to the positive aspects of the study.

Conclusion

In overview, fasting blood glucose, higher TSH levels, and subclinical hypothyroidism was among the factors leading to GDM and can be considered important risk factors. The benefits of regular screening for thyroid function during pregnancy are controversial. Based on the findings of this study, regular screening for thyroid function in pregnant women is beneficial and safe for timely prevention and providing more effective treatments. Nevertheless, there is a requirement for more randomized-prospective studies to be conducted.

Ethics

Ethics Committee Approval: Ethics Committee Approval of the research was obtained from University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Hospital (date: 07.08.2023, decision no: 2023-15).

Informed Consent: The need for informed consent was waived under the approval of the local ethics committee due to the retrospective design.

Peer-review: Internally and externally peer-reviewed.

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ORIGINAL RESEARCH

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Investigating the 25(OH) Vitamin D Levels and Impacts of Urinary Tract Infection in Geriatric Hematogenous Septic Arthritis Patients

Geriyatrik Hematojen Septik Artritli Hastalarda 25(OH) Vitamin D Düzeyleri ve İdrar Yolu Enfeksiyonunun Etkilerinin Araştırılması

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Abstract

Objective: Our study aimed to determine the serum level of 25(OH) vitamin D in geriatric hematogenous septic arthritis and to assess the potential presence of urinary tract infections in the same cohort.

Method: The study included 22 patients diagnosed with septic arthritis and 25 individuals selected to match the control group's age and gender distribution. Inclusion criteria for patients diagnosed with septic arthritis were the presence of monoarthritis, age over 60, swelling and pain in the joint, high C-reactive protein (CRP) levels, purulent joint fluid, and the presence of more than 50,000 neutrophils per mm^3 in the joint fluid or within the joint culture. In both the septic arthritis and control groups, a comprehensive assessment encompassed hemogram, CRP, whole blood biochemistry, complete urinalysis, urine culture, and 25(OH) vitamin D tests for comparative analysis.

Results: In the patient group, 25(OH) vitamin D levels were significantly lower than the control group ($p<0.05$). Urine analysis revealed a notably higher leukocyte count in the patient group compared to the control group ($p<0.05$). In addition, the patient group exhibited significantly lower blood albumin levels in contrast to the control group, along with a significant decrease in hemoglobin levels ($p<0.05$). There was no significant difference in urine culture distribution between the patient and control groups ($p>0.05$).

Conclusion: Our study has identified a notable correlation between severe vitamin D deficiency and hematogenous septic arthritis among elderly individuals. Furthermore, evidence of bacteriuria and pyuria emerged in the complete urinalysis of some subjects. These findings support our belief that certain instances of hematogenous geriatric septic arthritis may arise as a consequence of urosepsis.

Keywords: Geriatric, sepsis, septic arthritis, urinary tract infection, vitamin D

Öz

Amaç: Çalışmamızın amacı geriyatrik hematojen septik artritlerde 25(OH) vitamin D serum seviyesini saptamak ve aynı hastalarda idrar yolları enfeksiyonu olup olmadığını araştırmaktır.

Yöntem: Çalışmaya septik artrit tanısı almış 22 hasta ve kontrol grubu olarak benzer yaş ve cinsiyet dağılımı gösteren 25 denek dahil edilmiştir. Septik artrit tanısı konmuş olan hastalarda dahil edilme kriterleri monoartrit olması, 60 yaş üstü olması, eklemde şişlik ve ağrı olması, C-reaktif protein (CRP) yüksekliği, eklem sıvısının pürulan karekterde olması, eklem sıvısında mm^3'te 50000 üzerinde nötrofil olması ya da eklem kültüründe üretilmiş olması olarak belirlenmiştir. Hem septik artrit hem de kontrol grubundan, karşılaştırma yapmak için hemogram, CRP, tam kan biyokimya, tam idrar tahlili, idrar kültürü, 25(OH) vitamin D tetkikleri istenmiştir.

Bulgular: Olgu grubunda 25-(OH) vitamin D serum seviyeleri değeri kontrol grubundan anlamlı ($p<0,05$) olarak daha düşüktü. Olgu grubunda idrarda lökosit sayısı değeri kontrol grubundan anlamlı ($p<0,05$) olarak daha yüksekti. Olgu grubunda kandaki albümin değeri kontrol grubundan anlamlı ($p<0,05$) olarak daha düşüktü. Olgu grubunda hemoglobin değeri kontrol grubundan anlamlı ($p<0,05$) olarak daha düşüktü. Olgu grubu ve kontrol grubu arasında idrar kültürü dağılımı anlamlı ($p>0,05$) farklılık göstermemiştir.

Sonuç: Yaşlı bireylerdeki hematojen nedenli septik artritlerde ciddi D vitamini eksikliği ile beraber bir kısmında da tam idrar tahlilinde bakteriüri ve piyüri saptanmıştır. Hematojen geriyatrik septik artritlerin bir kısmının ürosepsis sonucunda geliştiğini düşünüyoruz.

Anahtar kelimeler: Geriyatrik, idrar yolları enfeksiyonu, sepsis, septik artrit, vitamin D

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Introduction

With advancing age, people become more susceptible to infections due to the weakening of their immune systems. Aging disrupts acquired immunity because of T-cell dysfunction and impaired cytokine-mediated inflammatory response (1). One common infection that affects the elderly is urinary tract infections (UTIs), which can lead to septicemia or sepsis (2). Another serious infection that is prevalent among the geriatric population is septic arthritis, which can sometimes be mistaken for acute exacerbation of osteoarthritis, leading to its underdiagnosis. The etiology of septic arthritis encompasses both exogenous and endogenous factors.

Exogenous causes involve invasive interventions such as intra-articular injections and joint arthroplasty (3-5). In contrast, endogenous causes occur as a result of hematogenous spread. The prevalence of diseases such as osteoarthritis and diabetes mellitus, in addition to diseases such as Alzheimer's and dementia, which reduce self-care in the elderly, paves the way for septic arthritis (2,5). In the elderly, septic arthritis most commonly affects the knee joint. Researchers have found a link between UTIs and the development of septic arthritis in older adults (2).

Furthermore, studies have suggested that vitamin D plays a crucial role in maintaining a healthy immune system and reducing the risk of infections. Vitamin D, functioning as a hormone, is primarily synthesized via exposure to ultraviolet sunlight. Vitamin D plays an important role in bone hemostasis, prevention of some cardiovascular diseases, stimulation of insulin secretion, and the regulation of the immune system and inflammatory processes (6,7). Individuals with vitamin D deficiency are prone to infection and sepsis (8,9). Vitamin D plays an important role in the regulation of immunomodulatory function through the presence of vitamin D receptors in most immune cells (10). Low vitamin D levels have been associated with an increased risk of infections and inflammatory diseases (3).

Given this context, our current study is geared toward evaluating vitamin D levels in elderly patients with UTIs and septic arthritis, to understand its potential impact on their conditions. This research endeavor holds significance in highlighting the importance of detecting and managing UTIs among geriatric patients, in addition to emphasizing the potential advantages of maintaining optimal vitamin D levels to prevent and manage infections. Understanding the relationship between UTIs, septic arthritis and vitamin D can help healthcare professionals provide better care and improve outcomes for their elderly patients.

Materials and Methods

This retrospective, cross-sectional study was carried out at University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital between 2020 and 2021. Our study involved 22 patients aged 60 and above, diagnosed with septic arthritis, as well as a control group comprising 25 individuals sharing similar age and gender characteristics. The control group was selected from patients who visited the outpatient orthopedic clinic.

Inclusion criteria for patients diagnosed with septic arthritis were the presence of monoarthritis, age over 60, swelling and pain in the joint, high C-reactive protein (CRP) levels, purulent joint fluid, and the presence of more than 50,000 neutrophils per mm^3 in the joint fluid or within the joint culture. Patients afflicted with rheumatologic disorders, chronic renal failure, septic arthritis following prior joint surgery, recent intra-articular injections, or localized skin infections near the joint were excluded from the study. Only septic arthritis cases thought to be of hematogenous origin were included in the study. Joint fluid was taken from all septic arthritis patients under sterile conditions and sent to the laboratory for neutrophil count, aerobic and anaerobic cultures, and Gram-staining. Synovial fluid and urine were inoculated on aerobic chocolate, blood agar, and anaerobic blood agar plates, then incubated for seven days aerobically at 37 °C with 5% CO_2 and anaerobically at 37 °C.

