Original Articles / *Özgün Araştırmalar*

Case Reports / *Olgu Sunumları*

Turkish Journal of Pediatric Disease / *Türkiye Çocuk Hastalıkları Dergisi*

Volume / *Cilt* 18 Number / *Sayı* 5 September / *Eylül* 2024

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ANKARA BİLKENT ŞEHİR HASTANESİ
ÇOCUK HASTANESİ

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Turkish Journal of Pediatic Disease
Türkiye Çocuk Hastalıkları Dergisi

ANKARA BİLKENT ŞEHİR HASTANESİ
ÇOCUK HASTANESİ

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Turkish Journal of Pediatric Disease has been a member of the DOI® system since March 2013.
Türkiye Çocuk Hastalıkları Dergisi Mart 2013 tarihinden itibaren DOI® sistemi üyesidir.

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Türkiye Çocuk Hastalıkları Dergisi TÜBİTAK/ULAKBİM Türk Tıp Dizini, EBSCOhost Research Databases, ve Türkiye Atıf Dizini tarafından indekslenmektedir.

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22 PAP

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Bu dergi geri dönüştürülebilir, imha etmek istediğinizde lütfen geri dönüşüm kutularına atınız.

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The Turkish Journal of Pediatric Disease is an open access and a scientific publication journal of the Ankara Bilkent City Hospital, Children's Hospital. The journal is published in accordance with independent, unbiased, and double-blind peer review principles. The journal is published bimonthly (January, March, May, July, September, November).

In the Turkish Journal of Pediatric Disease original articles, reviews, case reports, editorials, short reports, book reviews, biographies and letters to the editor are also published in the journal. Besides if related with pediatrics, articles on aspects of pedatric surgery, dentistry, public health, genetics, pshyciatrics and nursery could be published. The publication language of Turkish Journal of Pediatric Disease is English.

Manuscripts submitted to the Turkish Journal of Pediatric Disease will go through a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in the field, in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of manuscripts submitted by editors or by the editorial board members of the journal. The Editor in Chief is the final authority in the decision-making process for all submissions.

The Turkish Journal of Pediatric Disease is indexed in Turkish Medical Index of TÜBİTAK / ULAKBİM, EBSCOhost Research Databases and Türkiye Citation Index.

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Türkiye Çocuk Hastalıkları Dergisi, Ankara Bilkent Şehir Hastanesi Çocuk Hastanesi'nin açık erişimli bilimsel yayındır. Dergi bağımsız, tarafsız ve çift-kör hakemlik ilkelerine uygun olarak yayınlanır. Dergi iki ayda bir yayınlanmaktadır (Ocak Mart, Mayıs, Temmuz, Eylül, Kasım).

Türkiye Çocuk Hastalıkları Dergisi'nde orijinal makale, derleme, olgu sunumu, editöryal, çalışma yöntemi, kısa rapor, kitap incelemeleri, biyografiler ve editöre mektup yayınlanmaktadır. Ayrıca pediatri ile ilgili konulardaki genetik, pediatrik cerrahi, diş hekimliği, halk sağlığı, çocuk ve ergen psikiyatrisi ve hemşirelik makaleleri değerlendirmeye alınır. Türkiye Çocuk Hastalıkları Dergisi'nin yayın dili İngilizcedir.

Türkiye Çocuk Hastalıkları Dergisi'ne gönderilen yazılar çift kör hakemlik sürecinden geçecektir. Her bir yazı tarafsız bir değerlendirme süreci sağlamak için alanda uzman en az iki harici, bağımsız hakem tarafından incelenecektir. Baş editör, tüm başvurular için karar alma sürecindeki nihai otoritedir.

Türkiye Çocuk Sağlığı ve Hastalıkları Dergisi TÜBİTAK/ULAKBİM Türk Tıp Dizini, EBSCOhost Research Databases ve Türkiye Atıf Dizini tarafından indekslenmektedir.

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Yazarlar Türkiye Çocuk Hastalıkları Dergisi'ne bir yazı gönderirken, yazıların telif haklarını Türkiye Çocuk Hastalıkları Dergisi'ne devretmiş olmayı kabul ederler. Yayınlanmamak üzere reddedilirse veya herhangi bir sebepten yazı geri çekilirse telif hakkı yazarlara geri verilir. Türk Türkiye Çocuk Hastalıkları Dergisi'ne ait Telif Hakkı Devri ve Yazarlık Formları (https://dergipark.org.tr/tr/pub/tchd adresinden indirilebilir). Şekiller, tablolar veya diğer basılı materyaller de dahil olmak üzere basılı ve elektronik formatta daha önce yayınlanmış içerik kullanılıyorsa yazarlar telif hakları sahiplerinden gerekli izinleri almalıdır. Bu konudaki hukuki, finansal ve cezai yükümlülükler yazarlara aittir.

INSTRUCTIONS FOR AUTHORS

The Turkish Journal of Pediatric Disease is an open access and a scientific publication journal that is published from the Ankara Bilkent City Hospital, Children's Hospital. The journal is published in accordance with independent, unbiased, and double-blind peer review principles. The journal is published bimonthly (January, March, May, July, September, November)

The journal publishes original articles, reviews, case reports, short reports, editorials, book reviews, biographies and letters to the editor. Additionally, articles on topics related to pediatrics, including aspects of pediatric surgery, dentistry, public health, genetics, psychiatry and nursery, may be considered for publication. The publication language of the Turkish Journal of Pediatric Disease is English.

The editorial and the publication processes of the journal are shaped in accordance with the guidelines of the World Association of Medical Editors (WAME), the Committee on Publication Ethics (COPE), the International Council of Medical Journal Editors (ICMJE), the Council of Science Editors (CSE), the European Association of Science Editors (EASE) and National Information Standards Organization (NISO). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

The originality, high scientific quality, and the citation potential are the most important criterias for a manuscript to be accepted for the publication. Manuscripts submitted for the evaluation should not have been previously presented or already published in an electronic or printed medium. The journal should be informed if manuscript have been submitted to another journal for the evaluation and have been rejected for the publication. The submission of previous reviewer reports will expedite the evaluation process. Manuscripts that have been presented in a meeting should be submitted with a detailed information of the organization, including the name, date, and location of the organization.

Manuscripts submitted to the Turkish Journal of Pediatric Disease will go through a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in the field, in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of manuscripts submitted by editors or by the editorial board members of the journal. The Editor in Chief is the final authority in the decision-making process for all submissions. Articles accepted for publication in the Turkish Journal of Pediatrics are put in the order of publication, with at least 10 articles in each issue, taking into account the acceptance dates. If the articles sent to the reviewers for evaluation are assessed as a senior for publication by the reviewers, the section editor and the editor considering all aspects (originality, high scientific quality and citation potential), it receives publication priority in addition to the articles assigned for the next issue.

An approval of the research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, www.wma.net) is required for the experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts that are concerning experimental researchs on humans, a statement should be informed included that shows a written informed consent of the patients and the volunteers who were given a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information of the patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Materials and Methods section of the manuscript. It is the authors' responsibility to carefully protect the patients' anonymity carefully. For the photographs that may reveal the identities of the patients, releases signed by the patient or their legal representative should be enclosed.

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CONSORT	Randomised controlled trials
STROBE	Observational epidemiological research
STARD	Diagnostic accuracy
PRISMA	Systematic reviews and meta-analysis
ARRIVE	Experimental animal studies
TREND	Non-randomized public behavior

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Manuscripts submitted to the journal will go firstly through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions not conforming to the journal's guidelines will be returned to the submitting author with the technical correction requests.

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Manuscripts should be written using Microsoft Word™ (2010 and higher) software, in Times New Roman, 12 point size and double line spacing. There should be 2 cm margins on all sides on the pages. "System International" (SI) units should be used in manuscripts. Tables and graphics should be cited in the text. Abbreviations can be used provided that they are written openly at the first place they appear in the abstract and text, and the abbreviation is given in parentheses.

In the article, when giving the mean and percentile, 2 digits should be used after the decimal point (such as 231.69 or 231.70, instead of 231.7). In the representations other than integers, two digits should be written after the dot, and in the representation of statistical values (such as p, r, t, z values), three digits should be written after the dot. In the presentation of p values, instead of $p<0.05$ or $p>0.05$, the full p value should be given with three digits after the dot (eg $p=0.029$) with the test statistic. If this value is less than one thousandth, it should be displayed as $p<0.001$.

Preparation of the Manuscript Title page:

Title page should be submitted for all of the submissions and this page should include:

Title page of the manuscript should include the English title of the article. The title page should include the authors' names, degrees, ORCID number and the institutional/professional affiliations, a short title (max 50 character), abbreviations, financial disclosure statement, and the conflict of interest statement. For manuscripts sent by the authors in Türkiye, a title in Turkish is also required. If a manuscript includes authors from more than one institution, each author's name should be followed by a superscript number that corresponds to this/her institution, which is listed separately. Please provide a contact information for the corresponding author, including name, e-mail address, and telephone and fax numbers.

Important Notice: The title page should be submitted separately.

Keywords: Each submission must be accompanied by a minimum of three to a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html). For manuscripts sent by the authors in Türkiye, key words in Turkish are also required.

MANUSCRIPT TYPES

Original Articles:

Word count: up to 3,500 (Introduction, Methods, Results, Discussion)

Title: maximum of 20 words

Structured abstract: up to 250 (Objective, Materials and Methods, Results and Conclusion)

Keywords: 3-6 word, listed in alphabetical order.

Figures and tables: are not limited, but must be justified thoroughly

References: It should be at least 20 and at most 40.

It is required that original articles include an English title, an English structured abstract and English keywords. Additionally, the Turkish title, Turkish structured summary and Turkish keywords are required. It is widely acknowledged that the abstract is of critical importance to the majority of readers, as it is the first section they will read. Furthermore, a significant number of electronic databases only integrate abstracts into their index, which emphasises the importance of including key findings in the abstract. The remaining sections of the manuscript should include the following: Introduction, Materials and Methods, Results, Discussion, Conclusion, Acknowledgement (if required) and References. All sections of the manuscript should start on a new page.

Review Articles:

Word count: up to 5000

Abstract: up to 500 (Objective, Materials and Methods, Results and Conclusion)

Keywords: 3-6 word, listed in alphabetical order.

Figures and tables: are not limited, but must be justified thoroughly

References: up to 80

Review articles are comprehensive analyses of the specific topics in medicine, which are written upon the invitation due to extensive experience and publications of authors on the review subjects. All invited review articles will also undergo peer review prior to the acceptance.

Review articles should include; English title, English abstract and English key words. For manuscripts sent by authors in Türkiye, a Turkish title, Turkish abstract and Turkish key words are also required.

Case Reports:

Word count: up to 2000

Abstract: up to 200

Keywords: 3-6 word, listed in alphabetical order.

Figures and tables: total 5

References: up to 15

There is a limited space for the case reports in the journal and reports on rare cases or conditions that constitute challenges in the diagnosis and the treatment, those offering new therapies or revealing knowledge that are not included in the literature, and interesting and educative case reports are being/ will be accepted for publication. The text should include Introduction, Case Presentation and Discussion.

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Letters to the Editor:

Word count: up to 1500

Figures and tables: total 3

References: up to 15

This type of manuscript discusses about the important parts, overlooked aspects, or lacking parts of the previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a Letter to the Editor. Readers can also present their comments on published manuscripts in the form of a Letter to the Editor. An abstract and Keywords should not be included. Tables, Figures, Images, and other media can be included. The text should not include subheadings. The manuscript that is being commented on, must be properly cited in this manuscript.

Letters to the Editor should include; English title. For the letter to the editor sent by authors in Türkiye, a Turkish title also required.

Study Protocols:

The Turkish Journal of Pediatric Disease welcomes study protocols to improve the transparency of research and inform the scholarly community about the trials that are being underway. Publication decision of study protocols will be by editorial decision. Study protocols for the pilot or feasibility studies are not generally taken into consideration.

Study protocol articles should follow the SPIRIT guidelines that provides a detailed account of the hypothesis, rationale, and methodology of the study. All study protocols must provide an Ethics Committee Approval. All protocols for the clinical trials require a trial registration number and the date of registration.

Tables

Tables should be included in the main document, presenting after the reference list, and they should be numbered consecutively in the order they are referred in the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by the footnotes (even if they were defined within the main text). Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text. The following symbols should be used for abbreviations in sequence: *, †, ‡, §, ||, ¶, **, ††, ‡‡.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or in the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures should also be blind. Any information within the images that may indicate an individual or an institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses as in the following format: The skin prick tests were performed using a multi-prick test device (Quantitest, Panatrex Inc, Placentia, California, USA).

All references, tables, and figures should be referred in the main text, and they should be numbered consecutively in the order that they are referred in the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

REFERENCES

While citing publications, the preference should be given to the latest, most up-to-date publications. Authors should avoid using references that are older than ten years. The limit for the old reference usage is 20% in the journal. If an ahead-of-print publication is cited, the DOI number should be provided. Authors are responsible for the accuracy of the references. Reference numbers should be indicated at the end of the sentences in parentheses and references should be numbered consecutively in the order that they are mentioned in the text. Journal names should be abbreviated as listed in "Index Medicus" or in "ULAKBIM/Turkish Medical Index". References should be typed in consistence with the following examples. Native references should be used as much as possible.

If the reference is a journal;

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of an article is more than 6 followed by "ve ark." in Turkish references and "et al." in international references). Title of the article, title of the manuscript abbreviated according to Index Medicus

(http://www.ncbi.nlm.nih.gov/sites/entrez/query.fcgi?db=nlmcatalog). Year;Volume:First and last page number.

Example: Benson M, Reinholdt J, Cardell LO. Allergen-reactive antibodies are found in nasal fluids from patients with birch polen-induced intermittent allergic rhinitis, but not in healthy controls. Allergy 2003;58:386-93.

If the reference is a journal supplement;

Author(s)' surname and initial(s) of the first name. Title of the article. Title of the manuscript abbreviated according to Index Medicus (http://www.ncbi.nlm.nih.gov/sites/entrez/query. fcgi?db =nlmcatalog). Year;Volume (Suppl. Supplement number): First and last page number.

Example: Queen F. Risk assessment of nickel carcinogenicity and occupational lung cancer. Envirol Health Perspect 1994;102 (Suppl. 1):S2755-S2782.

If the reference is a book;

Author(s)' surname and initial(s) of the first name. Title of the book. Edition number. City of publication; Publisher, Year of Publication.

Example: Ringsven MK, Bond N. Gerontology and leadership skills for nurses. 2nd ed. Albany, NY: Delmar Publishers, 1996.

If the reference is a book chapter;

Surname and initial(s) of the first name of the author(s) of the chapter. Title of the chapter. In: Surname and initial(s) of the first name(s) of the editor(s) (ed) or (eds). Title of the book. Edition number. City of

publication: Publisher, Year of publication: First and last page numbers of the chapter.

Example: Phillips SJ, Whistant JP. Hypertension and stroke. In: Laragh JH, Brenner BM (eds). Hypertension: Pathophysiology, Diagnosis and Management. 2nd ed. New York: Raven P, 1995:466-78.

If the reference is a conference paper presented in a meeting;

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of a conference paper is more than 6 followed by "et al.". Title of the conference paper, If applicable In: Surname and initial(s) of the first name(s) of the editor(s) (ed) or (eds). Title of the abstract book. Title of the meeting; Date; City of the meeting; Country. Publisher; Year: Page numbers.

Example: Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Reinhoff O (eds). MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland. North-Holland; 1992: 1561-5.

If the reference is an online journal:

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of an article is more than 6 followed by "ve ark." in Turkish references and "et al." in international references).Title of the article, title of the manuscript abbreviated according to Index Medicus Year; Volume (Number). Available from:URL address. Accessed date:day.month. year.

Example: Arrami M, Garner H. A tale of two citations. Nature 2008;451(7177): 397-9. Available from: URL:www.nature.com/nature/journal/v451/n7177/full/451397a.html. Accessed 20 January 2008.

If the reference is a website:

Name of the web site. Access date. Available from: address of the web site.

Example: Centers for Disease Control and Prevention (CDC). Acsess date: 12 March 2013. Available from: http://www.cdc.gov/

If the reference is a thesis:

Author's surname and initial of the first name. Title of the thesis (thesis). City; Name of the university (if it is a university); Year.

Example: Özdemir O. Fibrillin-1 gene polymorhism and risk of mitral valve disorders. (Thesis). *Ankara*: Gazi University, 2006.

REVISIONS

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue were raised by the reviewers, and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be cancelled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial 30-day period is over.

Accepted manuscripts are copy-edited for the grammar, the punctuation, and the format. Once the publication process of a manuscript is completed, it will be published online on the journal's webpage as an ahead-of-print publication before being included in it's scheduled issue. A PDF proof of the accepted manuscript will be sent to the corresponding author and their publication approval will be requested within 2 days of their receipt of the proof.

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In a case where a manuscript has taken more than six months' time for the review process, that this allows the author for withdrawing the manuscript.

YAZARLAR İÇİN BİLGİ

Türkiye Çocuk Hastalıkları Dergisi, Ankara Şehir Hastanesi Çocuk Hastanesi'nin açık erişimli bilimsel yayındır. Dergi bağımsız, tarafsız ve çift-kör hakemlik ilkelerine uygun olarak yayınlanır. Dergi iki ayda bir yayınlanmaktadır (Ocak Mart, Mayıs, Temmuz, Eylül, Kasım)

Türkiye Çocuk Hastalıkları Dergisi'nde orijinal makale, derleme, olgu sunumu, editöryal, çalışma yöntemi, kısa rapor, kitap incelemeleri, biyografiler ve editöre mektup yayınlanmaktadır. Ayrıca pedatrik cerrahi, diş hekimliği, halk sağlığı, genetik, çocuk ve ergen psikiyatrisi ve hemşirelik konularında makaleler yayınlanabilir. Türkiye Çocuk Hastalıkları Dergisi'nin yayın dili İngilizcedir.

Derginin yayın ve yayın süreçleri, Dünya Tıbbi Editörler Derneği (World Association of Medical Editors (WAME)), Yayın Etiği Komitesi (Committee on Publication Ethics (COPE)), Uluslararası Tıbbi Dergi Editörleri Konseyi (International Council of Medical Journal Editors (ICMJE)), Bilim Editörleri Konseyi (Council of Science Editors (CSE)), Avrupa Bilim Editörleri Birliği (EASE) ve Ulusal Bilgi Standartları Organizasyonu (National Information Standards Organization (NISO) (NISO)) kurallarına uygun olarak şekillendirilmiştir. Dergi, Bilimsel Yayıncılıkta Şeffaflık ve En İyi Uygulama İlkeleri'ne (Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice)) uygundur.

Yazıların yayına kabulü için en önemli kriterler özgünlük, yüksek bilimsel kalite ve atıf potansiyelidir. Değerlendirme için gönderilen yazılar daha önce elektronik veya basılı bir ortamda yayınlanmamış olmalıdır. Dergi, değerlendirilmek üzere başka bir dergiye gönderilen ve reddedilen yazılar hakkında bilgilendirilmelidir. Önceki inceleme raporlarının sunulması değerlendirme sürecini hızlandıracaktır. Kongre ve toplantılarda sunulan yazılarda yazının sunulduğu toplantının kongrenin adı, tarihi ve yeri de dahil olmak üzere ayrıntılı bilgi ile birlikte sunulmalıdır.

Türkiye Çocuk Hastalıkları Dergisi'ne gönderilen yazılar çift kör hakemlik sürecinden geçecektir. Her bir yazı tarafsız bir değerlendirme süreci sağlamak için alanda uzman en az iki harici, bağımsız hakem tarafından incelenecektir. Baş editör, tüm başvurular için karar alma sürecindeki nihai otoritedir. Türkiye Çocuk Hastalıkları Dergisinde yayınlanmak üzere kabul edilmiş makaleler kabul tarihleri dikkate alınarak her sayıda en az 10 makale olacak şekilde yayın sırasına alınır. Değerlendirilmek üzere hakemlere gönderilen makaleler tüm yönleri (özgünlük, yüksek bilimsel kalite ve atıf potansiyeli) dikkate alınarak hakemler, alan editörü ve editör tarafından öncelikli olarak yayınlanmaya aday bir makale olarak değerlendirilir ise bir sonraki sayıda o sayı için atanmış makalelere ek olarak yayınlanma önceliği alır.

Yazarlardan deneysel, klinik ve ilaç çalışmaları ve bazı vaka raporları için gerekirse, etik kurul raporları veya eşdeğer bir resmi belge istenecektir. İnsanlar üzerinde yapılan deneysel araştırmalarla ilgili yazılar için, hasta ve gönüllülerin yazılı bilgilendirilmiş olurlarının alınabileceği prosedürlerin ayrıntılı bir açıklamasının ardından elde edildiğini gösteren bir ifade eklenmelidir. Hayvanlar üzerinde yapılan çalışmalarda, hayvanların acı ve ıstıraplarını önlemek için alınan önlemler açıkça belirtilmelidir. Hasta onamı, etik komite adı ve etik komite onay numarası hakkında bilgi de makalenin Materyal-Metod bölümünde belirtilmelidir. Hastaların anonimliklerini dikkatlice korumak yazarların sorumluluğundadır. Hastaların kimliğini ortaya çıkarabilecek fotoğraflar için, hasta veya yasal temsilcisi tarafından imzalanan bültenler eklenmelidir.

Tüm makale başvurularında DergiPark ile intihal.net ile arasında yapılan işbirliği uyarınca intihal açısından benzerlik raporu istenecektir. Makale gönderim adımlarında yazarlar bilgilendirlecek ve dosya yükleme adımında sistem tarafından rapor hazırlanarak sonuç e-posta ile yazara bildirlecektir. Rapor açıklandığında yazar gönderim işlemini tamamlayabilecektir. Türkiye Çocuk Hastalıkları Dergisi'ne makale gönderebilmek için benzerlik oranı en fazla %20 olmalıdır.

İntihal, atıf manipülasyonu ve gerçek olmayan verilerden şüphelenilmesi veya araştırmaların kötüye kullanılması durumunda, yayın kurulu COPE yönergelerine uygun olarak hareket eder.

Yazar olarak listelenen her bireyin Uluslararası Tıp Dergisi Editörleri Komitesi (ICMJE - www.icmje.org) tarafından önerilen yazarlık kriterlerini karşılaması gerekir. ICMJE yazarlığın aşağıdaki 4 kritere dayanmasını önerir:

1. Çalışmanın tasarımı, verilerin elde edilmesi, analizi veya yorumlanması

2. Dergiye gönderilecek kopyanın hazırlanması veya bu kopyayının içeriğini bilimsel olarak etkileyecek ve ileriye götürecek şekilde katkı sağlanması

3. Yayınlanacak kopyanın son onayı.

4. Çalışmanın tüm bölümleri hakkında bilgi sahibi olma ve tüm bölümleri hakkında sorumluluğu alma

Bir yazar, yaptığı çalışmanın bölümlerinden sorumlu olmanın yanı sıra, çalışmanın diğer belirli bölümlerinden hangi ortak yazarların sorumlu olduğunu bilmeli ayrıca yazarlar, ortak yazarlarının katkılarının bütünlüğüne güvenmelidir.

Yazar olarak atananların tümü yazarlık için dört kriteri de karşılamalı ve dört kriteri karşılayanlar yazar olarak tanımlanmalıdır. Dört kriterin tümünü karşılamayanlara makalenin başlık sayfasında teşekkür edilmelidir.

Yazı gönderim aşamasında ilgili yazarların, yazarlık katkı formunun imzalı ve taranmış bir versiyonunu (https://dergipark.org.tr/en/pub/tchd adresinden indirilebilir) Türkiye Çocuk Hastalıkları Dergisi'ne göndermesini gerektirir. Yayın kurulu yazarlık şartarını karşılamayan bir kişinin yazar olarak eklendiğinden şüphe ederse yazı daha fazla incelenmeksizin reddedilecektir. Makalenin gönderilmesi aşamasında bir yazar makalenin gönderilmesi ve gözden geçirilmesi aşamalarında tüm sorumluluğu üstlenmeyi kabul ettiğini bildiren kısa bir açıklama göndermelidir.

Türkiye Çocuk Hastalıkları Dergisi'ne gönderilen bir çalışma için bireylerden veya kurumlardan alınan mali hibeler veya diğer destekler Yayın Kuruluna bildirilmelidir. Potansiyel bir çıkar çatışmasını bildirmek için, ICMJE Potansiyel Çıkar Çatışması Bildirim Formu, katkıda bulunan tüm yazarlar tarafından imzalanmalı ve gönderilmelidir. Editörlerin, yazarların veya hakemlerin çıkar çatışması olasılığı, derginin Yayın Kurulu tarafından COPE ve ICMJE yönergeleri kapsamında çözümlenecektir.

Derginin Yayın Kurulu, tüm itiraz durumlarını COPE kılavuzları kapsamında ele almaktadır. Bu gibi durumlarda, yazarların itirazları ile ilgili olarak yazı işleri bürosu ile doğrudan temasa geçmeleri gerekmektedir. Gerektiğinde, dergi içinde çözülemeyen olayları çözmek için bir kamu denetçisi atanabilir. Baş editör itiraz durumlarında karar alma sürecinde alınacak kararlarla ilgili nihai otoritedir.

Yazarlar Türkiye Çocuk Hastalıkları Dergisi'ne bir yazı gönderirken, yazıların telif haklarını Türkiye Çocuk Hastalıkları Dergisi'ne devretmiş olmayı kabul ederler. Yayınlanmamak üzere reddedilirse veya herhangi bir sebepten yazı geri çekilirse telif hakkı yazarlara geri verilir. Türk Türkiye Çocuk Hastalıkları Dergisi'ne ait Telif Hakkı Devri ve Yazarlık Formları (https://dergipark.org.tr/tr/pub/tchd adresinden indirilebilir). Şekiller, tablolar veya diğer basılı materyaller de dahil olmak üzere basılı ve elektronik formatta daha önce yayınlanmış içerik kullanılıyorsa yazarlar telif hakları sahiplerinden gerekli izinleri almalıdır. Bu konudaki hukuki, finansal ve cezai yükümlülükler yazarlara aittir.

Yazıların sonuçlarının rapor edilemesi sırasında genellikle istatistiksel analizler gereklidir. İstatistiksel analizler uluslararası istatistik raporlama standartlarına uygun olarak yapılmalıdır (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Tıp dergilerine katkıda bulunanlar için istatistiksel yönergeler. Br Med J 1983: 7; 1489-93). İstatistiksel analizler hakkında bilgi, Materyal ve Metot bölümünde ayrı bir alt başlık ile açıklanmalı ve bu süreçte kullanılan istatistiksel yazılımlar mutlaka belirtilmelidir.

Türkiye Çocuk Hastalıkları Dergisi'nde yayınlanan yazılarda belitilen ifade veya görüşler, editörlerin, yayın kurulunun veya yayıncının görüşlerini yansıtmaz; editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez. Yayınlanan içerikle ilgili nihai sorumluluk yazarlara aittir.

YAZININ HAZIRLANMASI

Yazılar, Tıbbi Çalışmalarda Bilimsel Çalışmanın Yürütülmesi, Raporlanması, Düzenlenmesi ve Yayınlanması için Uluslararası Tıbbi Dergi Editörleri Konseyi (International Council of Medical Journal Editors (ICMJE)) Önerileri'ne uygun olarak hazırlanmalıdır (Aralık 2019'da güncellenmiştir - http://www.icmje.org/icmje-recommendations). Bu liste aşağıda görülebilir.

CONSORT	Randominize kontrollü çalışma
STROBE	Gözlemsel epidemiyolojik çalışmalar
STARD	Tanı yöntemleri
PRISMA	Sistemetik derleme ve metaanaliz
ARRIVE	Deneysel hayvan çalışmaları
TREND	Randomize olmayan tutum ve davranış çalışmaları

Yazılar yalnızca derginin çevrimiçi (online) makale gönderme ve değerlendirme sistemi aracılığıyla gönderilebilir.

https://dergipark.org.tr/tr/journal/2846/submission/step/manuscript/new Başka herhangi bir araç aracılığıyla gönderilen yazılar değerlendirmeye alınmayacaktır.

Dergiye gönderilen yazılar öncelikle sekreterlik tarafından yazının

derginin kurallarına uygun olarak hazırlanıp hazırlanmadığı yönünden teknik bir değerlendirme sürecinden geçecektir. Derginin yazım kurallarına uymayan yazılar, düzeltme talepleriyle birlikte gönderen yazara iade edilecektir.

Yazarların yazıları hazırlarken ve sisteme yüklerken aşağıdaki konulara dikkat etmesi gerekmektedir:

Telif Hakkı Devri ve Yazarlık Formunun Kabulü ve ICMJE tyarafından önerilen Potansiyel Çıkar Çatışması Bildirim Formu İlk başvuru sırasında (katkıda bulunan tüm yazarlar tarafından doldurulmalıdır) sisteme yüklenmelidir. Bu formları www.dergipark.org.tr/tr/pub/tchd adresinden indirebilirsiniz.

Yazılar, Microsoft Word™ (2010 ve üstü) yazılım programı kullanılarak, Times New Roman karakterinde, 12 punto büyüklüğünde ve çift satır aralığı ile yazılmalıdır. Sayfalarda her yönden 2 cm boşluk bırakılmalıdır. Yazılarda "System International" (SI) birimleri kullanılmalıdır. Tablo ve grafiklere metin içinde atıf yapılmalıdır. Kısaltmalar öz ve metinde ilk geçtikleri yerde açık yazılıp, parantez içinde kısaltma verilmek kaydıyla kullanılabilirler.

Makale içinde, ortalama ve yüzdelik verilirken, ondalıklı hanelerin gösteriminde noktadan sonra 2 basamak kullanılması gerekmektedir (231.7 yerine; 231.69 veya 231.70 gibi). Tam sayı dışındaki gösterimlerde noktadan sonra iki hane, istatistiksel değerlerin gösteriminde ise (p, r, t, z değerleri gibi) noktadan sonra üç hane yazılması gerekir. p değerlerinin sunumunda $p<0.05$ veya $p>0.05$ yerine test istatistiği ile birlikte tam p değerinin noktadan sonra üç hane içerek şekilde verilmesi (ör: $p=0.029$) gerekmektedir. Bu değerin binde birden küçük olması durumunda $p<0.001$ şeklinde gösterim yapılmalıdır.

Kapak sayfasının hazırlanması:

Kapak sayfası tüm yazılarla birlikte gönderilmeli ve bu sayfa şunları içermelidir:

Yazının kapak sayfasında yazının İngilizce başlığı bulunmalıdır. Kapak sayfası yazarların adlarını, akademik ünvanlarının, ORCID numaralarını, kurumsal/mesleki bağlantılarını, yazının kısa başlığını (en fazla 50 karakter), kısaltmaları, finansal açıklama bildirimini ve çıkar çatışması bildirimini içermelidir. Yazı Türkiye'de bulunan bir merkez tarafından gönderilmişse yazılar için Türkçe bir başlık da gereklidir. Bir yazı birden fazla kurumdan yazar içeriyorsa, her yazarın adını, ayrı olarak listelenen kurumlarına karşılık gelen bir üst simge numarası izlemelidir. Tüm yazarlar için için isim soy isim, e-posta adresi, telefon ve faks numaraları dahili iletişim bilgileri verilmelidir. Ayrıca yazı ile ilgili olrak iletişim kurulacak sorumlu sorumlu yazarın kim olduğu belirtilmelidir.

Önemli Uyarı: Kapak sayfası ayrı bir belge olarak yüklenmelidir.

Anahtar kelimeler:
Özetin sonunda konu indeksleme için her gönderime en az üç en fazla altı anahtar kelime eklenmelidir. Anahtar kelimeler kısaltma olmadan tam olarak listelenmelidir. Anahtar kelimeler "National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html)" veritabanından seçilmelidir. Yazı Türkiye'de bulunan bir merkez tarafından gönderilmişse Türkçe anahtar kelimeler de gereklidir.

Yazı türleri:

Orijinal araştırma makalesi

Kelime sayısı: En çok 3500 kelime (Başlık, özet, anahtar kelimeler, kaynaklar, tablo ve figür yazıları hariç).

Ana metnin içereceği bölümler: Giriş, Yöntemler, Sonuçlar, Tartışma

Başlık: En çok 20 kelime

Yapısal özet: En çok 250 kelime. Bölümler: Amaç, Gereç ve Yöntem, Sonuçlar ve Tartışma

Anahtar kelimeler: En az 3 en fazla altı kelime, alfabetik olarak sıralanmıştır.

Şekiller ve tablolar: Sayı sınırı yok ancak tam olarak gerekçelendirilmeli ve açıklayıcı olmalıdır.

Referanslar: En az 20, en çok 40 olmalıdır.

Özgün makalelerin İngilizce başlık, İngilizce yapılandırılmış özet ve İngilizce anahtar kelimeler içermesi gerekmektedir. Ayrıca, Türkçe başlık, Türkçe yapılandırılmış özet ve Türkçe anahtar kelimeler de gereklidir. Özetin, okuyucuların çoğunluğu için, okuyacakları ilk bölüm olması nedeniyle kritik öneme sahip olduğu yaygın olarak kabul edilmektedir.

Ayrıca, elektronik veri tabanlarının önemli bir kısmı sadece özetleri indekslerine dahil etmektedir, bu da özette temel bulguların yer almasının önemini vurgulamaktadır. Makalenin geri kalan bölümleri aşağıdakileri içermelidir: Giriş, Materyal ve Yöntemler, Bulgular, Tartışma, Sonuç, Teşekkür (gerekiyorsa) ve Kaynaklar. Makalenin tüm bölümleri yeni bir sayfada başlamalıdır.

Derleme:

Kelime sayısı: En fazla 5000

Özet: En fazla 500 kelime

Anahtar kelimeler: En az üç en fazla altı kelime, alfabetik olarak sıralanmıştır.

Şekiller ve tablolar: Sayı sınır yok ancak tam olarak gerekçelendirilmeli ve açıklayıcı olmalıdır.

Referanslar: 80'e kadar

Derleme makaleleri, tıptaki belirli konuların kapsamlı olarak gözden geçirildiği, konunun tarihsel gelişimini, mevcut bilinenleri, araştırıma ihtiyacı olan alanları içeren yazılarır. Konu hakkında orijinal araştırmaları yazarlar tarafından yazılmalıdır. Tüm derleme yazıları kabulden önce diğer yazılara eşdeğer değerlendirme süreçlerine tabi tutulacaktır.

Derleme makaleleri şunları içermelidir; İngilizce başlık, İngilizce özet ve İngilizce anahtar kelimeler. Derleme Türkiye'de bulunan bir merkez tarafından gönderilmişse Türkçe başlık, Türkçe özet ve Türkçe anahtar kelimeler de gerekmektedir.

Olgu Sunumu:

Kelime Sayısı: En fazla 2000 kelime

Özet: En fazla 200 kelime

Anahtar Kelime: En az üç en fazla altı kelime

Tablo ve Şekil: Toplamda en fazla beş ile sınırlandırılmıştır.

Referans: En fazla 15

Dergiye sınırlı sayıda olgu sunumu kabul edilmektedir. Olgu sunumlarının tanı ve tedavide zorluk oluşturan, nadir, literatürde yer almayan yeni tedaviler sunan ilginç ve eğitici olguların seçilmesine dikkat edilmektedir. Olgu sunumu giriş, olgu sunumu ve tartışma içermelidir.

Olgu sunumları şunları içermelidir; İngilizce başlık, İngilizce özet ve İngilizce anahtar kelimeler. Türkiye'de bulunan bir merkez tarafından gönderilmişse Türkçe başlık, Türkçe özet ve Türkçe anahtar kelimeler de gereklidir.

Editöre mektup:

Kelime sayısı: En fazla 1500 kelime

Şekil ve tablolar: En fazla 3

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Tablolar

Tablolar, referans listeden sonra ana belgeye dahil edilmelidir ana metin içine yerleştirilmemelidir. Ana metinde atıfta bulundukları sırayla numaralandırılmalıdır. Tabloların üzerine açıklayıcı bir başlık konulmalıdır. Tablolarda kullanılan kısaltmalar ana metinde tanımlansalar bile tabloların altında dipnotlarla tanımlanmalıdır. Tablolarda sunulan veriler, ana metinde sunulan verilerin tekrarı olmamalı, ancak ana metni desteklemelidir. Kısaltmalar için aşağıdaki semboller sırayla kullanılmalıdır: *, †, ‡, §, ||, ¶, **, ††, ‡‡.

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Makalede kullanılan tüm kısaltmalar ve akronimler, hem özet hem de ana metinde ilk kullanımda tanımlanmalıdır. Kısaltma, tanımın ardından parantez içinde verilmelidir.