Before the initiation of empirical antibiotic therapy, all patients suspected of having septic arthritis underwent comprehensive diagnostic evaluations, including complete urinalysis, urine culture, 25(OH) vitamin D levels, whole blood biochemistry, hemogram, sedimentation, CRP, lung PA X-ray, and electrocardiography. Consultations with infectious diseases, internal medicine, cardiology, chest diseases, and anesthesia and reanimation departments were sought for all patients suspected of septic arthritis. Patients in the control group underwent hemogram, CRP, whole blood biochemistry, complete urinalysis, urine culture, and 25(OH) vitamin D tests. In both groups, serum vitamin D levels were measured using the electrochemiluminescence immunoassay method.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional

Review Board. All study participants provided informed consent before participating in the study. The confidentiality and privacy of the participants were ensured throughout the study.

Statistical Analysis

Taking into consideration the frequency of vitamin D deficiency and urinary trac infection in elderly septic patients in the literature, the study's sample size was determined through power calculations involving both qualitative and quantitative data, with a statistical power of over 80% and a margin of error of 5%. Mean, standard deviation, median, minimum, maximum, frequency, and percentage were used for descriptive statistics. The distribution of variables was checked with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for the comparison of the quantitative data, while the chi-square test was employed for the comparison of the qualitative data. The SPSS v.28.0 software was employed in all statistical analyses.

Results

The age distribution of patients exhibited no significant difference between the patient and control groups ($p>0.05$). Furthermore, the gender distribution among patients demonstrated no significant difference between the case and control groups ($p>0.05$). In the patient group, the 25(OH) vitamin D levels were significantly lower than the control group ($p<0.05$) (Figure 1). Urine analysis revealed a notably higher leukocyte count in the patient group compared to the control group ($p<0.05$) (Figure 2). Conversely, the urinary erythrocyte count didn't manifest any considerable distinction between the patient and control groups ($p>0.05$). In addition, the patient group exhibited significantly lower blood albumin levels in contrast to the control group, along with a significant decrease in hemoglobin levels ($p<0.05$). The CRP value in the patient group exceeded that of the control group, signifying a significant disparity ($p<0.05$). There was no significant difference in urine culture distribution between the patient and control groups ($p>0.05$) (Table 1). The mean leukocyte count per mm^3 in the joint fluid of septic arthritis patients reached 81,077, as indicated in Table 2.

Discussion

Our investigation unveiled a noteworthy prevalence of 25(OH) vitamin D deficiency alongside frequent occurrences of bacteriuria within the urinary tract of patients afflicted with hematogenous geriatric septic arthritis. Moreover, this patient cohort exhibited a significant reduction in mean hemoglobin and serum albumin levels when compared to the control group.

In the guideline for diagnosis and treatment of metabolic bone diseases published in 2012 by the Turkish Society of Endocrinology and Metabolism, 25(OH) vitamin D was evaluated in four categories based on serum concentration: significant deficiency for serum 25(OH)D levels <10 ng/mL, deficiency for levels between 11-20 ng/mL, insufficiency for levels between 21-30 ng/mL, and normalcy for levels >30 ng/mL. Remarkably, the serum vitamin D level in septic arthritis patients reached a mere 7.3 ng/mL, while it was observed that the mean vitamin D levels within the control group, albeit lower than the patient group, were significantly higher. Vitamin D deficiency (≤30 ng/mL) or insufficiency (≤20 ng/mL) is known to be associated with an increased risk of infection (11,12). Furthermore, vitamin D levels in septic patients in all age groups are lower than in other patients without sepsis (13,14).

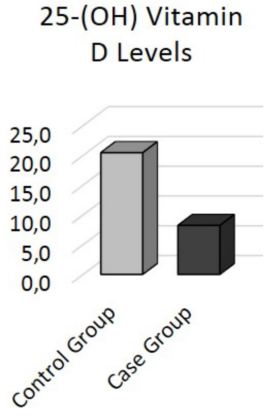

Figure 1. Serum vitamin D levels in the control and septic arthritis group

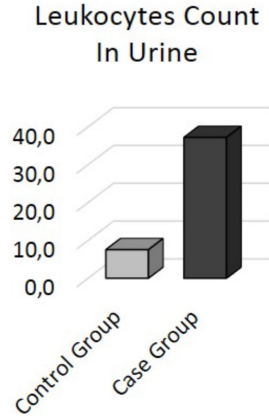

Figure 2. Mean leukocyte count in the urine of the control and septic arthritis groups

Table 1. Comparison of the 25(OH) vitamin D, albumin, CRP, and hemoglobin levels, and complete urinalysis and urine culture outcomes of both septic arthritis and control groups

		Control group		Patient group		p
Mean ± SD/n-%		**Median**	**Mean ± SD/n-%**	**Median**		
Age		71.9±7.3	71.0	74.9±7.8	74.0	0.208*
Gender	Female	19, 76.0%		11, 50.0%		0.064†
	Male	6, 24.0%		11, 50.0%		
Albumin levels in blood		4.0±0.4	4.1	3.3±0.57	3.3	**0.000***
CRP		5.1±5.1	3.6	162±65.0	167.0	**0.000***
Hemoglobin		12.3±1.8	12.5	11.3±1.8	11.7	**0.044***
25(OH) vitamin D		20.4±13.3	17.0	8.2±3.5	7.3	**0.000***
Leukocyte count in urine		7.6±17.9	2.0	37.2±137.9	3.0	**0.047***
Erythrocyte count in urine		3.5±4.8	1.0	12.6±33.6	3.5	0.067*
Bacterıa count in urine		3.4±13.7	0.0	10.6±23.3	0.0	0.050*
Urine culture						
(-)		22, 88.0%		15, 68.2%		0.098†
(+)		3, 12.0%		7, 31.8%		
Escherichia coli		3, 12.0%		5, 22.7%		
Candida albicans		0, 0.0%		1, 4.5%		
Proteus mirabilis		0, 0.0%		1, 4.5%		

SD: Standard deviation, *Mann-Whitney U test, †chi-square test, CRP: C-reactive protein, significant p-values are written in bold

Table 2. The number of leukocytes per mm³ in the joint fluid, the distribution of the bacteria grown in culture, and blood sedimentation averages in septic arthritis patients

	Patient group	
	Mean ± SD/n-%	**Median**
Sedimentation	66.2±27.2	65.5
Leukocyte count in joint fluid	81,077±55,301	59,401
Joint fluid culture		
(-)	16, 72.7%	
(+)	6, 27.3%	
Staphylococcus aureus	2, 9.1%	
Enterococcus faecalis	1, 4.5%	
Escherichia coli	1, 4.5%	
Staphylococcus haemolyticus	1, 4.5%	
Streptococcus dysgalactiae ssp. *equisimilis*	1, 4.5%	

SD: Standard deviation

Vitamin D's multifaceted role in regulating monocyte activation, attenuating inflammatory responses triggered by pathogens such as bacteria, viruses, and fungi, its bactericidal properties, facilitation of phagocytosis, and induction of B and T-cell proliferation and differentiation, have all been well-documented (9,15). In addition, the synthesis of cathelicidin, a strong antimicrobial peptide synthesized from neutrophils in the epithelia of the respiratory, bladder, and gastrointestinal tract, is stimulated by vitamin D (6). Notably, previous studies have shown that patients with low vitamin D levels have longer hospital stays and higher mortality rates than patients with normal vitamin D levels (7,12,16,17). In our study, the average hospitalization period of the patients ranged from 3 to 6 weeks, with one unfortunate fatality during this period.