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Tüm referanslar, tablolar ve şekiller ana metin içinde belirtilmeli ve ana metin içinde belirtildikleri sırayla numaralandırılmalıdır. Orijinal makalelerin kısıtlılıkları tartışma bölümü içinde sonuç paragrafından önce belirtilmelidir.

KAYNAKLAR

Yayınlara atıf yapılırken, en son ve en güncel yayınlar tercih edilmelidir. Yazarlar on yıldan eski referansları kullanmaktan kaçınmalıdır. Yazılarda 10 yıldan eski tarihli referans sayısının toplam referans sayısının %20'sini geçmemesine dikkat edilmelidir. Elektronik olarak yayınlanmış ancak cilt ve sayfa numarası verilmemiş yazılar atfedilirken DOI numarası verilmelidir. Yazarlar kaynakların doğruluğundan sorumludur. Referans numaraları metindeki cümlelerin sonunda parantez içinde metinde kullanıldıkları sıra ile numaralandırılmalıdır. Dergi adları "Index Medicus" veya "ULAKBIM/ Turkish Medical Index" de listelendiği gibi kısaltılmalıdır. Mümkün olduğunca yerel referanslar kullanılmalıdır. Kaynaklar aşağıdaki örneklere uygun olarak yazılmalıdır.

Kaynak dergi ise;

Yazar(lar)ın soyadı adının başharf(ler)i (6 ve daha az sayıda yazar için yazarların tümü, 6'nın üzerinde yazarı bulunan makaleler için ilk 6 yazar belirtilmeli, Türkçe kaynaklar için "ve ark.", yabancı kaynaklar için "et al." ibaresi) kullanılmalıdır. Makalenin başlığı. Derginin Index Medicus'a uygun kısaltılmış ismi

(http://www.ncbi.nlm.nih.gov/sites/entrez/query.fcgi?db=nlmcatalog) Yıl;Cilt:İlk ve son sayfa numarası.

Örnek: Benson M, Reinholdt J, Cardell LO. Allergen-reactive antibodies are found in nasal fluids from patients with birch polen-induced intermittent allergic rhinitis, but not in healthy controls. Allergy 2003;58:386-93.

Kaynak dergi eki ise;

Yazar(lar)ın soyadı adının başharf(ler)i. Makalenin başlığı. Derginin Index Medicus'a uygun kısaltılmış ismi (http://www.ncbi.nlm.nih.gov/sites/entrez/query.fcgi?db=nlmcatalog) Yıl;Cilt

(Suppl. Ek sayısı):İlk sayfa numarası-Son sayfa numarası.

Örnek: Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994; (102 Suppl 1):275–82.

Kaynak kitap ise;

Yazar(lar)ın soyadı, adının başharf(ler)i. Kitabın adı. Kaçıncı baskı olduğu. Basım yeri: Basımevi, Basım Yılı.

Örnek: Ringsven MK, Bond N. Gerontology and leadership skills for nurses. 2nd ed. Albany, NY: Delmar Publishers, 1996.

Kaynak kitaptan bölüm ise;

Bölüm yazar(lar)ının soyadı adının başharf(ler)i. Bölüm başlığı. In: Editör(ler)in soyadı, adının başharf(ler)i (ed) veya (eds). Kitabın adı. Kaçıncı baskı olduğu. Basım yeri: Yayınevi,

Baskı yılı:Bölümün ilk ve son sayfa numarası.

Örnek: Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM (eds). Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York: Raven P, 1995:466–78.

Kaynak toplantıda sunulan bildiri ise;

Yazar(lar)ın soyadı adının başharf(ler)i. (6 ve daha az sayıda yazar için yazarların tümü, 6'nın üzerinde yazarı bulunan bildiriler için ilk 6 yazar belirtilmeli, Türkçe kaynaklar için "ve ark.", yabancı kaynaklar için "et al." ibaresi kullanılmalıdır). Bildirinin başlığı. Varsa In: Editör(ler)in soyadı adının başharf(ler)i (ed) veya (eds). Kitabın adı. Toplantının adı; Tarihi; Toplantının yapıldığı şehrin adı, Toplantının yapıldığı ülkenin adı. Yayınevi; Yıl. Sayfa numaraları.

Örnek: Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet

P, Piemme TE, Reinhoff O (eds). MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland. North-Holland; 1992. p. 1561-5.

Kaynak elektronik dergi ise;

Yazar(lar)ın soyadı adının başharf(ler)i. (6 ve daha az sayıda yazar için yazarların tümü, 6'nın üzerinde yazarı bulunan makaleler için ilk 6 yazar belirtilmeli, Türkçe kaynaklar için "ve ark.", yabancı kaynaklar için "et al." ibaresi kullanılmalıdır). Makalenin başlığı. Derginin Index Medicus'a uygun kısaltılmış ismi Yıl; Cilt (Sayı). Available from: URL adresi. Erişim tarihi: Gün.Ay.Yıl.

Örnek: Arrami M, Garner H. A tale of two citations. Nature 2008;451(7177): 397-9. Available from: URL:www.nature.com/nature/journal/v451/n7177/full/451397a.html. Accessed 20 January 2008.

Kaynak web sitesi ise:

Web sitesinin adı. Erişim tarihi. Available from: Web sitesinin adresi.

Örnek: Centers for Disease Control and Prevention (CDC). Erişim tarihi: 12 Mart 2013.

Available from: http://www.cdc.gov/

Kaynak tez ise:

Yazarın soyadı adının baş harfi. Tezin başlığı (tez). Tezin yapıldığı şehir adı: Üniversite adı (üniversite ise); Yılı.

Örnek: Özdemir O. Fibrillin-1 gen polimorfizmi ve mitral kapak hastalığı riski. (Tez). Ankara: Gazi Üniversitesi, 2006."

Düzeltme istenmesi aşaması:

Bir makalenin hakemler tarafından istenen değişiklikler yapılmış kopyası gönderilirken yazar, hakemler tarafından istenen her açıklama/düzeltmeye cevap vermekle yükümlüdür. Yazarlar hakemlerin düzeltme/açıklama isteklerini her isteğin ardından olacak şekilde madde madde açıklmalı, düzeltilmiş kopyaya yazılacak metin bu açıklamanın altına eklemelidir. Düzeltme yapılmış kopya dergiye ayrı bir kopya olarak yüklenmelidir. Düzeltilmiş yazılar düzeltme isteğinin gönderilmesinden itibaren 30 gün içinde gönderilmelidir. Yazının düzeltilmiş kopyası istenilen sürede gönderilmezse yazı sistemden ototmatik olarak düşürülecektir ve tekrar başvuru yapılması gerekecektir. Eğer yazarlar ek zaman talep ediyorlarsa bu taleplerini ilk 30 günlük süre sona ermeden önce dergiye iletmelidir.

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Yazı gönderildikten sonra yazar listesinin/sırasının değiştirilmesi (yazar adlarının silinmesi veya yeni yazar adı eklenmesi gibi) talepleri yayın kurulunun onayına tabidir. Bu talep yazar değişiklik formunun doldurulup dergiye yüklenmesi ile talep edilebilir. Bu form aşağıdakileri içerecek şekilde doldurulmalıdır: Talebin gerekçesi, yani yazar listesi, tüm yazarlar tarafından (yeni ve eski) imzalanan yeni bir telif hakkı transfer formu, yeni yazar tarafından imzalanmış çıkar çatışması formu.

Yazının geri çekilmesi talebi

Türkiye Çocuk Hastalıkları Dergisi yüksek kaliteli yazılar yayınlamayı ve yayın etiğini korumayı taahhüt etmektedir. Yazarlardan, yayın etiğinde ve yazıların kalitesinde tavsiye edilen kurallara uymaları beklenmektedir.

Yazının geri çekilme talebi olağanüstü durumlarda talep edilmelidir. Bir yazının geri çekilmesi için yazarların dergiye geri çekme nedenlerini belirten ve tüm yazarlar tarafından imzalanan bir "Makale geri çekme Formu" yüklemeleri gerekmektedir. Bu form derginin web sayfasından indirilebilir. Yazarlar dergiden bu konuda olumlu bir cevap alana kadar makalelerinin geri çekilme işleminin tamamlanmadığını bilmelidir.

Bir makalenin inceleme süreci altı aydan uzun bir zaman almış ve yazarlara karar bildirilmemişse yazının geri çekilme talebi olumlu karşılanır.

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Original Articles / *Özgün Araştırmalar*

Case Reports / *Olgu Sunumları*

The Invisible Danger: Third-hand Smoke and Families' Knowledge Levels

Görünmez Tehlike: Üçüncü El Sigara Dumanı ve Ailelerin Bilgi Düzeyi

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ABSTRACT

Objective: The objective of this study was to idenitfy the knowledge levels of families regarding third-hand smoke (THS), which represents the most significant health risk currently, and to raise awareness of the subject.

Material and Methods: The 'Beliefs About Third-hand Smoke' (BATHS) scale was applied to 1016 caregivers. The BATHS scale and sub-factor scale results were compared in terms of participant-related variables such as smoking behaviors, THS awareness and beliefs, and sociodemographic findings.

Results: Awareness of the term THS was very low (8.7%). Statistically significantly low smoking habits and high BATHS scale scores were determined among participants who owned their own homes, those with higher levels of education and income, and in non-parent relatives ($p<0.001$). Parental THS awareness was lower among mothers. Being a university graduate increased awareness 19 times and owning one's own home 2.6 times. While not smoking at all resulted in a significant increase in BATHS scores, it did not affect THS awareness.

Conclusion: Despite the availability of numerous programs and educational material concerning the harm caused by first- and second-hand smoke, levels of information about TSH, a more important but invisible danger, are unfortunately very low in society and among health professionals. It is therefore essential to increase the requisite sensitivity to the issue and to encourage smoke-free society studies.

Key Words: Awareness, Exposure, Smoke, Tobacco

ÖZ

Amaç: Bu çalışmanın amacı, günümüzde sağlığa yönelik en önemli tehdit olan üçüncü el sigara dumanına (ÜSD) ilişkin ailelerin bilgi düzeylerini tespit etmek ve konuya ilişkin farkındalığı artırmaktı.

Gereç ve Yöntemler: 'Üçüncü El Duman Hakkında İnançlar' (ÜDHİ) ölçeği 1016 bakım verene uygulanmıştır. ÜDHİ ölçeği ve alt faktör ölçeği sonuçları, sigara içme davranışları, ÜSD farkındalığı ve inançları ve sosyodemografik bulgular gibi katılımcılarla ilgili değişkenler açısından karşılaştırılmıştır.

Bulgular: Üçüncü el sigara dumanı terimine ilişkin farkındalık çok düşüktü (%8.7). Kendi evi olanlarda, eğitim ve gelir düzeyi yüksek olanlarda ve ebeveyn olmayan akrabalarda istatistiksel olarak anlamlı düzeyde düşük sigara içme alışkanlıkları ve yüksek ÜDHİ ölçek puanları tespit edilmiştir ($p<0.001$). Ebeveynlerin ÜSD farkındalığı anneler arasında daha düşüktü. Üniversite mezunu olmak farkındalığı 19 kat, kendi evine sahip olmak ise 2.6 kat artırmıştır. Hiç sigara içmemek ÜDHİ puanlarında anlamlı bir artışa neden olurken, ÜSD farkındalığını etkilememiştir.

Sonuç: Birinci ve ikinci el dumanın yol açtığı zararlara ilişkin çok sayıda program ve eğitim materyali bulunmasına rağmen, daha önemli ancak görünmez bir tehlike olan ÜSD hakkında bilgi düzeyleri ne yazık ki toplumda ve sağlık çalışanları arasında çok düşüktür. Bu nedenle konuya ilişkin gerekli duyarlılığın artırılması ve dumansız toplum çalışmalarının teşvik edilmesi elzemdir.

Anahtar Sözcükler: Farkındalık, Maruziyet, Duman, Tütün

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Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by the Ethics Committee of Samsun Training and Research Hospital (BAE/2022/1/1-01.03.2022).

Contribution of the Authors / Yazarların katkısı: AKÇA G: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***AKÇA Ü:*** Planning methodology to reach the conclusions, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar.

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INTRODUCTION

Tobacco smoke exposure (TSE) is a major global health problem. This is particularly important in terms of children, who are more susceptible to toxicity present in environments where tobacco smoking occurs (1). Such exposure leads to numerous health problems, including voice difficulties, upper and lower respiratory tract infections, ear infections, asthma, cardiovascular diseases, and even sudden baby death (2).

It is estimated that 40% of children worldwide are exposed to tobacco in their homes (3). This exposure results not only from second-hand smoke (SHS), the passive intake of tobacco smoke, but also from the effect of third-hand smoke (THS), the waste residues created by such smoke (4). These waste residues consist of various components of tobacco smoke not found in fresh smoke but capable of reacting with toxic substances by adhering to surfaces in the environment.

The toxication caused by the accumulation of tobacco smoke on surfaces is more harmful than the smoke itself and SHS. While exposure to SHS results from the involuntary respiration of smoke, exposure to THS occurs via involuntary respiration, swallowing, or even absorption through the skin (5). The following tobacco-specific nitrosamines were detected: N′-Nitrosonornicotine (NNN), 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and 4-(methylnitrosamino)-4-(3-pyridyl) butanal (NNA) can remain in closed environments for several days or even months after tobacco has been smoked, while SHS is removed through ventilation. Indeed, some components can remain on clothing fibers for up to 19 months (6). While adults can choose whether or not to smoke tobacco, children are particularly vulnerable to THS in their play areas, homes, and cars (7). It is important for parents to be made aware of THS, and to the best of our knowledge, no previous studies have assessed Turkish families' knowledge of and attitudes toward the subject.

MATERIALS and METHODS

The data in this cross-sectional study were collected through face-to-face interviews in a tertiary training hospital between 1 February and 1 May, 2022. The requisite sample size was calculated at 384, with $Z\alpha = 1.96$ for a 95% confidence interval, a predicted acceptable margin of error $d = 0.05$, and a 50% estimated knowledge of THS. The study was approved by the Ethics Committee of Samsun Training and Research Hospital (BAE/2022/1/1-01.03.2022).

Care-giver relatives such as parents or grandparents presenting to the pediatric clinic were included in the study. Participants were informed about the purpose of the research, the duration of the survey, the identities of the researchers, and how the data would be stored by means of a special section at the beginning of the questionnaire. Written consent forms were obtained from the participants before the questionnaire was applied. The questionnaire was developed based on a scan of the relevant literature (8,9). The accuracy and clarity of the questionnaire was first tested on 15 parents. It contained 25 questions involving sociodemographic characteristics and the Beliefs About Third-Hand Smoke (BATHS) scale and was capable of completion in a mean seven minutes.

Sociodemographics

The parents were asked to state their age, sex, education level, income level, whether or not they owned their own home, and the age and sex of their children.

Participants' beliefs concerning THS were investigated using the BATHS scale (Table I). The validity and reliability of the Turkish-language version of the BATHS scale were investigated by Önal et al. (10). The scale assesses the persistence of THS in the environment (Factor 1) and the impact of THS on health (Factor 2). Factor 1 includes items describing THS in the built environment, including the persistence of smoke particles, the accumulation of THS, and the ineffectiveness of THS reduction by means other than refraining from smoking in the home. Factor 2 includes the health impact of THS and the transmission of THS other than through the air (11). Participants were asked whether they strongly disagreed, disagreed, were undecided, agreed, or strongly agreed with statements coded on a scale of 1-5. Following a brief explanation of the term THS, participants were then asked whether they believed that this was deleterious to the health of their children.

Smoking behaviors

Participants were asked for the following details concerning smoking:

- Smoking status: 1) I have never smoked, 2) I smoke, or 3) I used to smoke but quit.
- Rules regarding smoking in the home: 1) Nobody can smoke in the home, 2) smoking is only allowed on the balcony, 3) smoking is allowed in specific locations in the home (such as the living room or in front of windows), and 4) there is no set rule, and smoking is allowed everywhere.
- Children's exposure to smoking in the previous two weeks in the home, outside the home (in a closed environment), and in the car was also investigated.

Statistical analyses

A check of the data revealed that <10% were missing. Rows with missing data were eliminated when performing the data analyses. Data were verified for normality of distribution and equality of variances on IBM Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). Descriptive statistics were calculated for participant demographics. Quantitative variables are presented as mean and standart deviation and qualitative data as frequency and percentage. The Independent Samples T-test/ANOVA (in case

Table I: Comparison of smoking behaviors and sociodemographic findings

Smoking behavior	Smoker*	Quit smoking*	Never smoked*	X^2	p†
Sex					
Female	134 (16.5) [a]	223 (27.4) [b]	456 (56.1) [c]	107.678	0.001
Male	94 (46.3) [a]	67 (33.0) [b]	42 (20.7) [c]		
Caregiver					
Mother	133 (17.1) [a]	209 (26.9) [b]	435 (56.9) [c]	116.823	0.001
Father	91 (48.7) [a]	57 (30.5) [b]	39 (20.9) [c]		
Other	4 (7.7) [a]	24 (46.2) [b]	24 (46.2) [a, b]		
Education status					
Elementary school	73 (26.3) [a]	92 (33.1) [a]	113 (40.6) [b]	30.247	0.001
Middle school	53 (29.3) [a]	33 (18.2) [b]	95 (52.5) [a]		
High school	65 (18.7) [a]	114 (32.9) [b]	168 (48.4) [b]		
University equivalent	37 (17.6) [a]	51 (24.3) [a, b]	122 (58.1) [b]		
Caregiver age group				15.098	0.001
<30 years	71 (24.9) [a]	66 (23.2) [a]	148 (51.9) [a]		
30-50 years	151 (22.6) [a]	196 (29.3) [a]	322 (48.1) [a]		
>50 years	6 (9.7) [a]	28 (45.2) [b]	28 (45.2) [a, b]		
Home-owner					
Yes	85 (15.7) [a]	171 (31.5) [b]	287 (52.9) [b]	31.001	0.001
No	143 (30.2) [a]	119 (25.2) [b]	211 (44.6) [b]		
Income					
Lower than expenditure	108 (29.9) [a]	92 (25.5) [b]	161 (44.6) [b]	19.194	0.001
Equal to expenditure	103 (18.3) [a]	174 (31.0) [b]	285 (50.7) [b]		
Higher than expenditure	17 (18.3) [a]	24 (25.3) [a]	52 (55.9) [a]		
Smoke exposure in the car					
Yes	45 (50.0) [a]	13 (14.4) [b]	32 (35.6) [b]	43.947	0.001
No	183 (19.8) [a]	277 (29.9) [b]	466 (50.3) [b]		
Smoke exposure at home					
Yes	119 (55.6) [a]	34 (15.9) [b]	61 (28.5) [b]	171.371	0.001
No	109 (13.6) [a]	256 (31.9) [b]	498 (49.0) [b]		
Outdoor smoke exposure					
Yes	71 (51.8) [a]	16 (11.7) [b]	50 (36.5) [b]	81.768	0.001
No	157 (17.9) [a]	274 (31.2) [b]	498 (49.0) [b]		

***:** *n(%)* **†:** *Pearson's chi-squared test.* **[a,b,c]:** *Each subscript letter denotes a subset of categories whose column proportions do not differ significantly from each other at the 0.050 level.*

of normal distribution) were applied to evaluate differences between scale scores in terms of participant characteristics. Multivariate analysis was then conducted to explore the factors influencing the BATHS scale and subscales, using the generalized linear model. Independent variables included demographics and variables identified as exhibiting a statistically significant association with BATHS scores at univariate analysis. Odds ratios, adjusted for parent gender, parent age, parental education level, and family income were calculated for each dependent variable. Significance tests were bilateral, and p values <0.05 were regarded as significant for all analyses.

RESULTS

Participant characteristics

One thousand sixteen caregivers were included in the study. Eighty percent of the participants were women, and 76.6% were mothers. Individuals defined as the 'others' group, relatives such as grandfathers and grandmothers, represented 5.1% of the participants. The mean age of the parents was 35.36 ±8.9 years (min 18, max 70), 34.2% were high school graduates, and 20.7% were university graduates. The mean age of the children was 72.54± 54.04 months (min 1, max 210), and 55.6% were girls. In terms of income, 35.5% of parents had income lower than outgoings, while 9.2% had income higher than outgoings. More than half (53.4%) of the participants owned their own homes, and 22.4% were active smokers. Evaluation showed that 21.1% of participants reported that their children had been exposed to cigarette smoke in the home in the previous two weeks, while 13.5% reported exposure to smoke outside the home, and 8.9% in the car. In terms of rules regarding smoking within the home, 32.5% of participants reported that no smoking was permitted anywhere, while 42.5% only allowed smoking on an outside balcony (either opening onto the home or closed off from it). In addition, 48.7% of fathers, 17.1% of mothers, and 7.7% of other relatives were smokers, while 26.9% of mothers, 30.5% of fathers, and 46.2% of other

Table II: Comparison of the differences between the BATHS scale and subscale scores of the participants

Category	n (%)	Total BATHS score ±SD	p	Factor1 persistence average ±SD	p	Factor 2 Health average ±SD	p
Caregiver							
Mother	777 (76.6)	3.78±0.53	<0.001*	3.78±0.57	0.001*	3.78±0.53	0.001*
Father	187 (18.4)	3.85±0.83		3.57±0.85		3.60±0.86	
Other	52 (5)	3.86±0.65		3.82±0.72		3.92±0.68	
Education status							
Elementary school	278 (27.3)	3.54±0.62	<0.001*	3.51±0.66	0.001*	3.58±0.69	0.001*
Middle school	181 (17.7)	3.67±0.74		3.61±0.82		3.74±0.76	
High school	347 (34.1)	3.83±0.67		3.79±0.74		3.89±0.68	
University equivalent	210 (20.6)	4.23±0.56		4.22±0.57		4.24±0.61	
Income							
Lower than expenditure	361 (35.4)	3.53±0.67	<0.001*	3.52±0.68	0.001*	3.55±0.68	0.001*
Equal to expenditure	562 (55.2)	3.93±0.66		3.88±0.75		4.00±0.68	
Higher than expenditure	93 (9.1)	4.12±0.67		4.09±0.70		4.15±0.72	
Smoking status							
Smoker	228 (22.3)	3.50±0.58	<0.001*	3.44±0.86	0.001*	3.58±0.63	0.001*
Quit smoking	290 (28.69)	3.73±0.76		3.72±0.70		3.74±0.68	
Never smoked	498 (48.9)	3.99±0.59		3.95±0.65		4.04±0.63	
Home owner							
Yes	543 (53.2)	3.94±0.66	<0.001*	3.90±0.72	0.001*	3.99±0.68	0.001*
No	473 (46.5)	3.65±0.69		3.61±0.74		3.70±0.73	
Age group							
<30 years	285 (28.2)	3.75±0.69	0.325*	3.70±0.74	0.467*	3.81±0.73	0.487*
30-50 years	669 (65.7)	3.83±0.70		3.80±0.76		3.87±0.72	
>50 years	62 (6.2)	3.82±0.58		3.82±0.59		3.82±0.64	
Smoking rules							
No smoking anywhere	330 (30.2)	4.15±0.58	<0.001*	4.12±0.65	0.001*	4.20±0.59	0.001*
Smoking allowed only on the balcony	432 (39.6)	3.65±0.55		3.62±0.63		3.68±0.60	
Smoking allowed in some areas	227 (20.9)	3.63±0.82		3.57±0.82		3.70±0.87	
Smoking allowed everywhere	26 (2.4)	3.53±1.00		3.50±0.98		3.57±1.05	
Exposure at home							
Yes	214 (21.0)	3.49±0.84	<0.001†	3.43±0.89	0.001†	3.57±0.90	0.001†
No	802 (79.0)	3.89±0.62		3.86±0.68		3.93±0.64	
Outdoor exposure							
Yes	137 (13.5)	3.62±0.87	<0.001†	3.56±0.92	0.001†	3.71±0.94	0.001†
No	879 (86.5)	3.83±0.65		3.80±0.71		3.87±0.67	
Exposure in the car							
Yes	90 (8.9)	3.42±0.86	<0.001†	3.34±0.93	0.001†	3.52±0.92	0.001†
No	926 (91.1)	3.84±0.65		3.81±0.71		3.88±0.69	
Aware of third-hand smoke							
Yes	88 (8.7)	4.36±0.62	<0.001†	4.33±0.73	0.001†	4.40±0.55	0.001†
No	928 (91.3)	3.75±0.67		3.72±0.72		3.80±0.71	

***:** *ANOVA,* **†:** Independent Samples T-Test

relatives had subsequently quit, and 56.9% of mothers, 20.9% of fathers, and 46.2% of other relatives had never smoked. In terms of education, 17.6% of smokers and 58.1% of those who had never smoked were university graduates. Smokers constituted 15.7% of parents who owned their own homes and 30.2% of non-home owners. Finally, 8.7% of participants had heard of THS. A comparison of the participants' demographic data according to smoking status is shown in Table I.

Higher BATHS scale scores were observed among non-parent caregivers (3.86±0.65, p<0.001), and among individuals with a higher level of education (university, 4.23±0.56, p<0.001), whose income exceeded their outgoings (4.12±0.67, p<0.001), and who had never smoked (3.99±0.59, p<0.001). Higher scores were also registered by those who owned their own homes (3.94±0.66, p<0.001), in whose homes nobody was allowed to smoke (4.15±0.58, p<0.001), whose children were not exposed to smoking in the home (3.89±0.62, p<0.001), outside the home (3.83±0.65, p<0.001), or in the car (3.84±0.65, p<0.001), and who had heard of THS (4.36±0.62, p<0.001). No significant age difference was determined in BATHS scale scores. Mean total scale scores were 3.75±0.69 among participants aged under 30, 3.83±0.70 for those aged 30-50, and 3.82±0.58 for those aged over 50 (p=0.325) (Table II).

Table III: Logistic regression analysis of the factors affecting participants' awareness of third-hand smoke

Category	B	SE	OR	95% CI	p
Caregiver					
Mother			1		
Father	1.78	.46	5.91	2.42-14.46	0.001
Other	1.62	.51	5.03	1.84-13.71	0.002
Education status					
Elementary school			1		
Middle school	1.27	.31	3.56	1.95-6.51	0.001
High school	1.90	.63	6.64	1.92-22.96	0.003
University equivalent	2.94	.66	18.84	5.21-68.19	0.001
Income					
Lower than expenditure			1		
Equal to expenditure	.95	.32	2.60	1.40-4.84	0.003
Higher than expenditure	1.46	.55	4.28	1.45-12.63	0.009
Smoking status					
Never smoked			1		
Quit smoking	-0.29	.44	.75	.32-1.79	0.517
Smoker	-0.54	.30	.59	.33-1.05	0.074
Home owner					
No			1		
Yes	-1.01	2.96	2.67	1.38-5.19	0.004

SE: *Standart Error,* ***OR:*** *Odds Ratio,* ***CI:*** *Cofidence Interval*

Awareness of the term third-hand smoke

In the logistic regression model, university graduates were approximately 18 times more aware of the term THS than primary school graduates. Individuals with high income were four times more aware of the term than those with low income, fathers six times more than mothers, and those who own their own homes three times more than home owners (Table III).

At the end of the survey, participants were given information about THS and were asked whether or not it is harmful; 83.8% responded that it is harmful, with 12.2% being undecided, and 3.8% describing it as not harmful.

DISCUSSION

Mortality and morbidity deriving from tobacco use and exposure remain a global threat to child health. Although smoking has decreased steadily among adults aged 18 and over in the last 50 years, the prevalence of smoking in Europe as a whole is still approximately 24%. Although public awareness of the damage to health caused by primary and secondary smoking has increased, awareness of exposure to THS, defined as that part of the smoke remaining in the environment long after the cigarette itself has been extinguished, is still inadequate (12). Studies that commenced in 1991 under the auspices of the world's largest cigarette manufacturer are still being published today. These have shown that even if ventilation is performed after a regular eight-hour smoking period, high concentrations of nicotine, nitrosamines, and carcinogenic substances remain in the air for 12 hours, and on carpets, curtains, clothes, and wallpaper for more than two months (13).

Although one child in five worldwide is reported to be exposed to tobacco smoke, the true figure is thought to be much higher because parents under-report smoking in the home and in their cars (14). Cigarette smoking traditionally began as male behavior and a show of strength. However, manipulation on the part of the powerful tobacco industry also encouraged women to smoke, as a supposed symbol of freedom and gender equality (15). Global smoking rates are still higher among men than women (16). Taking up smoking at a young age is directly correlated with low income, low education levels, and membership of the working class (17). In agreement with the previous literature, the prevalence of smoking in the present study was 21%, with a male/female ratio of 2.81, and exposure to smoking was observed at an approximate level of 21.1%. Higher rates of starting and quitting smoking were determined among non-parent caregivers (grandfathers and grandmothers). We attribute this to increasing age-related health and financial limitations and to regret over having smoked in the past.

Lower socioeconomic status, whether in terms of income or education, has been identified as a risk factor for exposure to cigarette smoke (18). This explains the lower exposure to THS associated with higher income, a higher level of education, and owning one's own home. In the present study, being a university graduate was associated with 19-fold higher awareness of THS, a high-income level with four-fold higher awareness, and home ownership with three-fold greater awareness.

Homes and cars represent the principal closed spaces in which children are exposed to passive smoking. Potential areas of exposure to THS include homes in which residents smoke, apartments and houses previously inhabited by smokers, and cars in which people have smoked (19,20). One in three of the participants in this study reported that smoking was not permitted anywhere in the home, which represents the most favorable situation in terms of exposure to THS. Reported rates of smoking prohibition in the home and car among smokers and non-smokers in previous studies were 55.1% and 64.2%, respectively, in Japan, 45.6% and 61.6% in Spain, and 83.7% and 78.1% in the USA (21-23). Some parents in the present study smoked in some or all parts of the home. A study from Israel reported that 39% of smoker parents smoked on the balcony, 34.1% anywhere in the home, and 26.8% only outdoors (7). Smoking in the home, even on the balcony, impacts on children in terms of both SHS and THS. Parents who smoke on the balcony may think that this is not harmful to their children since these are not present at the time. However, children are still exposed to toxic pollutants that adhere to smokers' skin, hair, and clothing. Some components of THS can remain in clothing fibers for up to 19 months, even if smoking takes place in the open air. THS can thus still be harmful to babies and children if they come into contact with contaminated clothing, such as being picked up by smokers. Smoking when children are not present only prevents exposure to SHS, and does not obviate the harmful effects of THS.

Due to the restricted space involved, smoking in cars has been shown to be potentially 23 times more harmful than smoking in the home (24). Smoking in the car may also be an indirect reflection of heavy smoking at home. A recent survey from Ireland showed that one child in seven was exposed to smoking in cars (25). Consistent with the present study, Dai et al. (26) reported that half of smokers in Japan also smoked in their cars. Rates of smoking in cars in Turkey are generally low. We think that one factor in this is that vehicles in which nobody has smoked are easier to sell and fetch higher prices in the country.

One important finding of this study is the 8.7% level of awareness of the term THS. Awareness increased in proportion to education and income, but was lower in mothers. Higher awareness was also determined among individuals who did not permit smoking in the home, but no significant association was found with smoking. We think that the most important factors in this context are the lack of attention paid to THS on the radio, television and social media, the lack of eye-catching public information broadcasts, and the limited level of knowledge of the subject among research and health professionals.

Child health clinicians affect the beliefs of parents concerning the potential harm that THS can inflict on their children. Parents who are advised to quit smoking or to make their homes or cars smoke-free by a pediatrician are more likely to believe that THS is deleterious to their children's health (27). However, the level of awareness of the term THS among health workers in a study from Spain was only 34.8%, showing that awareness also needs to be raised among clinicians (28).

Fathers who smoke more on a daily basis (compared to mothers) are less likely to believe that THS is harmful to children (27). In the present study, too, parents who smoked were three times less likely to believe that THS is damaging to children. Effective educational messages and counseling for parents concerning THS can help promote no-smoking guidelines and encourage the acceptance of assistance for quitting.

All heath care environments must be entirely smoke-free. Bans on smoking will help protect children and the whole family against exposure to SHS and THS. It is particularly important that medically vulnerable children should be able to visit institutions that are free of all forms of tobacco smoke contamination.

CONCLUSION

Information about THS should be included in health promotion and educational campaigns aimed at reducing smoking. Stricter rules preventing smoking in public and private settings should be imposed in order to protect non-smokers and children against the adverse effects of SHS and THS. In addition, encouraging changes in smoking behaviors will not only protect non-smokers against the deleterious effects of SHS and THS, but will also help smokers avoid the effects of tobacco, and will ultimately result in smoke-free environments.

Limitations

This study involved a large number of participants in order to ensure that sound results could be obtained. However, it was performed with parents visiting our hospital's pediatric clinic. It is therefore limited by its single-center nature, and the findings cannot be generalized to the whole country. In addition, smoking history (active smoking and exposure to cigarettes in the home or car) and their effects on health were based on self-reports. Relying on parental self-reports may lead to bias error.

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Diagnosis and Treatment of Newborns Referred to the Metabolism Department from the National Newborn Screening Program in Türkiye: A 5-Year Single-Center Experience

Türkiye'deki Ulusal Yenidoğan Tarama Programı Tarafından Metabolizma Bölümüne Yönlendirilen Yenidoğanların Tanı ve Tedavisi: Beş Yıllık Tek Merkez Deneyimi

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ABSTRACT

Objective: The aims of this study were to investigate biochemical and genetic tests and treatment plans of newborns referred to our center with inherited metabolic disorders screened in Türkiye National Newborn Screening Program (NNSP).

Material and Methods: The medical records of babies referred by the NNSP between January 2019 and November 2023 were scanned retrospectively. Plasma biotinidase activity and the biotinidase gene (BTD) analysis results for suspected biotinidase deficiency (BD), the plasma phenylalanine and phenylalanine hydroxylase gene (PAH) analysis for a suspicion of phenylketonuria (PKU) were documented with treatment information.

Results: A total of 143 babies, 78 (54.5%) with suspected BD and 65 (45.5%) with suspected PKU were included. A PAH gene analysis was performed on 23 (35.4%) of those had high plasma phenylalanine levels, among which 86.9% were identified with the biallelic variant. Five patients were started on sapropterin-diet combined therapy, three on diet therapy and one on sapropterin therapy. In the first serum biotinidase activity measurement of babies referred with suspected BD, a heterozygous deficiency was detected in 48.7%, partial deficiency in 39.7% and profound deficiency in 10.3%. A BTD gene analysis was performed on 79.5% of those with suspected BD, and biallelic variants were detected in 50%. Forty-six patients (59.0%) underwent biotin treatment.

Conclusion: In our study, approximately one-third of the babies referred from NNSP over the five-year course of the study had biallelic variants of the relevant disease. Our research is one of the few studies on NNSP in our country and presents the diagnosis and treatment process of PKU and BD.

Key Words: Biotinidase deficiency, Neonatal Screening, Phenylketonuria, Türkiye

ÖZ

Amaç: Bu çalışmanın amacı, Türkiye Ulusal Yenidoğan Tarama Programı (UYTP)'de tarama yapılan kalıtsal metabolik hastalık şüphesiyle merkezimize yönlendirilen yenidoğanların biyokimyasal ve genetik testleri ile tedavi planlarını araştırmaktı.

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Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. This study was approved by the Ankara University ethics committee (İ01-32-24, 18.01.2024).

Contribution of the Authors / Yazarların katkısı*: *KOÇ YEKEDÜZ M: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***EMİNOĞLU FT***: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

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Gereç ve Yöntemler: Ocak 2019 ile Kasım 2023 tarihleri arasında UYTP tarafından yönlendirilen bebeklerin tıbbi kayıtları geriye dönük tarandı. Şüpheli biotinidaz eksikliği (BE) için plazma biyotinidaz aktivitesi ve BTD gen analiz sonuçları, fenilketonüri (FKÜ) şüphesi için plazma fenilalanin ve PAH gen analizi ile birlikte tedavi bilgileri araştırıldı.

Bulgular: Yetmiş-sekizi (%54.5) şüpheli BE ve 65'i (%45.5) şüpheli FKÜ olmak üzere toplam 143 bebek dahil edildi. Yüksek plazma fenilalanin seviyelerine sahip olanların 23'üne (%35.4) PAH gen analizi yapılmış, bunların %86.9'unda biallelik variant saptanmıştı. Beş hastada sapropterin-diyet kombinasyon tedavisine, üç hastada diyet tedavisine ve bir hastada sapropterin tedavisine başlanmıştı. Şüpheli BE ile yönlendirilen bebeklerin ilk serum biyotinidaz aktivite ölçümünde, %48.7'sinde heterozigot eksiklik, %39.7'sinde kısmi eksiklik ve %10.3'ünde derin eksiklik saptanmıştı. Şüpheli BE olan bebeklerin %79.5'ine BTD gen analizi yapılmış ve %50 oranında biallelik varyant saptanmıştı. Kırk altı hastaya (%59) biyotin tedavisi başlanmıştı.