The realm of sepsis reveals genitourinary infections as the second most prevalent cause. Furthermore, among the elderly, UTIs claim the position of the second most common ailment after respiratory tract infections (1). In addition, asymptomatic bacteriuria emerges as a prevalent occurrence within this demographic. In our study, while 20% bacteriuria was observed in the urine in the control group, the rate escalated to 50% in the septic arthritis group. The geriatric populace confronts various factors contributing to this trend, encompassing advanced age, the burden of diseases that impede cellular immunity, and complications stemming from conditions like dementia, stroke, and Parkinson's disease that instigate incontinence within the urinary bladder and intestines (18,19).

In females, estrogen deficiency within this age group causes vaginal and urinary incontinence, and thus bacterial flow into the sterile urinary tract. In addition,

the deficiency further disrupts the protective colonization of *Lactobacillus* bacteria in the vagina, which normally suppresses the growth of pathogenic bacteria (20). On the male front, prostatic hypertrophy causes post-void urinary retention, predisposing them to chronic prostatitis. On the other hand, a chronically inflamed prostate causes recurrent UTIs by forming stones that trap bacteria (21). Thus, our findings postulate that the recurrence of UTIs in the elderly causes sepsis and paves the way for septic arthritis development.

While one or more leukocytes were observed in the urine of all but one of the septic arthritis patients, there were no leukocytes in the urine of six participants in the control group. Pyuria, denoting the emergence of leukocytes surpassing 10 HPF (high-power field) in urine, was identified in eight septic arthritis patients, as opposed to four from the control group. Although there was no difference in microscopic hematuria (erythrocyte count ≤50 HPF) in both groups, one patient in the septic arthritis group had gross hematuria. Nonetheless, it's crucial to acknowledge that the presence of asymptomatic bacteriuria, pyuria, and microscopic hematuria alone does not suffice for a UTI diagnosis (2). Antibiotic treatment is not recommended in asymptomatic bacteriuria because of multidrug-resistant bacteria growth and high recurrence rate (2,22). Nonetheless, we underscore the significance of vigilant monitoring via complete urinalysis, as changes in its content may be a precursor to sepsis. The diagnosis of UTI is mostly made in the presence of major symptoms such as dysuria or fever. McGeer et al. formulated diagnostic criteria for UTIs, encompassing indicators such as dysuria, fever, flank pain, suprapubic pain, chills, gross hematuria, new urinary incontinence, changes in urinary characteristics (hematuria, increased pyuria, altered odor, etc.), cognitive and functional decline, and delirium. While dysuria or fever is sufficient alone for the diagnosis of UTI among these criteria, the authors stipulated that at least three of the other criteria should be present in non-catheterized patients in the absence of these two criteria (2,23). Notably, upon investigating the medical histories of septic arthritis patients, it emerged that a subset of them reported dysuria-related complaints.

Urine cultures of septic arthritis patients yielded *Escherichia coli* in five cases, *Proteus mirabilis* in one, and *Candida albicans* in another (Table 1). In the control group, *E. coli* grew in three cultures. The most isolated microorganism in UTI is *E. coli*, and its prevalence is reported to be 53% in the literature (24), followed by *Proteus* at 15% and *Klebsiella* at 14% (24,25). The causative pathogen was cultured in 28% of the joint fluid of septic arthritis patients, with *Staphylococcus aureus* being the prevailing microorganism (Table 2). For all age groups, *Staphylococcus aureus* ranks as the most prevalent cause of septic arthritis (5). Other produced microorganisms were *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus haemolyticus*, and *Streptococcus dysgalactiae* ssp. *equisimilis* (Table 2). All of these bacteria produced in the joint fluid can cause urosepsis in the elderly (26-28). The physiological balance of the urinary tract's flora is known to deteriorate with age, potentially leading to polymicrobial infections (2). Microorganisms such as *Staphylococcus epidermitis, Streptococcus faecalis*, non-pathogenic *Neisseria* species, *Corynebacterium*, as well as *Candida* fungi can be found in the urinary tract flora.

There may be a significant relationship between the serum level of vitamin D in the elderly and the risk of UTI, similar to observations in children (29). In addition, there are studies related to the fact that vitamin D may be effective in the management of UTI infection through different mechanisms (30,31). It has been shown that tightly bound proteins play an important role in preventing bacterial invasion of the epithelial barrier, and that vitamin D supplementation can strengthen the bladder lining and restore bladder epithelial integrity (30). In addition, vitamin D acts as a local immune response mediator in UTIs (32). In a randomized clinical trial, the subjects who received vitamin D3 (20,000 IU per week) for five years showed better prevention against UTIs (33).

In this present study, septic arthritis patients experienced joint involvement predominantly in the right knee (12 cases), followed by the left knee (seven cases), right ankle (two cases), and right shoulder (one case). Notably, septic arthritis patients exhibited lower albumin and hemoglobin levels compared with the control group (Table 1). In addition, due to the presence of comorbidities in these patients, the duration of emergency surgery was prolonged in some instances. While emergency arthroscopic saline flushing and debridement were performed in merely six out of the 22 patients, others underwent emergency aspiration and flushing via the lateral suprapatellar portal, performed at the bedside. Patients who underwent bedside emergency washing at the bedside were subject to follow-up involving serum CRP level and neutrophil count in the joint fluid and clinical examination. Patients displaying a less rapid healing response during follow-up were subjected to late arthroscopic washing and debridement.

Study Limitations

There were several limitations in our study, including the limited number of cases, the omission of procalcitonin investigation in septic arthritis patients, and the culturing of causative microorganisms in joint fluid in only a minority of cases.

Conclusion

Our study has identified a notable correlation between severe vitamin D deficiency and hematogenous septic arthritis among elderly individuals. Furthermore, evidence of bacteriuria and pyuria emerged in the complete urinalysis of some subjects. These findings support our belief that certain instances of hematogenous geriatric septic arthritis may arise as a consequence of urosepsis. This situation should be considered when choosing antibiotics for treatment and supplementing with vitamin D.

Ethics

Ethics Committee Approval: Granted by University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Clinical Research Ethics Committee of (12, 22, 2022-subject 2022/12/11/048).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Authorship Contributions

Surgical and Medical Practices: S.Ç., E.B., Concept: S.Ç., En.B., O.B., Design: S.Ç., O.B., Data Collection or Processing: E.B., En.B., Analysis or Interpretation: E.B., En.B., O.B., Literature Search: S.Ç., E.B., Writing: S.Ç.

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ORIGINAL RESEARCH

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Turkish Clinicians Opinions About COVID Treatment in 2nd and 3rd Level Hospitals What Did Change from 2021 to 2022? Results of 2 Years of Follow-up

İkinci ve Üçüncü Basamak Hastanelerin COVID Kliniklerinde Çalışan Doktorların Tedavi Seçeneklerine Bakışı 2021'den 2022 ye Ne Değişti? 2 Yıllık İzlemin Sonuçları

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Abstract

Objective: To determine the change in opinion about the treatment options of Turkish doctors who fight Coronavirus (COVID) in 2nd and 3rd level hospitals.

Method: A questionnary compromised of 14 questions is asked to clinicians who worked in COVID clinics of 2nd and 3rd level hospitals in March 2021 and March 2022.

Results: Prednisolone, IV use of 60 and 80 mg when added to standart therapies was observed more effective in 2022 than in 2021. Also, use of high doses of prednisolone (250 mg and higher) was also found more efective in 2022 than 2021. Acetyl salicilic acide (ASA) is used in routine treatment in both years, but there was a small decline of trust level in its effectiveness in 2022 than in 2021. Low molecular weight heparine, (especially enoxaparine) is also used in the treatment of COVID for both years and a relatively small decline of trust in its effectiveness was observed in 2022 than in 2021. For vaccines, use of BIONTECH was the golden choice of clinicians for themselves and to be used for their relatives.

Conclusion: During the pandemic, clinicians tried to find the right treatment option to gain control over COVID, at the end ofalmost 3 years, it is well understood that there was no specific treatment but vaccines, steroids, ASA, low molecular weight heparin were the best agents to be used to help COVID patients not to decline to more severe conditions. In Turkey, after our study we can conclude that Turkish clinicians used the similar treatment options and vaccines as their global colleagues and found those agents effective than the other options.

Keywords: Clinicians, COVID, opinion, options, treatment

Öz

Amaç: İkinci ve üçüncü basamak hastanelerin Koronavirüs (COVID) servislerinde çalışan hekimlerin 2 yıl içinde sağaltım seçeneklerine bakışlarındaki değişiklikleri belirlemektir.

Yöntem: On dört soruluk bir test 2021 ve 2022'nin Mart aylarında 2. ve 3. derece hastanelerimizin COVID kliniklerinde çalışan doktorlarına gönüllük esasına dayanarak uygulandı.

Bulgular: Prednizolon IV 60 VE 80 mg'nin standart tedavilere eklenmesi 2022 de 2021'e göre daha etkin bulundu. Ayrıca 250 mg ve üstü doz steroid uygulanması da 2022'de daha üstün bulundu. Asetilsalisilik asit (ASA) uygulanması her 2 yılda da etkin görülse de 2022'de güven aralığı biraz azalmış olarak gözlendi. Düşük moleküler ağırlıklı heparin ve özellikle enoksaparin her 2 yılda da uygulanmış ve 2022 de 2021'e göre etkinlik açısından daha güvenilir bulunmuştur. Aşılara güven açısından en güvenilir aşı BIONTECH olarak gözlenmiştir.

Sonuç: Tüm pandemi boyunda dünyada hekimler COVID'e karşı pek çok ilaç denemişlerdir. Sonuçta standart tedavilere ek olarak aşılar, steroid, ASA, düşük moleküler ağırlıklı heparin en güvenilir sonuçları vermiştir. Ülkemizde de çalışmamızın sonucunda, COVID kliniklerinde çalışan doktorlar da küresel meslektaşlarıyla aynı tedavileri uygulamış ve aynı ilaçları sağaltımda güvenilir bulmuşlardır.

Anahtar kelimeler: COVID, klinisyen, seçenek, tedavi, tercih

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Introduction

In 2023, globally, we are aimed to think that COVID pandemic is now not a very big concern in our life after 2 years of global fighting against it. But can it really be concluded as it? In August 2023 World Health Organization (WHO) warned the member countries about the new variant of COVID named ERIS due to its severe potential.

We tried many options in the treatment but not a specific agent has been found to be the right choice. Coronaviruses (CoV) are a very big virus family which can cause diseases from flu like syndrome and self restricting mild infections to more and deadly severe status like middle east respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) (1).

CoV have sub classes in humans which can pass easily from one patient to another (like HCoV- 229E, HCoV- 0C43, HCoV- NL63 and HKU1- CoV) (1).

SARS-CoV, an unknown virus has emerged in 2003, as the first international health emergency state which caused hundreds of deads. After 10 years MERS-CoV a member of COVID family which was unidentified neither in human nor in animals was identified in humans in Saudi Arabia and after that it was understood that first cases were in an hospital in Zarka, Jordan, April 2012 (1).

31 December 2019, China Office of WHO anounced pneumonia cases of unknown origin in Wuhan city of Hubei state. At 7th of January 2020, the cause is declared as a new CoV (2019-nCoV) which wasn't identified in human before (1).

2019-nCoV was later named Coronavirus disease-2019 (COVID-19) and due to its similarity to SARS-CoV it is then named as SARS-CoV-2.

After the spread of the virus to 113 other countries WHO declared the infection as a pandemic in 11th of March 2020.

In Turkey first meeting of Council of scientific advise council of ministery of health came together in 22nd of January 2020 (1).

First confimed Turkish case is declared in 11st of March 2020. Symptoms mostly are fever, cough, dispnea. Headache, soar throat, nausea, muscle and joint pain, dizziness, loss of smell and taste and diarrea can be seen also.

From asymptomatic status to severe pneumonia and lower respiratory tract infection, renal failure and death can be seen (1).

SARS-CoV-2 has been diagnosed in March 2020 but no specific antivirus treatment is confirmed to be succesfull since then (2).

Molnupavir treatment is recomended in patients (>18 years of age) with confirmed polymerase chain reaction, with low and medium severity, in the first five days of symptoms, and in patients with possibly of getting severe status with no regard of vaccination levels (2,3).

During the early stages of pandemic, it was advised to avoid using the steroids unless there is acute respiratory distress syndrome or resisant shock status (0.5-1 mg/kg doses of prednisolone in those cases only as advised in ESICM) (2-4).

Today, based on randomised controlled studies, the use of glucocorticoids in patients with severe breathing needs is needed to augment the chance of survival and to shorten the stay in hospital (2-4).

In case of patients with COVID related MAS, tocilizumab (IL-6 blocker) and anakinra (IL-1 blocker) can be used if steroid treatment is not enough (2-4).

In patients with no respons to anti- cytokine treatment the use of janus kinase inhibitors (ruksonotinib etc.) is advised (4-6).

Intravenous immunoglobulin treatment in adult patients, with the control of Ig levels (not to be used in IgA defficiency) is advised with the doses of 20 gr/day for 5 days, if clinically needed. Always remembering that 2 gr/kg/day dose can cause severe overdosing symptoms (5,6).

In COVID patients venous and arterial thromboembolic events can occur due to various mechanisms (7).

Low molecular weight heparin (enoxaparine) is advised more than standart heparine because it causes less thrombocytopenia and less injection is needed (7,8).

Dipridamol can be used in the treatment at the doses of 2x75 mg P.O. in the first 14 days of disease because it reduces the replication rate and viral load. It also has anti-aggregan and anti-inflamatory effects. Hypotension can be seen in some patients (8).

Aspirin, when used in 100 mg P.O. dose, there are studies showing that it reduces the lung damage effect of the disease (8).

Favipravir 200 mg P.O. osetalmivir 30 mg -45 mg-75 mg P.O. lopinavir 200 mg/ritonavir 50 mg P.O. are also used in the treatment but no enough benefits are shown (9-11).

Materials and Methods

In our study we tried to evaluate the opinion about the treatment options and changes of preferences of COVID treating Turkish doctors working in 2nd and 3rd degree hospitals during 2 years of follow-up. A questionnary compromised of 14 questions is asked to clinicians in March 2021 and March 2022. Ethics committee permission of University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital is dated 19.01.2022 and the code is 134-2021.

Statistical Analysis

The tests were sent to clinicians who joined the study volontarily. The lowest number of participant was calculated as 25 for each year for statistical efficacy. The results were collected with data alchemer, and the results are analyzed with IBM SPSS.

Results

In 2021 107 (69 female and 38 male), (60 from family medicine, 10 from infectious disease clinic, 24 from internal medicine, 6 anesthesiologists, 4 from pulmonary diseases clinic, 1 cardiologist, 2 practitioner from COVID clinic) and in 2022, 114 (71 female and 43 male) (59 from family medicine clinic, 6 from infectious diseases clinic, 24 from internal medicine clinic, 9 from emergency clinic, 9 anestesiologists, 4 from pulmonary diseases clinic, 2 urologists and 1 surgeon) doctors filled the questionnnary.

All doctors answering the questions were working in COVID clinics. In 2021, the use of hydroxyclorokine was dominant in out and inpatient clinics (7.4% and 29%) but in 2022 it was almost out of use because it was totally deleted from protocols due to its side effects and uneffectiveness (87% of clinicians were not trusting outpatient effect and 88.6% of untrustiness to inpatient use).

Favipravir was also used very frequently 2021 but in 2022 a straight decline was observed due to study results about its side effects and uneffectiveness and self experiences (trust to its effectiveness declined from 64.5% in 2021 to 14.5% in 2022).

Tocilizumab, use and trust to its effectiveness was very high in both years (80.4% in 2021, 89.7% in 2022).

Anakinra also was used in clinics in patients with severe symtomps and in macrophage activation syndrome (MAS) and was found effective in both years (81.3% in 2021 and 82.5% in 2022).