Sonuç: Çalışmamızda, beş yıllık süre boyunca UYTP tarafından yönlendirilen bebeklerin yaklaşık üçte birinde ilgili hastalığın biallelik varyantları bulunduğu gösterildi. Araştırmamız, ülkemizde UYTP üzerine yapılan az sayıdaki çalışmalardan biridir ve FKÜ ve BE'nin tanı ve tedavi sürecini sunmaktadır.

Anahtar Sözcükler: Biotinidaz eksikliği, Yenidoğan Tarama, Fenilketonüri, Türkiye

INTRODUCTION

Inherited metabolic disorders (IMD), while rare, are more common in Türkiye where the rate of consanguineous marriages is higher than in other countries (1). In Türkiye, two IMDs, namely phenylketonuria (PKU) and biotinidase deficiency (BD), are screened in the National Newborn Screening Program (NNSP). The Phenylketonuria Screening Program started regionally in 1987 and was expanded to all of Türkiye in 1993. In 2008, BD was added to NNSP (2). While the newborn screening rate in Türkiye was 4.7% in 1987, it has reached almost a total rate of 95% since 2008 (3). It is estimated that the application of the NNSP has led to the prevention of disability in approximately 4,500 babies per year through early diagnosis in Türkiye (2).

Phenylketonuria is an autosomal recessive IMD associated with high phenylalanine levels, 98% of which are caused by PAH gene mutations and 2% by mutations in the BH4 metabolism. Phenylketonuria is frequently associated with developmental delay, progressive cognitive deterioration, neuropsychiatric findings, autism, dysmyelination, and light skin, hair and eye color. Early diagnosis and treatment can support the patient in developing in line with their peers (4, 5). Biotinidase deficiency is another autosomal recessively inherited neurocutaneous IMD that is associated with such symptoms as seizures, sensorineural hearing loss, skin rash, skin dryness, alopecia and acidosis. Since these findings can be confused with many different diagnoses in the neonatal period, an accurate diagnosis would be difficult in the absence of a screening program. Early diagnosis and rapid treatment can prevent the development of neurological sequelae and other clinical findings, and for this reason, BD and PKU are both included in the NNSP in Türkiye (6-8).

Phenylketonuria is most frequently seen in Türkiye, with a prevalence of 0.0167% in the world (9). In a regional study conducted in Türkiye, the highest and lowest incidences of screened diagnoses for the last 10 years were reported as 1:657–1:8375 for PKU and 1:1861–1:6815 for biotinidase deficiency (10). In a 10-year study conducted in another region of Türkiye, the incidence of PKU was reported as 1:7878, and the incidence of BD as 1:2359. A further study found that 4.7% of babies referred with suspected PKU had the diagnosis confirmed, while 18.9% had hyperphenylalaninemia (HPA), and 29.7% of those referred with suspected BD had the diagnosis confirmed (11). In the limited number of studies conducted for the single regions, final diagnoses were made based on biochemical examinations.

In our study conducted in a tertiary center in Ankara, the capital of Türkiye, babies referred by the NNSP with suspected PKU or BD were subjected to both biochemical and genetic examinations to investigate not only the diagnosis, but also the treatment status.

MATERIALS and METHODS

This study was approved by the Ankara University ethics committee (İ01-32-24, 18.01.2024).

The medical records of babies referred to Ankara University Faculty of Medicine, Department of Pediatric Metabolism between January 2019 and November 2023 were reviewed retrospectively, and the baseline characteristics, screening values, and biochemical and genetic examination results, treatment status of the patients were documented. This study was descriptive study.

In the NNSP, if the initial phenylalanine value is ≥4mg/dL, or ≥2.1 mg/dL twice for PKU, and if the biotinidase activity is ≤65 MRU (microplate response units) twice for BD, referral to department of metabolism is recommended (2).

The plasma blood amino acids of babies referred to our center with suspected PKU were studied and a PAH gene analysis was performed in the presence of abnormal phenylalanine values. Additionally, patients with high phenylalanine levels were assessed for BH4 (tetrahydrobiopterin) metabolism disorders. Phenylalanine levels of >20 mg/dL are classified as classical PKU, 15–20 mg/dL as moderate PKU, 10–15 mg/dL as mild PKU, 6–10 mg/dL as mild hyperphenylalaninemia and 2–6 mg/dL as benign mild HPA (12). If a phenylalanine level of >6 mg/dL is recorded in newborns, the urgent onset of treatment

is recommended (13). Before initiating BH4 treatment, we evaluated our patient's variants on the BioPKU website to predict BH4 responsiveness. We conducted a 48-hour BH4 loading test and monitored the responsiveness of phenylalanine levels. For the present study, these data were adopted as the classification and treatment indication limits.

Plasma biotinidase activity was measured and a BTD gene analysis was performed on babies referred to our center with suspected BD. At our center, the level of biotinidase enzyme is studied using the fluorometric method. In which <0.7 U/L (<10%) was considered a profound deficiency, 0.7–2.1 U/L (10-30%) a partial deficiency, 2.1–5.1 U/L (30-70%) a heterozygous deficiency and>5.1 U/L (>70%) normal activity (14). Biotin treatment was started in patients who have a profound deficiency and partial deficiency for biotinidase activity. For the present study, these data were accepted as the classification and treatment indication limits.

The complete gene sequence analysis was conducted for PAH and BTD genes, and in the event of identifying two different variants in a patient, confirmation was carried out on their parents using Sanger sequencing. Patients with variants detected in two different alleles were presented as compound heterozygotes.

Statistical Analysis

IBM SPSS Statistics (Version 28.0. Armonk, NY: IBM Corp.) was used for the statistical analysis, for which numbers, percentages, 25th-75th quarters, mean, standard deviation, median, minimum, and maximum values were calculated.

RESULTS

Between January 2019 and November 2023, 143 babies were referred to our department by the NNSP, of whom 59 were female (41.3%) and 84 (58.7%) were male. The median (25–75th percentile) age of the patients upon presentation to our center was 23.0 (17.0–30.0) days, while the median (25–75th percentile) gestational age was 38.3 (37.4–39.40) weeks. Of the total, 27 (18.9%) were preterm, 112 (78.3%) were term and four (2.8%) were post-term. The median (25–75th percentile) birth weight was 3080 (2770–3500) grams, and the weight of 90.9% of the sample was within the normal range. Of the total, 13.3% of the patients had a history of hospitalization, 23.1% had a history of icterus, 24.5% were from consanguineous marriages, and 3.5% had a sibling history with the same diagnosis. Finally, 78 (54.5%) of the patients were referred to our center with suspected BD and 65 (45.5%) with suspected PKU (Figure 1) (Table I) .

The median values of the first, second and third samples garnered from the NNSP records of the patients referred with suspected PKU were 2.3 mg/dL (2.0–3.4), 2.4 (2.2–3.4) and 2.4 (2.1–2.7), respectively. The median values of the first, second samples of patients referred with suspected BD were 54.4 MRU [46.7–60.8] and 57.3 [46.1–62.0], respectively. Only one patient in the sample was examined for the third time for BD, with a recorded value of 52.8 MRU (Table II).

Table I: Baseline characteristics of the research group

Sex*	
Female	59 (41.3)
Male	84 (58.7)
Age at hospital admission, days	
mean±SD	26.43±14.8
median (min-max)	23.0 (4.0-89.0)
25–75th percentile	17.0-30.0
Gestational age group*	
Preterm	27 (18.9)
Term	112 (78.3)
Post-term	4 (2.8)
Gestational age, weeks	
mean±SD	38.28±1.78
median (min-max)	38.3 (32.0-42.3)
25–75th percentile	37.4-39.40
Birth weight group*	
<2500 grams	9 (6.3)
2500–4000 grams	130 (90.9)
>4000 grams	4 (2.8)
Birth weight, grams	
mean±SD	3096±575
median (min-max)	3080 (2770-3500)
25–75th percentile	2770-3500
Hospitalization history*	
Yes*	19 (13.3)
No	124 (86.7)
Jaundice history*	
Yes	33 (23.1)
No	110 (76.9)
Consanguineous marriage*	
Yes*	35 (24.5)
No	108 (75.5)
Sibling with the same diagnosis*	
Yes*	5 (3.5)
No	138 (96.5)
Disease suspicion*	
Biotinidase deficiency	78 (54.5)
Phenylketonuria	65 (45.5)

***:** *n(%)*

The examinations performed at our center revealed median phenylalanine values in the first sample in the serum of patients referred with suspected PKU of 1.9 mg/dL (1.2–3.3). Biotinidase activity in the serum of patients referred with suspected BD were compatible with a partial deficiency in 39.7% and a profound deficiency in 8% in the first sample, while in the second sample, 25.6% were consistent with partial deficiency and 3.8% with profound deficiency (Table II).

A PAH gene analysis was performed on 23 (35.4%) babies who were found to have high phenylalanine levels. Of the patients subjected to a PAH gene analysis, a compound heterozygous variant was detected in 14 (60.9%) and a homozygous variant in six (26.0%). Of the six patients with the homozygous

Table II: National Newborn Screening Program Results and Serum Measurements in Our Center

	1st sample		2nd sample		3rd sample	
	A*	B†	A*	B†	A*	B†
PKU suspected babies, Phe level, mg/dL						
Sample number	63	65	55	40	18	23
mean±SD	3.2±3.0	3.7±6.6	2.8±3.0	3.7±4.4	2.5±0.6	4.0±3.0
median (min-max)	2.3 (0.8–17.0)	1.9 (0.65–46.0)	2.4 (2.0–6.1)	1.9 (0.5–22.0)	2.4 (1.8–4.8)	3.5 (0.9–12.4)
25–75th percentile	2.0–3.4	1.2–3.3	2.2–3.4	1.2–4.4	2.1–2.7	1.6–5.4
BD suspected babies, biotinidase activity, MRU						
The number of the sample	76	78	68	59	1	38
mean±SD	49.5±16.5	2.01±0.9	53.7±19.2	2.3±1.0	52.8	3.0±1.6
median (min-max)	54.4 (0.0–65)	2.0 (0.1–5.0)	57.3 (0.0–122)	2.2 (0.1–5.6)	-	2.8 (0.4–9.7)
25–75th percentile	46.7–60.8	1.3–2.6	46.1–62.0	1.8–2.8	-	2.0–3.7
The group of biotinidase activity, n (%)						
Profound deficiency (<0.7)		8 (10.3)		3 (3.8)		1 (1.3)
Partial deficiency (0.7–2.1)	-	31 (39.7)		20 (25.6)		11 (14.1)
Heterozygous deficiency (2.1–5.1)		38 (48.7)		33 (42.3)		22 (28.2)
Normal (>5.1)		1 (1.3)	-	1 (1.3)	-	3 (3.8)

***A:** National Newborn Screening Program Results, †**B:** Serum Measurements in Our Center, **BD:** Biotinidase deficiency, **Phe:** Phenylalanine, **PKU:** Phenylketonuria*

Table III: PAH and BTD gene analysis

	Total analysis	Homozygous variant	Compound heterozygous variant	Heterozygous variant	No variant
In the group of babies referred with suspected PKU PAH gene analysis)	23 (35.4)	6 (26.0)	14 (60.9)	2 (8.7)	1 (4.4)
In the group of babies referred with suspected BD BTD gene analysis*	62 (79.5)	21 (33.9)	10 (16.1)	27 (43.5)	4 (6.5)

***:** n (%), **BD:** Biotinidase deficiency, **PKU:** Phenylketonuria*

Table IV: Treatment approach to patients with suspected PKU and BD

	Suspected PKU, treatment*	Suspected BD, treatment*
Total number	9 (13.8)	46 (59.0)
Diet	3 (4.6)	-
Saptopterin	1(1.5)	-
Diet + saptopterin	5 (7.7)	-
No treatment	56 (86.2)	1 (1.3)
Biotin	-	46 (59.0)
Biotin treatment discontinued during follow-up	-	31 (39.7)

***:** n(%), **BD:** Biotinidase deficiency, **PKU:** Phenylketonuria*

variant in the PAH gene, treatment had already been started in five as a phenylalanine level of >6 mg/dL was recorded at admission. While three patients with the homozygous variant were receiving combined saptopterin and diet treatment, two were being monitored with diet therapy alone. Although the variant of a male patient with a homozygous variant in the PAH gene [PAH: NM_000277.3 c.533A>G (p.Glu178Gly)] is pathogenic, treatment has not been started as phenylalanine levels of 1.8–2.1 mg/dL have been recorded, but follow-up continues. Of the 14 patients with a compound heterozygous variant in the PAH gene, 10 were found to be compatible with benign mild HPA (phenylalanine levels of between 2–6 mg/dL) and were being monitored without treatment. Of the four patients with the compound heterozygous variant, two were continued with a saptopterin and diet combined treatment, one with diet and one with saptopterin (Tables III and IV). A total of nine cases of PKU and 21 cases of HPA were diagnosed. All patients were evaluated for BH4 metabolism disorders, and no abnormal results were found. One patient with no variant in the PAH gene was diagnosed with citrin deficiency based on the identification of high levels of citrulline and arginine in a blood amino acid analysis revealing simultaneous cholestasis and hyperammonemia findings. The patient's diagnosis was confirmed with the detection of a pathogenic homozygous variant in the SLC25A13 gene, for which the patient was started on a combined diet and pharmacological treatment based on a diagnosis of neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) type citrin deficiency.

A BTD gene analysis was performed on 62 (79.5%) of the patients referred with suspected BD, revealing a heterozygous variant in 27 (43.5%), a homozygous variant in 21 (33.9%) and a compound heterozygous variant in 10 (16.1%), while no BTD variant was identified in four (5.1%). All patients were started on biotin except one baby with a normal initial biotinidase level. The biotin treatment was subsequently discontinued in 31 babies (39.7%) identified with no biallelic variant after a BTD

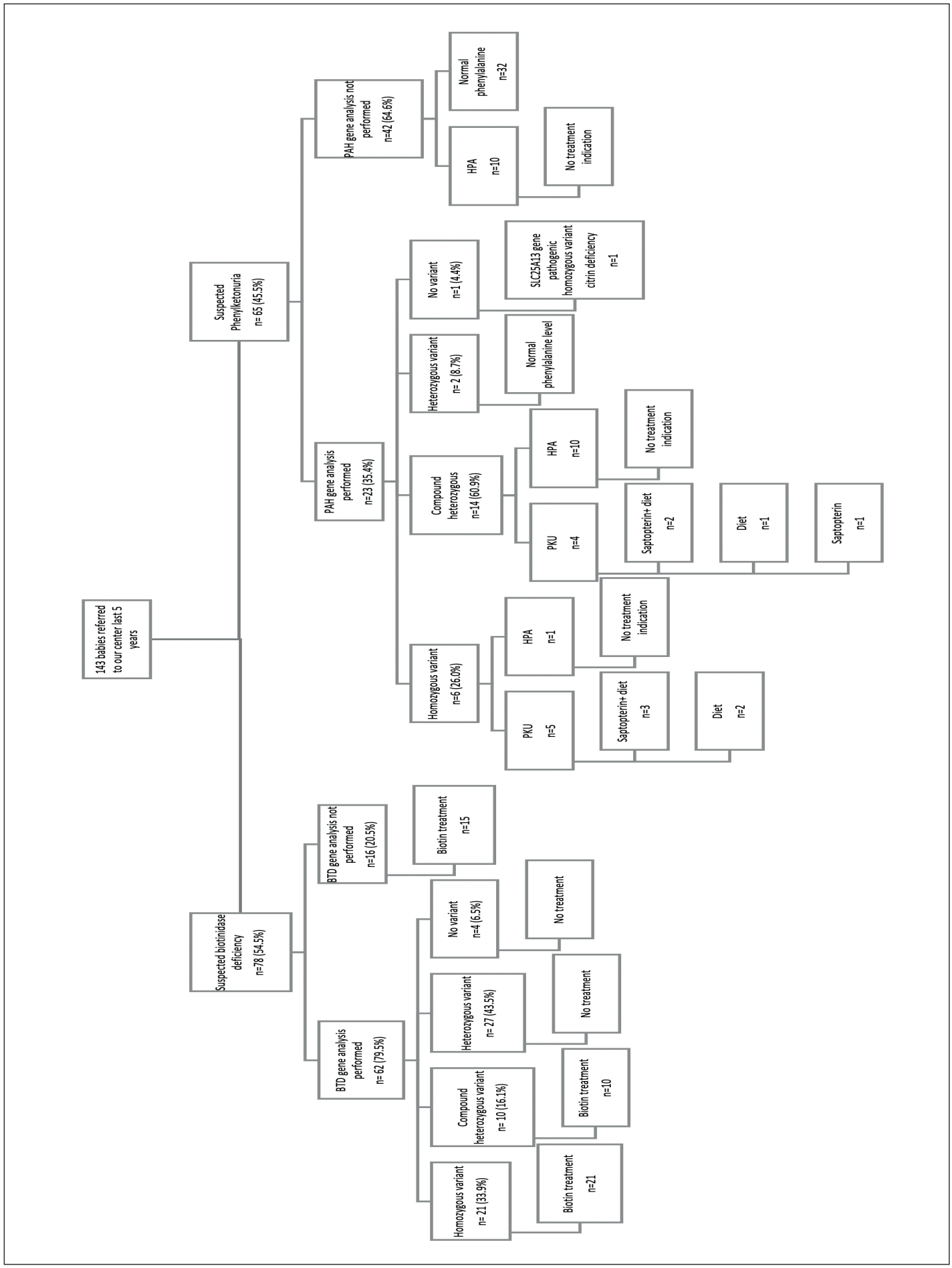

Figure 1: The flowchart of the study

gene analysis, and whose follow-up biotinidase activities were compatible with the carrier level. Finally, the biotin therapy of 46 patients (59.0%) was continued (Tables III and IV).

DISCUSSION

In this study, carried out in a tertiary center in Ankara, the capital of Türkiye, approximately one-third of the babies referred to our center by the NNSP over the last five years were found to be carrying biallelic variants of the relevant disease. Treatment indication was determined for 13.8% of the babies referred with suspected PKU and 59% of those with suspected BD.

A rate of consanguineous marriage in Türkiye of 23.2% has been reported, although rates of 42.6% have been reported in the Southeastern Anatolia region (15). The rate of consanguineous marriage in the present study was found to be 24.5%, which is similar to the general country rate. Türkiye is a country where a higher incidence of PKU and BD can be expected than in the rest of the world, and there are few studies in the field of NNSP (9-11). The present study is the first to include genetic examination and treatment processes, in addition to biochemical evaluations of babies with suspected PKU and BD.

Assuming a global prevalence of 1:23930, there are an estimated 0.45 million cases of PKU around the world, and prevalence studies have been conducted in many countries to date reporting different figures, including Italy (1:4000), Ireland (1:4545), Denmark (1:13434), Finland (1:112000), Thailand (1:227273), Japan (1:125000) and the Philippines. (1:116006) (4). Studies for PKU conducted in our country have produced different rates of 1:657, 1:8375, 1:6667 and 1:1861, reported regionally and yearly (4, 9-11). It is estimated at 1:60000 live births in BD (16). A study conducted in Italy reported a prevalence of BD of 1:61000, while as 1:28316 in Saudi Arabia, which is the rate of consanguineous marriage was reported similar to our country (17,18). Regional studies in our country have reported a prevalence of BD of 1:1861, 1:2359 and 1:6815, depending on the year and region (10,11). In the present study, the general research population was babies referred to our center with suspected PKU or BD, however this cannot be considered a prevalence study, as there is a lack of data on the number of positive cases among the screened patients, and what percentage of them applied to our center. Since our research population is a center in the capital that accepts patients from all over the country, accessing accurate data is also challenging, and this can be considered a limitation of our research.

A study conducted in a single region in our country reported that 4.7% of the babies referred with suspected PKU had the diagnosis confirmed, while 18.9% were diagnosed with hyperphenylalaninemia, and 29.7% of the babies referred with suspected biotinidase deficiency were diagnosed with BD (11). In the present study, 13.8% of the babies referred with suspected PKU had diagnosis confirmed, while 32.3% were diagnosed with hyperphenylalaninemia. A BTD gene analysis was performed on 79.5% of the babies referred with suspected BD in the present study, and biallelic variants were detected in half of them. The higher rates of prevalence reported in the present study indicate the potential for regional variations, revealing a need to garner data from each region in the country to identify the prevalence and distribution of positive cases geographically. The creation of a national registry would provide a clear understanding of the regions in Türkiye where pediatric metabolism specialists are needed.

Zeybek et al. (19) reported a case of citrin deficiency detected incidentally in NNSP upon the identification of a compound heterozygous variant in the SLC25A13 gene in whom cholestasis, coagulopathy, hyperammonemia and high citrulline were detected during follow-up for suspected PKU. In the present study, a female baby was examined for the development of cholestasis while being investigated for suspected PKU and was diagnosed with citrin deficiency due to the very similar clinical findings and the detection of a homozygous pathogenic variant in the SLC25A13 gene. Our study also revealed the second case in Türkiye to be referred by NNSP with suspected PKU and diagnosed with citrin deficiency (19). Also, sister of the patient was examined due to the history of cholestasis in infancy, and she was also diagnosed with citrin deficiency. Two siblings were started on a high-protein, low-carbohydrate diet and followed up. Ünal et al. (20) reported diagnoses of Maple Syrup Urine Disease (MSUD) in four patients, galactosemia in two patients and tyrosinemia type 1 in one patient referred from NNSP with high phenylalanine levels who underwent a detailed examination. It has been suggested that any condition that causes liver dysfunction can increase plasma phenylalanine levels (20). In the light of the above cases diagnosed with IMD other than PKU, we recommend that measurements of phenylalanine levels should not be carried out with limited parameters in patients coming from NNSP with suspected PKU, all plasma amino acids should be analyzed, and patients should be examined in detail and evaluated holistically.

Since the incidence of autosomal recessive diseases is higher in regions where consanguineous marriages are common, patients need to be diagnosed and started on treatments early in the asymptomatic period. The launch of an expanded newborn screening program in our country would contribute to a decrease in the death and sequelae rates of many patients, as only two IMDs (PKU and BD) are currently being screened for today.

Newborns with phenylalanine levels >6 mg/dL should be started on treatment as soon as possible (13). In the present study, this cut-off value was adopted as the treatment indication, and led to the start of treatment in nine (13.8%) patients. Since patients with BD can have neurocutaneous consequences if left

untreated, prompt treatment decisions are essential (7, 21, 22). Biotin is a safe and non-toxic drug (23). Biotin was started in all of the patients in the present study whose biotinidase levels were lower than normal. The importance of repeated measurements of biotinidase activity and genetic analysis for a final diagnosis has been demonstrated (14). Biotin treatment was started and discontinued only after excluding a BD diagnosis in babies with no biallelic variant in their genetic analysis, and whose repeated measurements of biotinidase activity were within the normal range during follow-up.

This is one of the few studies of the NNSP to date in our country and has provided genetic analysis and treatment follow-up data related to babies. Multi-center, large-scale studies would provide a clearer understanding of the current situation in the country.

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The Effect of Ultrasound-guided Central Venous Catheterization on Complications and Success Rate in Critically-ill Children: A Multicenter Study

Kritik Hasta Çocuklarda Ultrason Eşliğinde Santral Venöz Kateterizasyonun Komplikasyonlar ve Başarı Oranına Etkisi: Çok Merkezli Çalışma

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ABSTRACT

Objective: The aims of this study were to compare the results of ultrasound (US) guidance and the landmark (LM) technique for central venous catheter (CVC) placement in pediatric intensive care units (PICUs) as performed by clinicians.

Material and Methods: The patients were divided into two groups according to the technique used: an LM group (459 patients) and a US-guided group (200 patients). We evaluated the success rate, the number of attempts, and the complication rates based on each patient's age and weight.

Results: The time required for the successful placement of the CVC was significantly different between the two groups: 10.9±10.8 min in the LM group and 8.1±7.6 min in the US-guided group (p=0.012). Additionally, the average number of attempts for successful catheterization was 1.8±0.8 in the US-guided group; and 2.5 ± 1.4 in the LM group (p=0.024). A total of 115 (17.3%) complications were noted: 24 (3.6%) in the US-guided group and 91 (13.7%) in the LM group (p=0.014). The frequency of complications decreased as the age and weight of the patients increased. When the inserted catheters used by ultrasound were evaluated, 59.5% of them were placed by clinicians who had ultrasound training while 40.5% were inserted by clinicians who did not have ultrasound training. There was no significant difference in the complication rate, number of punctures, and success rates between the ultrasound-trained and untrained clinicians (p=0.476).

Conclusion: This is the largest multicenter study comparing the US-guided vs. LM technique for CVC placement in children. We believe that the US-guided CVC procedure is more safe and takes less time than the LM technique. Also, point-of-care ultrasound is useful, beneficial, and easily available for pediatric intensivists.

Key Words: Central venous catheter, Ultrasound, Pediatric intensive care units

ÖZ

Amaç: Bu çalışmada çocuk yoğun bakım ünitelerinde ultrasonografi eşliğinde yapılmış olan santral venöz kateter uygulamalarının değerlendirilmesi ve ultrason kullanılmadan takılan kateterizasyonlarla karşılaştırılması amaçlanmıştı.

Gereç ve Yöntemler: Hastalar, kullanılan tekniğe göre iki gruba ayrıldı: Ultrason kullanılmayan hasta grubu (459 hasta) ve US kullanılan hasta grubu (200 hasta). Başarı oranını, girişim sayısını ve komplikasyon oranlarını her hastanın yaşına ve kilosuna göre değerlendirdik.

Bulgular: SVK'nın başarılı bir şekilde yerleştirilmesi için gereken süre iki grup arasında önemli ölçüde farklıydı: Ultrason kullanılmayan grupta 10.9±10.8 dakika ve ultrason kılavuzluğundaki grupta 8.1±7.6 dakika (p=0.012). Ek olarak, başarılı kateterizasyon için ortalama girişim sayısı, ultrason kılavuzluğundaki grupta 1.8±0.8'di; ultrason kullanılmayan grupta 2.5±1.4 (p=0.024). Toplam 115 (%17.3) komplikasyon kaydedildi: Ultrason kullanılan grupta 24 (%3.6) ve ultrason kullanılmayan grupta 91 (%13.7) (p=0.014). Hastaların yaşı ve kilosu arttıkça komplikasyon sıklığı azaldığı saptandı. Ultrason kullanılarak takılan kateterler değerlendirildiğinde %59.5'inin ultrason eğitimi almış klinisyenler tarafından, %40.5'inin ultrason eğitimi almamış klinisyenler tarafından yerleştirildiği görüldü. Ultrason eğitimi almış ve almamış klinisyenler arasında komplikasyon oranı, girişim sayısı ve başarı oranları açısından anlamlı fark yoktu (p=0.476).

Sonuç: Çalışmamız çocuklarda ultrason eşliğinde ve ultrason kullanılmadan SVK yerleştirmesini karşılaştıran en büyük çok merkezli çalışmadır. Ultrason eşliğinde takılan SVK işleminin daha güvenli ve daha az zaman aldığına inanıyoruz. Ayrıca, yatakbaşı ultrason pediatrik yoğun bakım uzmanları için yararlı ve kolayca elde edilebilir bir yöntemdir.

Anahtar Sözcükler: Santral venöz kateter, Ultrason, Çocuk yoğun bakım

INTRODUCTION

In the past ten years, ultrasound (US) use has been increasing with the application point of care ultrasound (POCUS) in emergency care and pediatric intensive care units (PICUs). Nowadays, POCUS is frequently used for central venous catheter (CVC) insertion, cardiac, and abdominal-related focused assessment with sonography in trauma (FAST), thorax, and lung assessment. POCUS is safe, easy to use, and readily available at any time. US-guided CVC insertion has been widely used in recent years in PICUs and pediatric emergency services (1,2).

Central venous catheters (CVCs) are extensively used in Pediatric Intensive Care Units (PICUs) and emergency care units to facilitate hemodynamic monitoring, prolonged and multiple fluid therapy, administration of medications and blood products, total parenteral nutrition, plasma exchange, renal replacement therapy, and vascular access (3). Commonly utilized sites for central venous catheterization in pediatric patients encompass the internal jugular vein (IJV), femoral vein (FV), and subclavian vein (SCV). The placement of a CVC is technically more challenging in pediatric patients than in adults: unsuccessful attempts, arterial puncture, bleeding, and long attempts are seen frequently in infants. The success rate for CVC placement in the pediatric population varies between 81% and 95%, accompanied by reported complication rates ranging from 2.5% to 22% (4). Complications during central venous catheterization, such as arterial puncture, pneumothorax, hemothorax, and hematoma, have the potential to result in fatal outcomes. Many complications are correlated with the iterative

needle cannulation of the central vein (5). Recent studies have indicated that ultrasound-guided central venous catheterization exhibits a heightened success rate and fewer complications when compared to alternative techniques (3-5).

US-guided central venous catheterization has become widespread with technological improvements, allowing for the selection of the most appropriate and safe blood vessel, and the safe puncture of the target vessel. Frequently, IJV is the preferred vein, followed by FV; SCV is rarely used. We aimed to compare the results of US guidance and the landmark (LM) technique for CVC placement in PICUs as performed by clinicians. Furthermore, we aimed to evaluate the success rate, the time required for successful cannulation, the number of attempts, and the complication rates. This is the largest multicenter study comparing the US-guided vs. LM technique for central venous catheterization in children. In addition, we described the current practices for central venous catheterization used in many PICUs in Türkiye.

US-guided central venous catheterization has become widespread with technological improvements, allowing for the selection of the most appropriate and safe blood vessel, and the safe puncture of the target vessel. Our objective was to conduct a comprehensive comparative analysis of outcomes between ultrasound-guided (US) and landmark (LM) techniques for CVC placement in PICUs, performed by skilled clinicians. This study aimed to evaluate and contrast the success rates, time durations for successful cannulation, number of attempts, and complication rates between the US-guided and LM techniques. Notably, this research represents the most extensive multicenter investigation to date, directly comparing the two aforementioned methodologies for central venous catheterization in the pediatric population. Additionally, we described the current practices for central venous catheterization used in many PICUs in Türkiye.

MATERIALS and METHODS

A prospective, multicenter, observational study was undertaken spanning the period from September 1, 2018, to December 31, 2018, involving 14 Pediatric Intensive Care Units (PICUs). The study cohort comprised 659 critically ill children necessitating central venous catheterization (CVC) due to diverse clinical imperatives, such as the administration of multiple fluids and medications, infusion requirements, vasoactive drug administration, prolonged intravenous therapy, hemodialysis, plasma exchange, total parenteral nutrition. It heightened susceptibility to extravasation, among other indications. The patients were divided into two groups according to the technique used: an LM group (459 patients) and a US-guided group (200 patients).

Central venous catheterization was conducted utilizing the internal jugular vein (IJV), subclavian vein (SCV), and femoral vein (FV). The catheterization procedures encompassed the insertion of conventional double-lumen catheters or hemodialysis catheters, with diameters spanning from 4 Fr to 12 Fr, contingent upon the child's weight and vascular dimensions, into either the IJV, SCV, or FV. The selection of the catheterization site was determined by the patient's specific attributes, the rationale for catheterization, and the cumulative experience of the medical facility.

The procedures were performed by pediatric intensivists, fellows, and pediatricians. All the clinicians who participated in the study had at least one year of experience in CVC placement. In addition, some of the clinicians underwent formal US-guided training (hands-on training by radiologists), and their peers trained some of the clinicians. Formal ultrasound training given by qualified radiologists included the use of ultrasound, ultrasound settings, and evaluation of vessels and organs by ultrasound imaging.

Various parameters were recorded during the study, encompassing the patient's demographic information, the chosen access site, the number of attempts made, and the time required for catheter placement. The procedure time, delineated from the initial skin puncture to the successful placement of the guidewire, was recorded. Clinicians assessed and reported insertion-related complications, including pneumothorax, hematoma, and arterial puncture. The procedural timing was conducted by Pediatric Intensive Care Unit (PICU) personnel utilizing a stopwatch, commencing from the instant the needle first penetrated the skin. The number of skin entries and the time of successful guidewire placement were systematically documented. Termination of the procedure was designated as the moment of successful guidewire insertion. A procedure was deemed successful when the catheter was effectively placed into the vein. Instances of procedure failure were defined as either exceeding six attempts, irrespective of arterial puncture occurrence, or surpassing 40 minutes of cannulation time.

The identification of a pulsatile flow characterized by bright red blood emanating from the needle served as an indicative marker for an arterial puncture. Hematoma formation, exceeding a diameter of 1 cm, at the skin access site was documented. In cases where catheters were positioned in the internal jugular vein (IJV) and subclavian vein (SCV), a chest X-ray was performed. Sedation protocols were implemented for patient comfort. The patient cohort was stratified into two distinct groups based on age (i.e., <2 years vs. >2 years old) and weight (<10 kg vs. >10 kg). The success rate, number of attempts, and complication rates were systematically assessed and compared across these delineated age and weight categories.

LM Technique

For internal jugular vein (IJV) catheterization, anatomical landmarks included the medial border of the sternocleidomastoid muscle and the pulsations of the carotid artery. Subclavian vein (SCV) catheterization was executed 1 cm below the junction of the medial one-third and lateral two-thirds of the clavicle.

In the case of femoral vein (FV) catheterization, the superior anterior thigh served as the entry point, situated just below the level of the inguinal ligament and approximately 1 cm medial to the point of maximal pulsation of the femoral artery (6,7). To maintain aseptic conditions, the entry site was disinfected using a 2% chlorhexidine solution and subsequently covered with a sterile drape. The catheterization needle was cautiously advanced towards the anticipated position of the targeted vein, with simultaneous aspiration. Upon observation of venous blood entering the syringe, the needle guide was placed, and the procedure was concluded (6-8).

US-guided Technique

For the IJV catheterization, the US probe was applied to the lateral aspect of the neck. For subclavian vein (SCV) catheterization, the probe was positioned on the anterolateral aspect of the thorax, precisely 1 cm below the clavicle. Regarding femoral vein (FV) catheterization, the probe was situated on the anterolateral aspect of the femoral region, approximately 2 cm below the inguinal ligament (6,7). The US-guided technique employed two primary approaches for vascular access: the long-axis and short-axis techniques, with emphasis given to the latter in this study. In the short-axis technique, the probe orientation was vertical to the vessel, not parallel to the skin. To optimize visibility within the ultrasound beam's area, the needle was inserted as closely as possible to the probe. Following vein selection, the puncture site was shielded, and the US probe (linear transducer: 5 MHz to 10 MHz) was aseptically covered with a sterilized sheath or glove, along with the application of the conductive gel. Subsequently, the clinician or practitioner manually manipulated the probe to delineate the artery and vein on the ultrasound image. Additionally, by aligning a large-bore needle beneath the center of the probe, the clinician or practitioner confirmed the needle trajectory and proceeded with cannulation attempts. Upon encountering a visual indication of blood, the US probe was retracted, and the conventional Seldinger technique was implemented (8,9).

This study was approved by an ethics committee of the University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital (no: 2018:117). Furthermore, written consent was obtained from each patient's family to include them in this study.

Statistical Analyses

Statistical analyses were conducted utilizing the SPSS 22.0 version for Windows (SPSS Inc., Chicago, IL, USA). Demographic data underwent assessment employing both parametric and non-parametric tests. Continuous variables were presented as mean and standard deviation (SD), while categorical variables were represented as frequencies and percentages. The Student's t-test was utilized to assess differences in the time required for catheterization and the number of attempts, both treated as continuous variables. The comparison of success rates and the incidence of complications among patients was executed through Fisher's exact test. A significance level of $p \leq 0.050$ was deemed statistically significant.

RESULTS

The study cohort included 289 males and 370 females, ranging from one month to 232 months (mean: 58.8±63.2 months). Of the 659 critically ill children in this study, mechanical ventilation was performed in 392 patients (59.5%). The body weight of the patients ranged from 2 kg to 94 kg (mean: 17.5±16.5 kg). There was respiratory failure in 324 (49.1%) patients, neurological diseases in 47 (7.2%) patients, metabolic problems in 43 (6.5%) patients, sepsis in 36 (5.4%) patients, heart disease in 33 (5.2%) patients, renal diseases in 29 (4.4%) patients, hematologic diseases in 28 (4.2%) patients, and electrolyte abnormalities in 24 (3.6%) patients (Table I).