Dexamethasone use and trust in its effectiveness was higher in 2022 than in 2021 (88.8% in 2021 and 90.4% in 2022).

Prednisolone, IV use of 60 and 80 mg when added to standart therapies was observed more effective in 2022 than in 2021 (for 60 mg IV use, in 2021, 82.2% and in 2022, 85.1% trust levels were found. For 80 mg IV use, in 2021, 50.4%, in 2022, 84.2%).

Also, use of high doses of prednisolone (250 mg and higher) in patients with sevre pulmonary symptoms and MAS. It was cofidently used in both years (clinicians trust levels; 74.7% in 2021 and in 2022, 74.6%).

ASA is used in routine treatment in both years. But there was a decline of thrust in its effectiveness in 2022 than in 2021 (60.7% in 2021 to 57% in 2022).

Low molecular weight heparine (LMWH), (especially enoxaparine) is also used in the treatment of COVID for both years and an obvious augmentation of trust to its effectiveness was observed in 2022 more than in 2021 (trust to its effectiveness, 88.6% in 2021 and in 2022, 93.9%).

For vaccines, use of BIONTECH is dominantly preferred by doctors, for themselves and to be used for their relatives (In 2021, 37.4% of clinicians have chosen it and in 2022, 81.6%. In 2021 the percentage of clinicians who have chosen sinovac was 62.6% and in 2022, it was 11.4%). For outpatients of 55 years and older, molnupavir is advised but during our study it wasn't in use.

Discussion

Since the beginning of COVID pandemic, clinicians worked hard to find an effective treatment to stop the virus. A lot of medicaments of every class that could be usefull are applied to patients but at the end of almost 3 years it was obvious that there was no specific treatment to cure it. But some medicaments were found usefull to help the patients who intend to worsen.

In our study we tried to collect datas of clinicians of 2nd and 3rd level hospitals who worked in COVID sections and their opinion about the pharmacologic options that they used to treat patients (Tables 1-3).

The first drug was hidroxychlorokine. In 2021 quite high levels of its use was observed but in 2022 it was no longer in use in Turkey due to its side effects and uneffectiveness. Also during the trials in Brasil, France side effects like QT prolongation and sudden death was observed and it was out of use globally (12). In our study also its use was strictly declined in 2022 than 2021 (Table 4).

For favipravir, its use was in high levels in 2021 because it was thought that it could help patients to get saved of COVID but in 2022 an obvious and clear diminution of its use was observed due to study results all around the World (13) and national experiences. Our results were similar, in 2022 it was almost out of procedures (Table 5).

Tocilizumab use and its effectiveness were very high in both years. Also, IL-6 receptor blocker Tosilizumab is used for severe patients with COVID in almost all the clinics globally and couraging results were added to literature (14). In our study also, clinicians concluded that tocilizumab was effective in severe pulmonary disease and also in MAS (Table 6, 7).

Khani et al. (15) in their study exlained that anakinra which is a IL-1 receptor blocker, can be more beneficial in the early stages of the disease when higher levels of cytokines are yet to be observed, which could prevent progression to severe illness and mechanical ventilation. Four items are shown to be important for achieving the optimal therapeutic effects of anakinra in COVID-19 patients. These items include duration of treatment ≥10 days, doses ≥100 mg, intravenous administration, and early initiation of therapy (15). In our study, we have concluded that in 2021 and specially in 2022 in Turkey, clinicians were in favor of its use based on such datas (Table 8, 9).

Dexamethasone and methylprednisolone (in multiple doses as 60 mg, 80 mg) use were augmented during the pandemic and it was observed that their use in patients with severe pulmonary symptoms and possibly declining to MAS were in favor for the patient. Its use was favored all around the world after study results. Engel et al. (16) described the anti-inflammatory impact of dexamethasone on the pathways contributing to cytokine hyperresponsiveness observed in severe manifestations of COVID-19, including type I/II IFN signaling. They remarked that dexamethasone could have adverse effects in COVID-19 patients with mild symptoms by inhibiting IFN responses in early stages of the disease, whereas it exhibited beneficial effects in patients with severe clinical phenotypes by efficiently diminishing cytokine hyperresponsiveness. That results were smilar to our study results showing that in 2022 their use were more obvious than 2021 (Table 10, 11).

Table 1. Evaluation of Turkish clinicians opinion for COVID treatment options

Statistical analysis				
Answer statistics				
	1st period		**2nd period**	
Completed	100.00%	107	100.00%	114
Partial	0.00%	0	0.00%	0
Refused	0.00%	0	0.00%	0
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 2. Evaluation of Turkish clinicians opinion for COVID treatment options

Gender				
	1st period		**2nd period**	
Female	64.50%	69	62.30%	71
Male	35.50%	38	37.70%	43
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 3. Evaluation of Turkish clinicians opinion for COVID treatment options

Treating COVID confirmation				
	1st period		**2nd period**	
Yes	100.00%	107	100.00%	114
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 4. Clinicians opinion about using hydroxyclorokine in the treatment of COVID

	Definetly trust				**Trust**				**Neither trust nor not trust**				**Don't trust**			**Definetely don't trust**				
	1st period		**2nd period**		**1st period**		**2nd period**		**1st period**		**2nd period**		**1st period**		**2nd period**	**1st period**			**2nd period**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Outpatients only	1	0.9%	0	0.00%	7	6.5%	1	0.90%	35	32.7%	13	11.40%	42	39.3%	51	44.70%	22	20.6%	49	43.00%
Monotherapy inpatient	0	%	0	0.00%	3	2.8%	0	0.00%	37	34.6%	13	11.40%	47	43.9%	47	41.20%	20	18.7%	54	47.40%
Inpatient, combined with steroid	1	0.9%	0	0.00%	28	26.2%	15	13.20%	35	32.7%	30	26.30%	31	29.0%	35	30.70%	12	11.2%	34	29.80%

COVID: Coronavirus

Table 5. Clinicians opinion about favipravir use in the treatment of COVID

	Definetly trust				Trust				Neither trust nor not trust				Don't trust				Definetely don't trust			
	1st period		2nd period		1st period		2nd period		1st period		2nd period		1st period		2nd period		1st period		2nd period	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Inpatients, combined with steroid	9	8.4%	4	3.50%	77	72.0%	23	20.20%	17	15.9%	42	36.80%	4	3.7%	31	27.20%	0	%	14	12.30%
Montherapy, inpatient	6	5.6%	1	0.90%	63	58.9%	16	14.00%	30	28.0%	35	30.70%	7	6.5%	42	36.80%	1	0.9%	20	17.50%
At home.mono	6	5.6%	0	0.00%	64	59.8%	18	15.80%	26	24.3%	34	29.80%	9	8.4%	42	36.80%	2	1.9%	20	17.50%

COVID: Coronavirus

Pinzón et al. (17) howed that, the treatment of severe COVID-19 pneumonia with high-dose methylprednisolone for three days followed by oral prednisone for 14 days, compared with 6 mg dexamethasone for 7 to 10 days, statistically significantly decreased the recovery time, the need for transfer to intensive care and the severity markers C-reactive protein, D-dimer and LDH .

Table 6. Use of tocilizumab for the COVID patients with no respons to routine therapy or general status worsening

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Yes, apllied	52.30%	56	58.80%	67
No, I did not applied	35.50%	38	32.50%	37
I do not know	12.10%	13	8.80%	10
Total	100.00%	107	100.0%	114

COVID: Coronavirus

Table 7. Clinicians opinion about tocilizumab treatment effectiveness in the treatment of COVID

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Yes	80.40%	45	89.70%	61
No	8.90%	5	5.90%	4
I do not know	10.70%	6	4.40%	3
Total	100.00%	56	100.00%	68

COVID: Coronavirus

Table 8. Use of anakinra for the COVID patients with no respons to routine therapy or general status worsening

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Yes, apllied	29.90%	32	54.40%	62
No, not applied	58.90%	63	37.70%	43
I do not know	11.20%	12	7.90%	9
Total	100.00%	107	100.00%	114

COVID: Coronavirus

In our study, in 2022 (more clearly than 2021), clinicians were adapted to use these doses also (Table 12, 13).

About LMWH; Spyropoulos et al. (18) in their randomized clinical trial, showed that therapeutic-dose LMWH reduced major thromboembolism and death compared with institutional standard heparin thromboprophylaxis among inpatients with COVID-19 with very elevated D-dimer levels. In our study also, clinicians are observed trusting to LMWH' s effectiveness in protecting COVID patients from thromboembolic side effects (Table 14).

Tantry et al. (19), in their study explained that, aspirin targets the intracellular signaling pathway that is essential for viral replication, and resultant inflammatory

Table 9. Clinician's opinion about Anakinra's effectiveness in the treatment of COVID

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Yes	81.30%	26	82.50%	52
No	6.30%	2	11.10%	7
I do not know	12.50%	4	6.30%	4
Total	100.00%	32	100.00%	63

COVID: Coronavirus

Table 10. Opinion about dexamethasone's effectiveness in the treatment of COVID?

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Definetely trust	24.30%	26	29.80%	34
Trust	64.50%	69	60.50%	69
Neither trust nor not trust	11.20%	12	7.00%	8
Don't trust	0.00%	0	0,90%	1
Definetely don't trust	0.00%	0	1.80%	2
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 11. Clinician's opinion about the effectiveness of methyl prednisolone in COVID patients

	Definetly trust				Trust				Neither trust nor not trust				Don't trust				Definetely don't trust			
	1st period		2nd period		1st period		2nd period		1st period period		2nd period		1st period period		2nd period		1st period period		2nd period	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
60 mg IV	21	19.6%	35	30.70%	67	62.6%	62	54.40%	17	15.9%	15	13.20%	0	1.9%	0	0.00%	0	%	2	1.80%
80 mg IV	22	20.6%	34	29.80%	70	65.4%	62	54.40%	11	10.3%	16	14.00%	4	3.7%	0	0.00%	0	%	2	1.80%

COVID: Coronavirus

responses, hypercoagulability, and platelet activation. With these multiple benefits, aspirin can be a credible adjunctive therapeutic option for the treatment of COVID-19. In addition, inhaled formulation with its rapid effects may enhance direct delivery to the lung, which is the key organ damaged in COVID-19 during the critical initial course of the disease, whereas the 150-325 mg/day can be used for long-term treatment to prevent thrombotic event occurrences. Being economical and widely available, aspirin can be exploited globally, particularly in underserved communities and remote areas of the world to combat the ongoing COVID-19 pandemic (19). In our study also ASA is used in routine treatment in both years. But there was a diminishing pattern of trust to its effectiveness in 2022 regarding to 2021 (Table 15).

Finally for the vaccinnes; since antiquity clinicians are aware of the effectiveness of vaccination versus disease. It is obvious about COVID also as it is a pandemic caused with virus. The search for an effective vaccine versus COVID was the main concern of all the researchers all aorund the World. After a period of research and studies 4 main vaccines were globally accepted effective and started to be applied to citizens. In Turkey, first Sinovac then like almost all around the World, Biontech and at last Turkovac was applied.

Graña et al. (20) in their study concluded that; compared to placebo, most vaccines reduce, or likely reduce, the proportion of participants with confirmed symptomatic

Table 12. Clinician opinion about the use of pulse steroid treatment (250 mg and higher) in COVID patients

	1st period		2nd period	
Statement	**Percentage**	**n**	**Percentage**	**n**
Definetly trust	30.80%	33	31.60%	36
Trust	43.90%	47	43.00%	49
Neither trust nor not trust	19.60%	21	19.30%	22
Don't trust	5.60%	6	4.40%	5
	0.00%	0	1.80%	2
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 13. Opinion about the use of ASA in patients with COVID disease

	1st period		2nd period	
Statement	**Percentage**	**n**	**Percentage**	**n**
Definetly trust	12.10%	13	10.50%	12
Trust	48.60%	52	46.50%	53
Neither trust nor not trust	29.90%	32	30.70%	35
Don't trust	7.50%	8	8.80%	10
Definetely don't trust	1.90%	2	3.50%	4
Total	100.00%	107	100.00%	114

COVID: Coronavirus

Table 14. Opinion about the use of low molecular weight heparine in the treatment of COVID patients

	1st period		2nd period	
Statement	**Percentage**	**n**	**Percentage**	**n**
Definetly trust	46.70%	50	39.50%	45
Trust	43.90%	47	54.40%	62
Neither trust nor not trust	8.40%	9	4.40%	5
Don't trust	0.90%	1	0.00%	0
Definetely don't trust	0.00%	0	180%	2

COVID: Coronavirus

Table 15. Vaccine preferation to be used for self and relatives against COVID

	1st period		2nd period	
Statement	Percentage	n	Percentage	n
Sinovac	62.60%	67	11.40%	13
Pfizer Biontech	37.40%	40	81.60%	93
Astra Zeneca	0.00%	0	0.90%	1
Moderna	0.00%	0	2.60%	3
Turkovac	0.00%	0	3.50%	4
Total	100.00%	107	100.00%	114

COVID: Coronavirus

COVID-19, and for some, there is high-certainty evidence that they reduce severe or critical disease. There is probably little or no difference between most vaccines and placebo for serious adverse events. Over 300 registered RCTs are evaluating the efficacy of COVID-19 vaccines, and this review is updated regularly on the COVID-NMA platform (covid-nma.com). Implications for practice Due to the trial exclusions, these results cannot be generalized to pregnant women, individuals with a history of SARS-CoV-2 infection, or immunocompromized people. Most trials had a short follow-up and were conducted before the emergence of variants of concern. Implications for research Future research should evaluate the long-term effect of vaccines, compare different vaccines and vaccine schedules, assess vaccine efficacy and safety in specific populations, and include outcomes such as preventing long COVID-19.

Ongoing evaluation of vaccine efficacy and effectiveness against emerging variants of concern is also vital (20).

In our study we observed that BIONTECH was the favorite vaccine chosen by our clinicians to be used for themselves and relatives from 2021 to 2022.

Study Limitations

About our study's limitation we can admit that the number of participants to our clinic study is enough for making a first step to understand Turkish clinicians opinion about their treatment options for COVID, studies with larger numbers of clinicians would be more precise. Also with more participants we can analyse if there is statistical differences in their opinion regarding to their medical branches but also as the COVID treatment protocols are clear and standartised for all clinicians in the world and in Turkey, maybe it will not be needed. For our study there was no statistical difference in clinicians number between 2 years but as we mentioned before, studies with more clinicians can precisely show each clinics opinion about their options for COVID treatment.

Conclusion

Our results showed that, the opinion about the treatment choices of Turkish doctors who work in COVID clinics of 2nd and 3rd degree hospitals are similar to their global colleagues.

From 2021 to 2022 LMWH, ASA, steroid use is augmented due to the study results and clinical observations of their effectiveness in the treatment of COVID. Also after 2 years, there is no specific antiviral treatment option for COVID and the suspicions about the effectiveness of routine antiviral drugs such as favipravir or remdesevir etc. is still a medical problem to be solved.

Anakinra and tocilizumab were used in patients with severe symptoms and MAS and were found effecitve in higher levels both in 2022 than in 2021.

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Ethics

Ethics Committee Approval: Ethics committee permission of University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital is dated 19.01.2022 and the code is 134-2021.

Informed Consent: Not needed for this study.

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ORIGINAL RESEARCH

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Evaluation of Body Image in Patients Diagnosed with Fibromyalgia

Fibromiyalji Tanısı Alan Hastalarda Beden İmajının Değerlendirilmesi

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Abstract

Objective: The aim of this study was to determine the extent to which body image is affected by pain severity in patients diagnosed with fibromyalgia (FM).

Method: A total of 51 patients who were selected from the psychiatry and algology outpatient clinics and had their informed consent obtained were included in the study. All patients were evaluated using the numeric rating scale, body image scale (BIS), Rosenberg self-esteem scale (RSES), Beck depression inventory (BDI), and Beck anxiety inventory (BAI).