Significant disparities were observed in the time required for successful Central Venous Catheter (CVC) placement between the two groups, with durations of 10.9±10.8 minutes for the

Table I: Demographics and baseline characteristics for 659 children in whom central venous catheters (CVC) were placed by landmark or ultrasound-guided approach

Demographics	
Age (month)*	58.8 ± 63.2 (1-232)
Weight (kg)*	17.5 ±16.5 (2-94)
Gender†	
Female	289 (43.9)
Male	370 (56.1)
Intubation†	
Yes	392 (59.5)
No	267 (40.5)
Weight (kg)†	
≤3.5	49 (7.4)
3.51-10 kg	279 (42.3)
10.01-20 kg	151 (23)
> 20 kg	180 (27.3)
Diagnosis†	
Respiratory failure	324 (49.1)
Sepsis	36 (5.4)
Neurologic	47 (7.2)
Cancer	17 (2.5)
Renal	29 (4.4)
Trauma	22 (3.4)
Gastrointestinal diseases	18 (2.7)
Heart diseases	33 (5.2)
Hematologic	28 (4.2)
Electrolyte abnormalities	24 (3.6)
Metabolic diseases	43 (6.5)
Drug intoxication	18 (2.8)
Central nervous system infections	12 (1.8)
Immunodeficiency	8 (1.2)

**: mean ± SD (minimum-maximum), †: n(%)*

Table II: Comparison of outcome measure in the landmark technique and ultrasound technique

Variable	Landmark (n=459)	Ultrasound (n=200)	p
Catheter type*			
Double lumen	364 (79.3)	152 (76)	
Hemodialysis	95 (20.7)	48 (24)	
Insertion site*			
Jugular vein	150 (32.6)	146 (73)	
Subclavian vein	87 (19)	9 (4.5)	
Femoral vein	222 (48.4)	45 (22.5)	
Success rate*			
All	448 (97.6)	197 (98.5)	0.568‡
Jugular vein	147 (98)	144 (98.6)	0.685‡
Subclavian vein	84 (96)	9 (100)	0.354‡
Femoral vein	217 (97)	44 (97)	0.296‡
Success rate*			
First attempt	196 (42.7)	120 (60)	0.015‡
Complication rate*			
All	91 (13.7)	24 (3.6)	0.014‡
Jugular vein	33 (5)	9 (1.3)	0.001‡
Subclavian vein	16 (2.4)	0 (0)	0.001‡
Femoral vein	42 (6.3)	15 (2.2)	0.032‡
Number of attempts†			
All	2.5 ± 1.4	1.8 ± 0.8	0.024§
Jugular vein	2.5 ± 1.6	1.7± 0.7	0.012§
Subclavian vein	2.8 ± 1.8	2.1 ± 1.2	0.068§
Femoral vein	2.6 ± 1.6	2.2 ± 1.4	0.184§
Procedure time, minutes†			
All	10.9 ±10.8	8.1 ± 7.6	0.012§
Jugular vein	9.3 ±9.1	7.3 ± 7.2	0.022§
Subclavian vein	12 ± 11.1	12.1 ± 8.8	0.124§
Femoral vein	11.6 ± 10.6	9.9 ± 7.7	0.325§

***:** *n (%),* **†:** *mean±SD,* **‡:** *Fisher's exact test,* **§:** *Student's t-test*

Landmark (LM) group and 8.1±7.6 minutes for the Ultrasound-guided (US-guided) group (p=0.012). Notably, the time needed for successful Internal Jugular Vein (IJV) catheterization exhibited a statistically significant difference, with 7.3±7.2 minutes for the US-guided group and 9.3±9.1 minutes for the LM group (p = 0.022). The US-guided group demonstrated a superior success rate at the first attempt, with 60% compared to 42.7% in the LM group (p=0.015). The average number of attempts for successful catheterization was 1.8±0.8 in the US-guided group, whereas it was 2.5±1.4 in the LM group (p=0.024). Additionally, the US-guided group necessitated fewer puncture attempts to access the IJV compared to the LM group (1.7±0.7 vs. 2.5±1.6, respectively; p=0.012). Regarding complications, the incidence of arterial puncture was 8% for the LM group and 2.4% for the US-guided group. In comparison, hematoma formation was 4.7% for the LM group and 1% for the US-guided group. Pneumothorax occurred in 1% of the LM group and 0% in the US-guided group. A total of 115 complications were noted in the study, accounting for 17.3% of cases, with 24 complications (3.6%) in the US-guided group (nine for IJV, 15 for FV) and 91 complications (13.7%) in the LM group (33 for IJV, 42 for FV, 16 for SCV) (p=0.014) (Table II).

We evaluated the success rate, the number of attempts, and the complication rates based on the age and weight of the patients. The success rate was 96.7% for children < 2 years old and 99.1% for children > 2 years old (p=0.038). When the number of attempts was evaluated in the age groups, the percentage for two or more attempts was 38.3% for children < 2 years old and 26% for children > 2 years old (p=0.026) (Figure 1). When the number of attempts was evaluated based on the weight groups, the percentage for two or more attempts was 38.5% for the low-weight group (<10 kg) and 25.9% for the high-weight group (>10 kg) (p=0.014) (Figure 2). Technique, complication rates, catheter type, insertion site according to patient's weight, and type of catheter are shown in Table III.

In addition, 59% of the CVC insertions were performed by fellows, 32% were performed by pediatric intensivists, and 9% were performed by pediatricians. When the catheters inserted using the US-guided technique were evaluated, 59.5% were inserted by clinicians with formal US-guided training and 40.5% were inserted by clinicians who had been trained by their peers. There was no significant difference in the complication rate, the number of punctures, and the success rates between the formally trained and the peer-trained clinicians (p=0.476).

Table III: Technique, catheter type, insertion site, complication rate compared with weight

Variable	Total*	≤3.5 kg*	3.51-10 kg*	10.01-20 kg*	>20 kg*
Technique					
Landmark technique	459 (69.7)	34 (7.5)	192 (41.8)	107 (23.3)	126 (27.4)
US-guided	200 (30.3)	15 (7.5)	87 (43.5)	44 (22)	54 (27)
Catheter type†					
Single-double lumen	516 (78.3)	43 (8.4)	253 (49)	114 (22)	106 (20.6)
Hemodialysis	143 (21.7)	6 (4.2)	26 (18.2)	37 (25.8)	74 (51.8)
Insertion site†					
Internal jugular vein					
Right	195 (29.6)	18 (9.2)	88 (45.2)	44 (22.6)	45 (23)
Left	101 (15.3)	7 (7)	51 (50.4)	27 (26.8)	16 (15.8)
Subclavian vein					
Right	63 (9.6)	11 (17.5)	23 (36.5)	13 (20.6)	16 (25.4)
Left	33 (5)	6 (18.2)	13 (39.4)	7 (21.2)	7 (21.2)
Femoral vein					
Right	197 (29.9)	4 (2)	78 (39.5)	42 (21.4)	73 (37.1)
Left	70 (10.6)	3 (4.2)	26 (37.2)	18 (25.8)	23 (32.8)
Complication rate†					
Artery puncture	59 (9)	4 (6.8)	27 (45.8)	14 (23.7)	14 (23.7)
Hematoma	29 (4.4)	0(0)	18 (62)	6 (20.6)	5 (17.4)
Pneumothorax	5 (0.8)	0(0)	2 (40)	2 (40)	1 (20)
Artery puncture and hematoma	19 (2.9)		12 (63.2)	4 (21)	3 (15.8)
Artery puncture and pneumothorax	2 (0.3)	1 (50)	1 (50)		
No complication	545 (82.6)	44 (8)	219 (40)	125 (23)	157 (29)

**n (%)*

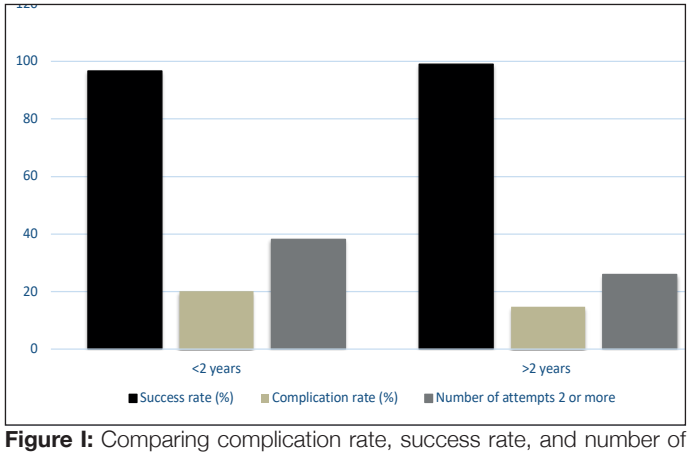

Figure I: Comparing complication rate, success rate, and number of attempts between <2 versus >2 years old in all patients.

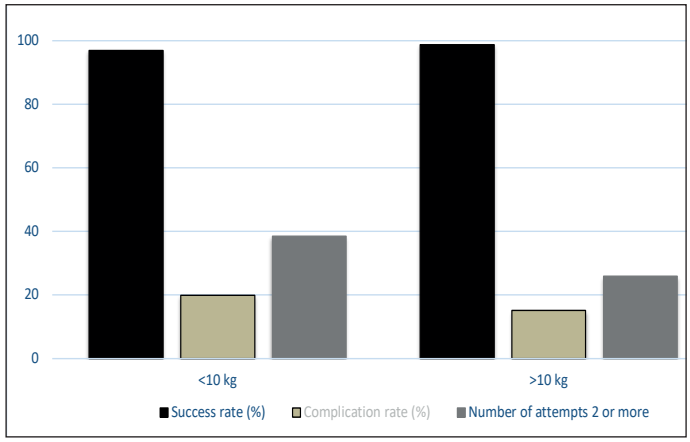

Figure 2: Comparing complication rate, success rate, and number of attempts between <10 kg versus >10 kg in all patients.

DISCUSSION

This study is the largest multicenter comparison of US-guided and LM techniques for central venous catheterization in critically ill children. We found that the US-guided technique reduces the complication rate and increases the first attempt success rate.

Anomalies in anatomy, prior Central Venous Catheter (CVC) placement, and conditions such as venous thrombosis or a small vessel diameter may detrimentally impact the success rate and augment the risk of complications during catheterization (10). Consistent with numerous prior investigations, the Ultrasound-guided (US-guided) technique has demonstrated superiority over the Landmark (LM) technique, manifesting in decreased complication rates and increased success rates. Several studies employing both techniques support this assertion (5,10,11). For instance, Kayir et al. (12) reported a complication rate of 24% for the LM group as opposed to 6% for the US-guided group, while Sazdov et al. (13) found a complication rate of 14.5% for the LM group and 4% for the US-guided group. The findings of the present study align with the existing literature, substantiating that the US-guided technique mitigates complications associated with central venous catheterization in Pediatric Intensive Care Unit (PICU) patients compared to the LM technique. Specifically, complications such as arterial puncture, pneumothorax, hemothorax, and hematoma were notably lower in the US-guided group than in the LM group. Arterial puncture emerged as the most prevalent complication for Internal Jugular Vein (IJV) and Femoral Vein (FV) catheterizations, while pneumothorax was most commonly

associated with Subclavian Vein (SCV) catheterization (10,14). In the literature, the reported incidences of these complications range between 10% and 14% for arterial puncture, 4% and 9% for hematoma formation, and 1% and 8% for pneumothorax (4,5,10,13,15). Importantly, the complication rates observed in our study closely resemble those reported in prior investigations.

Oulego-Erroz et al. (16) conducted a multicenter study demonstrating that the Ultrasound-guided (US-guided) technique significantly reduced the number of punctures and complication rates, while concurrently increasing the success rate when compared to the Landmark (LM) technique. In a study by Froehlich et al. (4), the cannulation success rate was reported as 88.2% in the LM group and 90.8% in the US-guided group, with no significant difference noted (p=0.540). In our cohort, the success rates for US-guided cannulation and anatomically LM-guided cannulation were 97.6% and 98.5%, respectively, and these rates were not found to be significantly different (p= 0.568). Several studies have reported a shorter duration for central vein cannulation using the US-guided technique compared to the LM technique, ranging from 4.2 minutes to 14.3 minutes (10,13,17). In alignment with these findings in the literature, our study indicates that the US-guided technique contributed to a reduction in the number of attempts and the duration of successful placement. The real-time nature of ultrasound application is notably advantageous for clinicians in localizing the vein during the procedure, leading to a more efficient process with reduced attempts and duration for successful catheter placement.

The impact of patient weight and age on cannulation success is well-documented in the literature. Leyvi et al. (17) reported varying success rates in their study group, with an overall success rate of 91%, 94.7% for children older than 1 year, and 77.8% for children younger than 1 year. Similarly, Froehlich et al. (4) observed that children in the low-weight group (median weight < 16.25 kg) exhibited lower success rates and required more placement attempts for both techniques compared to children in the high-weight group (median weight >16.25 kg). In this study, we analyzed success rates, the number of attempts, and complication rates with consideration of the age and weight of the patients. Our study findings align with existing literature, providing support for the notion that as patients age and weight increase, the number of attempts decreases, and the success rate increases. This aligns with the common understanding that placing a central catheter in infants is often more challenging than in older children due to factors such as a lack of patient cooperation and smaller vein size.

The literature consistently highlights that fellows and residents utilizing ultrasound (US) for cannulation experience a significant reduction in the number of attempts. Froehlich et al. (4) reported a noteworthy decrease in the required time for successful Central Venous Catheter (CVC) placement among resident physicians (405 vs. 919 seconds, p=0.020) when employing the US-guided technique, as opposed to the fellows or attending physicians, in comparison to the Landmark (LM)-guided technique. Sigaut et al.(18) demonstrated that the US-guided technique effectively reduced complication rates and failures in Internal Jugular Vein (IJV) catheterization in children, even when performed by physicians with limited experience in venous catheterization. Additionally, Zanolla et al. (19) indicated that specialists trained in ultrasound techniques exhibited reduced time requirements for successful placement, fewer attempts, and lower complication rates. In contrast, our study did not identify a significant difference in access time, success rate, or the incidence of complications for US-guided CVC placement between formally-trained and peer-trained clinicians (p=0.568). However, these findings are not surprising given that many clinicians acquire catheterization skills through peer training. Therefore, peer training can be equally effective as formal training in the context of US-guided CVC placement.

CONCLUSSION

In PICUs and emergency care units, POCUS is used for many invasive procedures in critically ill children. US-guided CVC placement is the technique that is most frequently used and it is beneficial for POCUS. Our large multicenter study confirms that, as evidenced by some studies, the use of US results in a higher rate of first-attempt success, a lower average number of attempts, a shorter access time, and lower complications (such as arterial puncture, hematoma, and pneumothorax) in the children. Hence, a US-guided central venous catheterization is safer and takes less time than the LM technique. Therefore, this technique should be preferred during CVC placement in critically ill children in PICUs.

Limitations

The limitations of this study are as follows. First, patient groups were not standardized. Second, patients and techniques were selected according to the center's experience.

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Evaluation of Patients Complaining of Staring Spells: Single Center Experience

Göz Dalması Şikayetiyle Başvuran Hastaların Değerlendirilmesi: Tek Merkez Deneyimi

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ABSTRACT

Objective: This study aimed to analyze the demographic characteristics, spell semiology, and electroencephalographic characteristics of children with a complaint of staring spells and determine the factors that differentiate epileptic and non-epileptic etiology.

Material and Methods: Fifty-six patients were included retrospectively between October 1, 2022, and December 1, 2023. The patients' age, gender, co-morbidities, and other characteristics of the staring spells (duration, frequency, automatism, and presence of post-attack symptoms), access time to the pediatric neurologist, referring unit and access time to the final diagnosis were also recorded. Electroencephalography (EEG) was performed on all patients.

Results: Fifty-six patients were divided into two according to epileptic and non-epileptic etiology. Thirty-three patients (59%) were diagnosed with non-epileptic staring spells, 15 (26.7%) were diagnosed with generalized epilepsy, and 8 (14.3%) were diagnosed with focal epilepsy. The non-epileptic group had a longer spell time and spell frequency, the presence of verbal stimulation response, and no post-attack symptoms ($p<0.001$). The access time to the pediatric neurologist was detected as 5.5 days, and the access time to the final diagnosis was 6.6 days. EEG was diagnostic in 100% of the epileptic group. Most of the patients were referred by pediatricians and family physicians ($p<0.001$).

Conclusion: Identifying the cause of staring spells is crucial for further follow-up. In this study, we emphasized that history and routine EEG are important to determine the etiology. It has been observed that access time to pediatric neurologists and final diagnosis are shorter in our country compared to the literature. It can be concluded that pediatricians and family physicians have a high awareness of staring spells.

Key Words: Childhood, Epilepsy, Staring spells, Epileptic seizure

ÖZ

Amaç: Bu çalışmanın amacı, göz dalması atakları şikayeti olan çocukların demografik özelliklerini, atak semiyolojisini ve elektroensefalografik özelliklerini analiz ederek epileptik ve epileptik olmayan etiyolojiyi ayıran faktörleri belirlemektir.

Gereç ve Yöntemler: 1 Ekim 2022-1 Aralık 2023 arasında göz dalması şikayetiyle başvuran 56 hasta, retrospektif olarak incelendi. Hastaların yaşı, cinsiyeti, komorbiditeleri, dalmanın diğer özellikleri (süre, sıklık, otomatizma ve atak sonrası

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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The study was provided by the Ankara Etlik City Hospital Ethics Committee (AEŞH-EK1-2023-646).

Contribution of the Authors / Yazarların katkısı*: *ÖZBUDAK P: Constructing the hypothesis or idea of research and/or article, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***KARGIN MENDERES D:*** Planning methodology to reach the conclusions, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***ÜSTÜN C:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***ÖNCEL EP:*** Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar. ***YÜKSEL D:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar.

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semptom varlığı), çocuk nöroloji hekimine ulaşma süreleri ve kim tarafından refere edildikleri sorgulandı. Tüm hastalara elektroensefalografi (EEG) uygulandı.

Bulgular: Ellialtı hasta epileptik ve epileptik olmayan etiyolojiye göre ikiye ayrıldı. Otuz-üç hastaya (%59) epileptik olmayan göz dalması, 15 hastaya (%26.7) jeneralize epilepsi, 8 hastaya (%14.3) ise fokal epilepsi tanısı konuldu. Epileptik olmayan gruptaki hastaların dalma süresinin ve atak sıklığının daha fazla olduğu, verbal uyarı yanıtının görüldüğü, atak sonrası semptomunun olmadığı saptandı (p<0.001). Dalma şikâyetiyle başvuran hastaların çocuk nöroloji hekimine ulaşma süresi 5.5 gün, hastaların sonuçlandırılma süresi 6.6 gün olarak hesaplandı. EEG epileptik grubun tamamında tanısaldı. Hastaların çoğu pediatrist ve aile hekimleri tarafından yönlendirilmişti (p<0.001).