Results: A moderate positive correlation was found between BAI scores and BDI and RSES scores, while a moderate negative correlation was found between BIS scores ($p<0.05$). Negative correlations were also observed between BDI scores and BIS and RSES scores.

Conclusion: In our study, it was observed that as depression and anxiety levels increased in FM patients, their perceptions of body and self-decreased, and the presence of a family history in patients also drew attention

Keywords: Body image, chronic pain, fibromyalgia, self-esteem

Öz

Amaç: Fibromiyalji (FM) tanısı alan hastalarında beden imajının ağrı şiddeti ile ne oranda etkilendiğinin ortaya koyulması amaçlanmıştır.

Yöntem: Bilgilendirilmiş onamları alınan, psikiyatri ve algoloji polikliniğinden kontrolleri ve takipleri yapılan toplam 51 hasta seçildi. Tüm hastalar nümerik değerlendirme skalası, beden imajı ölçeği (BİÖ), Rosenberg benlik saygısı ölçeği (RBSÖ), Beck depreyon ölçeği (BDÖ) ve Beck anksiyete ölçeği (BAÖ) ile değerlendirildi.

Bulgular: BAÖ puanları ile BDÖ ve RBSÖ puanları arasında pozitif yönde orta kuvvette, BİÖ puanları arasında negatif yönde orta kuvvette korelasyon olduğu belirlendi. BDÖ puanları ile BİÖ ve RBSÖ puanları arasında negatif yönde orta kuvvette korelasyon olduğu belirlendi ($p<0,05$).

Sonuç: Çalışmamızda, FM hastalarının depresyon ve anksiyete düzeyleri artıkça, beden ve benlik algıları düşüş gözlenmiş olup hastalarda aile öyküsünün varlığı da dikkati çekmiştir.

Anahtar kelimeler: Beden imajı, benlik saygısı, fibromiyalji, kronik ağrı

Introduction

Fibromyalgia (FM) is a chronic pain syndrome characterized by a range of symptoms, including muscle sensitivity, often accompanied by fatigue, sleep disturbances, and depressive moods (1). This condition affects around 2-3% of the population, with more than 90% of cases occurring in women. It also leads to various associated symptoms, including cognitive and functional challenges such as mood fluctuations, fatigue, sleep disruptions, headaches, and a notable impact on mental well-being (1-3).

Body image, an individual's perception of their physique, is intertwined with personality, while self-esteem involves feelings of self-worth and competence compared to others, implying that negative body perception may lead to reduced self-esteem. In contrast, self-esteem is defined as recognizing one's value and positivity without inferiority-superiority comparisons (4,5). Recognized as vital for

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contentment with one's body, body image's impact is more pronounced among women. Issues with body satisfaction have psychological implications, especially in relation to depressive symptoms, while positive body image enhances well-being and quality of life. Conversely, negative body satisfaction might lead to adverse health effects (5).

Within this context, it is hypothesized that while the etiological factors of FM may encompass negative body image and perception in patients, the diagnosis of FM might further exacerbate these negative perceptions regarding body image.

Materials and Methods

Sampling and Procedure

This cross-sectional study was conducted between July 1, 2018, and December 31, 2018, after receiving approval from the Ethics Committee (University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, approval no: KAEK/2018.6.23).

Patients who presented at the algology polyclinic with widespread body pain persisting for at least 6 months or more, without any prior treatment or diagnosis, and who met the FM diagnosis criteria as per the ACR-2016 guidelines, were invited for this study (6). Psychiatric interviews were conducted based on the DSM-5 criteria (7).

Obtaining "informed consent" was a fundamental step for this study, and it was secured from all participating patients. Utilizing a semi-structured form designed by the researcher, essential data regarding the patients' socio-demographic characteristics, diagnoses, and family history were systematically gathered. Each patient underwent comprehensive assessments employing the numerical rating scale (NRS), body image scale (BIS), Rosenberg self-esteem scale (RSE), Beck depression scale (BDI), and Beck anxiety scale (BAI).

Patients aged 18 and above were invited to participate in the study on a voluntary basis. Individuals with language impairments, insufficient educational background that could hinder diagnostic interviews, intellectual disabilities, ongoing use or addiction to psychoactive substances, or any mental disabilities attributed to medical factors were excluded from the study.

Measurement Instruments

Body image scale: BIS was developed to gauge satisfaction with various aspects and functions of the body (8). Comprising 40 items, this scale utilizes a five-point rating system to assess body parts or functions. No specific cut-off score was established. The cumulative scores fall within the range of 40 to 200. At the assessment's conclusion, results are categorized as "low", "medium", or "high". Lower scores denote higher levels of dissatisfaction. The scale's validity has been established through a study conducted in Turkey (9).

RSE: RSE is designed to measure self-esteem (10). This scale encompasses 63 questions divided into 12 sub-categories, all featuring multiple-choice questions. The initial 10 items are employed to assess self-esteem. A score of 0-1 in the "self-esteem" subtest suggests "high" self-esteem; scores of 2-4 indicate "moderate" self-esteem, while scores of 5-6 signify "low" self-esteem. The scale's validity has been established through research carried out in Turkey (11).

Beck depression inventory: BDI is a self-report measure designed to evaluate emotional, cognitive, somatic, and motivational facets. It serves as a widely used tool in research and clinical settings to comprehensively assess depression symptoms and cognitive content. Consisting of 21 items, the scale addresses emotions, cognition, behavior, physical symptoms, and interpersonal symptoms. The survey form contains 21 questions, with patients selecting the most suitable response. Scores between 0 and 63 are obtained by assigning values of 0, 1, 2, and 3 to each question. Results are categorized as follows: 0-9 for no/minimal depression, 10-18 for mild depression, 19-29 for moderate depression, and 30-63 for severe depression (12). The BDI's validity and reliability, as a measure of depression intensity, have been confirmed for Turkish society (13).

Beck anxiety inventory: BAI functions as a self-assessment tool used to determine the frequency of anxiety symptoms experienced by individuals (14). Comprising 21 items, this Likert scale assigns scores between 0 and 3 to each item. The scale's validity and reliability for Turkish usage have been established (15).

Pain intensity: NRS is a widely adopted and straightforward tool in clinical practice for assessing pain intensity. The scale's baseline corresponds to the absence of pain, while its upper limit represents the worst pain experienced. Patients are asked, "On a scale of 0 to 10, how would you rate your pain currently?" and are guided on how to evaluate their pain within this scale (16). NRS scores between 0-4 indicate mild pain, scores of 5-7 denote moderate pain, and scores of 8-10 signify severe pain.

Statistical Analysis

IBM SPSS Version 25 was used in the statistical analysis of this study (17). Mean, standard deviation, median, minimum, maximum and quartile values were used to present the descriptive data. Chi-square (X^2) analysis was used for comparison of categorical variables. Since the scores obtained from the scales did not show a normal distribution, the Mann-Whitney U test was used to compare the mean scores. Spearman Correlation analysis was used to compare scale scores. Linear regression model was used to evaluate the factors affecting the data with continuous variable characteristics. Logistic regression analysis was used to evaluate the factors affecting the variable expressed in pairs. The limit of statistical significance was accepted as $p<0.05$ (18).

Results

Socio-demographic Characteristics

Fifty-one participants [aged 18-67, 50 (98%) females, one (2%) male] completed the study. The mean age was calculated as 44.71±10.74 years. The number of people currently working was significantly less than those who did not work (n=6). Mean body mass index was 28.10±4.97. The most common chronic disease accompanying was thyroid dysfunction [22 (43.2%)]. Other socio-demographic and some physical characteristics are summarized in Table 1.

Pain Intensity Evaluation

Pain Intensity distribution in FM patients is given in Table 2. As seen, 12 patients (23.5%) had moderate pain intensity and 39 patients (76.5%) had severe pain intensity.

Anxiety, Depression, Body Image, and Self-esteem Evaluation

The total scores obtained from the study's utilized scales were as follows: 27.80±13.16 (moderate anxiety) for BAI; 21.61±8.21 (moderate depression) for BDI; 122.61±20.37 for BIS; 1.31±0.76 for RSE (Table 3).

When the correlations (Spearman Correlation analysis) between BAI, BDI, BIS and RSE scores, it was determined that there was a positive correlation between the BAI scores and the BDI and RSE scores, and a negative correlation between the BIS scores ($p<0.05$ for each). It was determined that there was a negative correlation between BDI scores and BIS and RSE scores ($p<0.05$ for each) (Table 4).

The comparison of the BAI, BDI, BIS and RSE scores of the groups divided into moderate and severe according to the

Table 1. Demographic findings of the patients

Parameters	n	%	Mean	SD	Min	Max	IQR 25	IQR 75
Gender								
Male	1	2						
Female	50	98						
Age (years)			44.71	10.74	18.00	67.00	36.00	53.00
Education (years)			7.00	4.25	0.00	15.00	5.00	11.00
Working status								
Still working	6	11.8						
Left job	23	45.1						
Never worked	22	43.1						
Marital status								
Single	3	5.9						
Married	40	78.4						
Widow	2	3.9						
Divorced	4	7.8						
Living together	2	3.9						
BMI			28.10	4.97	18.00	41.00	25.00	31.00
Physical trauma								
Yes	13	25.5						
No	38	74.5						
Physical permanent problem								
Yes	6	11.8						
No	45	88.2						
Suicidal attempt								
Yes	5	9.8						
No	46	90.2						

N: Number, SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index, BMI calculated using the formula kg/m^2.

intensity of pain in the study. As a result of Mann-Whitney U, there was no difference between the two groups in terms of BDI, BAI, BIS and RSE scores (p>0.05 for each) (Table 5).

Binary logistic regression analysis revealed that socio-demographic status, anxiety, depression, body image, and self-esteem were not associated with whether the pain intensity moderate or severe.

Discussion

The presence of numerous symptoms, primarily pain, in individuals with FM leads to a reduced quality of life, curtailing their daily activities. These symptoms might also alter how FM patients perceive themselves and their bodies, potentially exerting a detrimental influence on the disease progression and potentially paving the way for subsequent psychiatric issues (19,20). Hence, our study aims to comprehensively assess the interplay of body perception, self-esteem, as well as socio-demographic and clinical attributes among FM patients.

Although the number of participants in our sample was not extensive, the socio-demographic characteristics we observed among FM patients are consistent with previous data (2,19,20) (with a higher proportion of female participants, lower education levels, and socio-economic status).

In the present study, we observed that patients diagnosed with FM exhibited coexisting moderate levels of depression (with a mean BDI score of 21) and moderate levels of anxiety (with a mean BAI score of 27). Furthermore, a substantial proportion (76.5%) of participants reported experiencing severe pain intensity in our sample.

The co-occurrence of anxiety and depression in FM patients is well-documented in the literature, and previous studies (19-21) have established a connection between anxiety, depression levels, and pain intensity. Our findings align with these historical data. However, it's important to note that our study did not explore the potential mediating role of anxiety and depression on pain intensity.

To address this gap, future research endeavors should aim to investigate the mediating role of anxiety and depression in influencing pain intensity among FM patients. Conducting larger-scale studies with diverse participant groups and incorporating control groups could offer a more comprehensive understanding of these relationships. Notably, none of the participants

Table 2. Pain intensity of the patients

Pain intensity	n	%
Moderate	12	23.5
Severe	39	76.5

Pain intensity assessed by numerical rating scale (NRS). NRS scores ranging from 5 to 7 indicate moderate pain, while scores of 8 to 10 represent severe pain

Table 3. The characteristics of the scores obtained by the study group from the scales

	Median	IQR 25	IQR 75
BAI	25.00	16.00	37.00
BDI	22.00	15.00	28.00
BIS	124.00	117.00	134.00
RSE	1.33	0.50	1.83

BAI: Beck anxiety inventory, BDI: Beck depression inventory, BIS: Body image scale, RSE: Rosenberg self-esteem scale, IQR: Interquartile range

Table 4. Correlations of the scores obtained by the study group from the scales

		BAI	BDI	BIS	RSE
BDI	r^s	0.533			
	p	<0.001			
BIS	r^s	-0.435	-0.475		
	p	<0.001	<0.001	.	
RSE	r^s	0.454	0.589	-0.534	
	p	<0.001	<0.001	<0.001	.
NRS	r^s	-0.080	-0.047	-0.045	0.064
	p	0.575	0.744	0.752	0.654

BAI: Beck anxiety inventory, BDI: Beck depression inventory, BIS: Body image scale, RSE: Rosenberg self-esteem scale, NRS: Numerical rating scale

Table 5. Comparison of the BDI, BAI, BIS and RSE scores of the groups that were divided into moderate and severe according to the intensity of pain in the study

	Moderate			Severe			p
	Median	IQR 25	IQR 75	Median	IQR 25	IQR 75	
BAI	26.00	17.50	34.50	25.00	16.00	37.00	0.903
BDI	20.50	15.00	26.50	22.00	15.00	29.00	0.563
BIS	124.00	116.50	132.50	124.00	117.00	134.00	0.747
RSE	1.04	0.38	1.75	1.33	0.75	1.99	0.379

BAI: Beck anxiety scale, BDI: Beck depression scale, BIS: Body image scale, RSE: Rosenberg self-esteem scale, NRS: Numerical rating scale

emphasized in our study had a prior psychiatric or pain diagnosis. Considering the existing literature on the link between psychiatric co-morbidities and chronic pain, our results underscore the significance of psychiatric screening tests and interventions that can be implemented in primary care settings. Such measures have the potential to contribute to the amelioration of chronic pain severity, thereby improving the overall quality of life for individuals with FM.

In this study, the reported body image values of FM patients were notably low, which aligns with similar findings in previous research (22-24). Notably, our study revealed a significant correlation between the duration of the disease and a negative impact on body image. This suggests that the evolving physical perception and pain associated with disease progression could potentially contribute to adverse changes in body image. Interventions targeting the enhancement of body image have been linked to pain reduction in certain chronic pain conditions (25,26). Recent investigations have explored the potential differential effects of specific exercises compared to general exercises on tactile acuity alterations in FM patients, albeit without significant outcomes (26). When considering the intricate interplay between body image and the severity of fibromyalgia, it is imperative to reconsider these treatment strategies. The results of such re-evaluation could lead to meaningful advancements in the field and offer valuable insights into managing FM more effectively.

FM profoundly restricts patients across various dimensions of life, diminishing their functional capacity in physical, social, and psychological realms. This holistic impact exerts a negative influence on individuals' self-perception in their daily existence. While the subject has been explored in a limited number of studies, there is consensus that self-esteem tends to be lower in FM patients (20,27). In the context of our study, we expect results consistent with previous studies, given the high levels of pain severity among patients and the lack of prior psychiatric supportive care. A comprehensive assessment, involving a substantial cohort of both patients and a well-matched control group, would provide a more robust foundation for understanding the intricate interplay between pain, psychiatric factors, and self-esteem in fibromyalgia.

Another significant outcome arising from the evaluation tests conducted in our study pertains to the notable influence of psychological factors on patients' body and self-perception. This finding is consistent with existing literature (20,28) and highlighting that beyond addressing physical symptoms, the provision of psychological support holds substantial value in enhancing patients' self-perception.

Conclusion

The depression and anxiety levels of FM patients negatively affect their body and self-perception, and family history plays an important role in the etiology of these patients.

Ethics

Ethics Committee Approval: This cross-sectional study was conducted between July 1, 2018, and December 31, 2018, after receiving approval from the Ethics Committee (University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, approval no: KAEK/2018.6.23).

Informed Consent: Informed consent obtained were included in the study.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.M.B., İ.A.Ş., Concept: H.M.B., İ.A.Ş., Design: H.M.B., İ.A.Ş., Data Collection or Processing: H.M.B., İ.A.Ş., Analysis or Interpretation: H.M.B., İ.A.Ş., Literature Search: H.M.B., İ.A.Ş., Writing: H.M.B., İ.A.Ş.

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