Sonuç: Göz dalması şikayetinin nedenini belirlemek daha sonraki takip için çok önemlidir. Bu çalışmada etyolojinin belirlenmesinde öykü ve rutin EEG'nin önemi vurgulanmıştır. Ülkemizde pediatrik nörologlara erişim ve kesin tanı süresinin literatüre göre daha kısa olduğu görülmüştür. Ayrıca çocuk doktorları ve aile hekimlerinin göz dalması atakları konusunda farkındalıklarının yüksek olduğu söylenebilir.

Anahtar Sözcükler: Çocuk, Epilepsi, Epileptik nöbetler, Göz dalması

INTRODUCTION

Staring spells frequently prompt referrals to pediatric neurology clinics, aiming to distinguish between epileptic seizures and non-epileptic paroxysmal events.

Staring spells typically manifest as inattention, unresponsiveness, and daydreaming. Similar symptoms can also manifest in individuals diagnosed with attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) (1,2). Staring spells might serve as the main symptom in individuals experiencing absence seizures, which comprise 10-17% of childhood-onset epilepsy (3).

Determining a diagnosis for a child experiencing staring spells can pose challenges since clinicians seldom witness these events directly. Instead, they rely on descriptions provided by the parent or the child regarding the occurrence (4). Identifying the underlying cause of these spells is vital for devising appropriate follow-up steps and implementing an effective treatment strategy.

Video-electroencephalography monitoring (VEEG) is the gold standard method for distinguishing between epileptic and non-epileptic causes of staring spells, as it provides the concurrent evaluation of both the clinical events and cerebral electrical activity (5). However, it is important to identify distinguishing factors between epileptic and non-epileptic staring spells due to the difficulty of accessing video EEG, the prolonged duration of recordings, and the higher cost involved.

This study aimed to review patients referred to a pediatric neurology outpatient clinic for staring spells and to identify the distinguishing features that would aid in the differentiation of non-epileptic from epileptic spells in clinics without video EEG monitoring units.

MATERIALS and METHODS

We included 73 patients who were diagnosed with staring spells in a tertiary-level pediatric neurology clinic between October 2022 and December 2023. The study focused on patients under 18 years old whose staring spells were captured during routine EEG monitoring. Patients with epilepsy diagnosis before the onset of staring spells, with incomplete data, and patients who did not take EEG results were excluded.

Various patient details were collected from 56 patients who met the inclusion criteria, including demographic data, clinical presentation, and staring spell features. The analysis of the staring spells involved evaluating their characteristics, such as duration, frequency, progression over time, response to stimuli, presence of automatisms, post-spell behaviors like crying or irritability, and postictal confusion. The 2017 International League Against Epilepsy (ILAE) guidelines were used to determine seizure types if applicable.

The patients were also examined for family history of epilepsy, psychiatric disorders, and staring spells, as well as relevant comorbidities like autism, attention deficit hyperactivity disorder (ADHD), developmental delays, and metabolic or organ dysfunction. The final diagnosis was established based on the clinical features observed and EEG changes during monitoring. A flowchart illustrating the study's methodology and patient selection process is provided in Figure 1. In addition, they were queried about who had referred the patients, reaching time to the pediatric neurology outpatient clinic, and the duration of reaching of final diagnosis.

Since the study was designed retrospectively, patient consent was not obtained, but ethical approval for the study was provided by the Ankara Etlik City Hospital Ethics Committee (AEŞH-EK1-2023-646). The study was conducted following the Declaration of Helsinki's ethical principles.

Statistical Analysis

All statistical analyzes were conducted using IBM Statistical Package for the Social Sciences, version 28.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). P values less than 0.050 were considered statistically significant. Descriptive statistics included mean and standard deviation for continuous variables and frequency and percentages for categorical variables. The data were analyzed for both epileptic and non-epileptic groups using Mann-Whitney U tests for continuous variables and chi-square or Fisher exact tests for categorical variables.

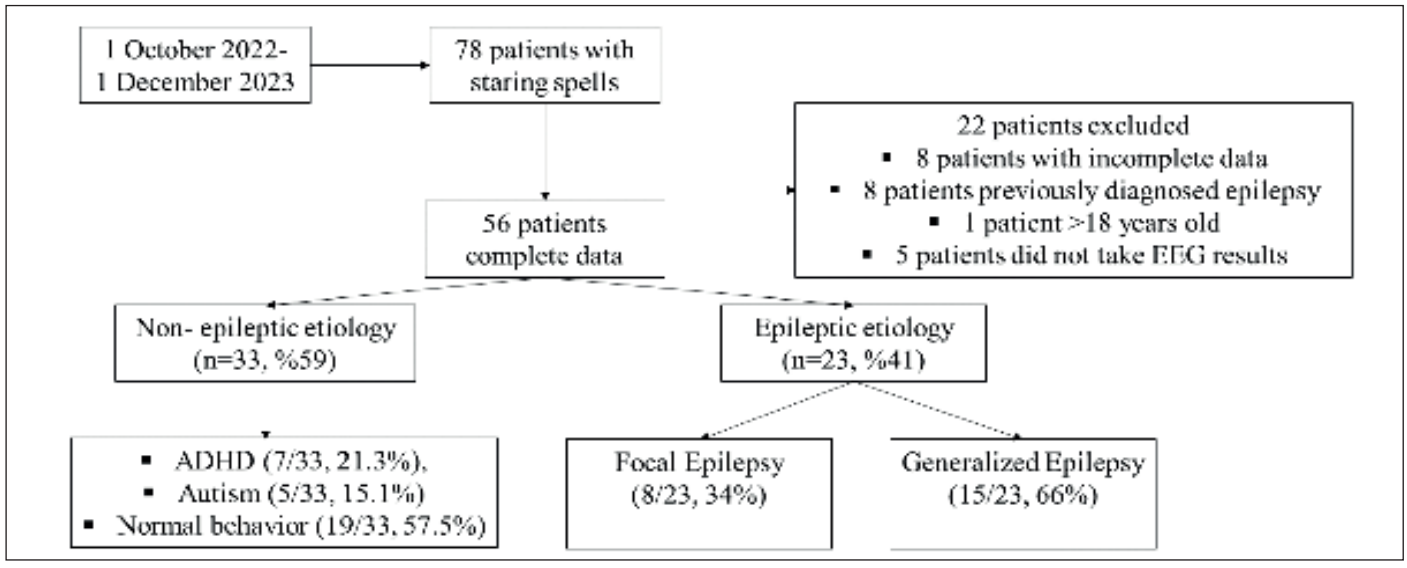

Figure 1: Shows the flowchart of study. **ADHD:** Attention deficit and hyperactivity disorder, **EEG:** Electroencephalography

RESULTS

In total, 56 patients were included in the study. The onset age of symptoms ranged from 24 to 142 months (82.10±24.9 months), with 53.7% of the patients (n=30) being male. Based on the etiology the patients were divided into two groups: epileptic (n=23, 41%) and non-epileptic (n=33, 59%) spell group. In all cohorts the most common comorbidity was detected as ADHD (n=7, 12.5%) and secondly ASD (n=6, 10.7%).

The average duration of spells was 95.2 seconds, with an average frequency of 8.4 per week. The presence of spells from onset was detected to be 14.25 ±7.83 weeks. Table I provides a summary of the entire cohort and the classification of patients based on their etiology as either epileptic or non-epileptic.

Table I: provides a summary of the entire cohort and the classification of patients based on their etiology as either epileptic or non-epileptic.

	All Cohort(n=56)	Epileptic (n= 23)	Non Epileptic (n= 33)	p
Demographic Datas				
Age (m)*	82.10±24.90 (24-142)	88.56±17.31 (65-132)	79.48±28.81 (24-142)	0.208‡
Gender (female)†	26 (46.5)	10 (43)	16 (48)	0.923§
Comorbidity†				
ADHD	7 (12.5)	-	7 (21.2)	
ASD	6 (10.7)	1 (3)	5 (15.1)	0.015§
ID	2 (3.5)	-	2 (6)	
Familial Epilepsy History†	4 (7.1)	2 (8)	2 (6)	0.547§
Familial Psychiatric Disorder History†	6 (10.7)	3 (13)	3 (9)	0.479§
Familial Staring Spell History†	3 (5.3)	1 (4)	2 (6)	0.635§
Staring Spells				
Duration (s)*	95.26±110 (10-600)	35.2±34.88 (10-120)	136.6±124.96(20-600)	<0.001‡
Frequency at onset (w)*	8.4±6.73 (1-30)	4.39±3.55 (1-15)	11.24±7.03 (2-30)	<0.001‡
Presence duration of staring spells (w)*	14.25±7.83 (3-35)	14.52±8.6 (3-35)	14.06±7.38 (4-34)	0.973‡
Increase in frequency†	17 (30.3)	16 (69.5)	1 (3)	<0.001§
Decrease in frequency†	17 (30.3)	-	17 (51.5)	<0.001§
Response to verbal stimulus†	28 (50)	-	28 (84.8)	<0.001§
Automatism†	12 (21.5)	9 (39.1)	3 (9)	<0.001§
Post-spell symptom† (crying/irritability/confusion)	6 (11)	6 (26)	-	<0.001§
Referral type†				
Other Families	3 (5.3)	2 (8)	1 (3)	
Internet	4 (7.1)	1 (4)	3 (9)	0.729§
Familiy Physician	9 (16)	4 (17.3)	5 (15)	
Pediatrician	35 (62.5)	16 (69.5)	24 (72)	
Access time to pediatric neurologist (d)*	5.53±3.23 (1-15)	4.39±3.38 (1-21)	4.63±3.17 (1-14)	0.662‡
Time until final diagnosis (d)	6.63±3.23 (2-16)	4.89±3.38 (2-24)	4.73±3.17 (2-15)	0.672‡

***:** mean±SD (Min-Max), **†:** n(%), **‡:** Mann Whitney U Test, **§:** Chi-square Test, ***ADHD:** Attention Deficit and Hyperactivity Disorder, **ASD:** Autism Spectrum Disorder, **ID:** Intellectual Disablity*

Table II: Displays the characteristics of the staring spells observed in these patients.

Epileptic Staring Spells n=23	Focal Epilepsy (n=8)	Generalized Epilepsy (n=15)	p
Duration (s)*	75 ± 31.16 (40-120)	14 ± 6.32 (10-30)	<0.001‡
Frequency at onset (w)*	4.35 ± 3.02 (1-10)	4.4 ± 4.67 (1-15)	0.767‡
Increase in frequency†	5 (62.5)	11 (73)	0.467§
Response to verbal stimulus	-	-	
Automatism†	5 (62.5)	4 (26.6)	0.110§
Post-spell symptom† (crying/irritability/confusion)	6 (75)	-	<0.001§
Presence of staring spells (w)*	18.37 ± 9.99 (7-35)	12.46 ± 8.05 (3-29)	0.137‡

*: *mean±SD (min-max),* †: *n(%)* ‡: Mann Whitney U Test, §: Chi-square Test

The final diagnoses for the non-epileptic group were ADHD (7/33, 21.2%), autism (5/33, 15.1%), and normal behavior (19/33, 57.5%). Generalized and focal epilepsy were diagnosed in 15/56 (26.7%) and 8/56 (14.2%) patients, respectively.

The leading non-epileptic diagnoses had longer spell durations, with a higher frequency averaging 136 seconds with 11.2 spells per week. Epileptic staring spell group patients had shorter spell durations (35.2 seconds) and less frequent spell episodes (4.4 per week). Longer spell durations (>120 seconds) were more prevalent among patients without an epilepsy diagnosis (p =0.001).

Response the verbal stimulation was more common in patients without an epilepsy diagnosis (p<0.001). Automatisms were observed in 12 patients and were detected higher prevalence in the epileptic group (9 out of 23; 39.1%) compared to the non-epileptic group (3 out of 33; 9%) (p<0.001). Additionally, post-spell symptoms were more commonly observed in the epileptic group (p<0.001).

The epileptic spell group was further divided into two subgroups based on EEG characteristics as generalized epilepsy group (n=15) and the focal epilepsy group (n=8). It is worth noting that all patients in the epilepsy group had EEG abnormalities (n=23). Table II displays the characteristics of the staring spells observed in these patients.

The study revealed a statistically significant difference in the duration of a spell between the focal and the generalized epilepsy group (75±31.16 vs 14±6.32, p=0.001). No response to verbal stimuli was detected in either group. There was no statistically significant difference between the groups in the frequency of spells at baseline, the increase in the frequency of spells at follow-up, or the presence of automatism (p=0.110). Postictal findings were more prevalent in the focal epilepsy group (p<0.001).

Upon questioning the units responsible for referring patients to the pediatric neurology department, it was observed that the majority of patients (62.5%) were referred by pediatricians, followed by family physicians (16%) (p<0.001). However, 8 out of 56 patients were referred by non-medical units. The mean access time to the pediatric neurology unit was 5.5 days and to reach the final diagnosis was calculated as 6.6 days.

DISCUSSION

Staring spells are one of the common paroxysmal non-epileptic events in children, often unrecognized by families (6). A definite diagnosis can be made with a VEEG recording of the spell. However, the availability of VEEG requires financial resources and is not always possible in non-specialized clinics (7).

In this study, we aimed to highlight the factors that may be crucial in distinguishing epileptic and non-epileptic causes in clinics without VEEG. To determine the etiology of newly emerging staring spells in our clinic, we routinely conduct a sleep and wakefulness EEG after a detailed evaluation of the patient's medical history and staring spell characteristics, including duration, frequency, automatisms, and post-spell symptoms. We ensure that the EEG results are normal or show specific interictal epileptiform findings.

Therefore, the development of more accessible diagnostic methods may aid in clarifying the etiology, preventing unnecessary fees for families and states, reducing the workload for physicians, and most importantly, identifying which patients may not require investigating.

The research illustrates that various underlying causes can manifest as staring spells, often resembling epileptic seizures. Among individuals experiencing newly occurring staring spells, 41% received a diagnosis of epileptic staring spells. Similar outcomes have been noted in prior studies, where rates have varied between 11% to 57%, indicating the diverse nature of conditions that can mimic or present similarly to epileptic staring spells (8,9).

The assessment of whether staring spells constitute epileptic seizures has focused on clinical factors. Patel et al. (9) devised a scoring system incorporating past EEG results, medication history, and the duration of the spell to determine which patients should undergo extended hospitalization for follow-up care. Among 276 admissions, only 29 patients (11%) received a diagnosis of seizures attributed to staring spells.

Our findings align with recent studies indicating that children experiencing nonepileptic staring spells were younger compared to those diagnosed with epileptic seizures. Additionally, individuals with nonepileptic staring spells were more prone to having neuropsychiatric comorbidities (8,10,11).

In the study conducted by Goenka et al. (12) staring spells were classified by age, and the most frequent diagnoses were summarized. The most common diagnoses for children aged 0-3 years were normal behavior and gratification response. However, diagnoses of epilepsy, attention deficit and hyperactivity disorder, and psychogenic non-epileptic seizures increased with age. Our study found that comorbidities, particularly attention deficit and hyperactivity disorder and autism spectrum disorder, were statistically more frequent in the non-epileptic group.

Additionally, the duration of spells was significantly lower in the epilepsy group compared to the non-epileptic group. Within the epilepsy group, focal seizures had a higher spell time than generalized seizures. Based on our analysis, we have concluded that the duration of spells lasting less than one minute are more significant in terms of generalized epileptic etiology while lasting more than two minutes are more significant in terms of non-epileptic etiology. These findings are consistent with those of Kim et al.(13). Furthermore, our study indicates a decrease in the frequency of non-epileptic etiology episodes over time, while the frequency of staring spells with epileptic etiology increased.

Another noteworthy finding is the lack of response to verbal stimulation in epileptic seizures, while 28 out of 33 (84.8%) non-epileptic seizures responded to verbal stimulation. This phenomenon has been observed in the literature across different age groups. In staring spells with epileptic etiology, there was no response to verbal stimulation. However, it was observed that 28 out of 33 attacks (84.8%) with non-epileptic etiology responded to verbal stimulation. This finding is consistent with similar observations in the literature across different age groups (12).

The epileptic group showed a statistically significant increase in the presence of automatisms and post-spell symptoms. Within the epileptic group, the focal epilepsy group had a higher incidence of these symptoms. However, it is important to note that although automatisms are more suggestive of an epileptic etiology, they may rarely accompany non-epileptic staring spells. The EEG showed a higher likelihood of abnormalities among children diagnosed with epilepsy. Among children experiencing focal seizures and displaying abnormal EEG results, the most frequent localization of epileptiform discharges was observed in the temporal lobe. Additionally, in all cases of absence seizures, EEG readings revealed 3-Hz generalized spike-and-wave discharges.

Our study revealed a new aspect, which is interesting for the literature. Although patients were generally referred by pediatricians or family physicians, a high rate of referrals from the internet and other families was observed. This suggests that while physicians are knowledgeable about staring spells, information from non-healthcare sources is also significant. It is worth noting that preschool teachers have also been reported to have a high awareness of this issue in the literature (14).

In comparison to the literature, our center has demonstrated a significantly shorter time to reach a pediatric neurologist and complete the diagnosis process. A recent article found that the mean time to reach a pediatric neurologist for children aged 0-17 years with staring spells was 0.7 years, which is much longer than our study.

In patients with staring spells, access time to initial neurological care appeared to be associated with race/ethnicity, insurance, and annual county per capita personal income. In our study, race/ethnicity, insurance, and annual county per capita personal income did not appear to be associated with access time to initial neurological care in patients with staring spells. These variables were among the reasons that significantly shortened the time for our patients, unlike in other centers (15).

In conclusion, the history, the semiology of spells, and routine EEG are important in the differential diagnosis of children presenting with staring spells. In addition, it has been observed that access time to pediatric neurologists and reaching time to final diagnosis are shorter in our country compared to the literature. With these results, it can be concluded that pediatricians and family physicians have a high awareness of staring spells.

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Hemogram Parameters of Children with Bell's Palsy at the Time of Admission and Their Findings in the Follow-up

Bell Paralizisi Tanılı Çocukların Başvuru Anında Hemogram Parametreleri ve İzlemdeki Bulguları

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ABSTRACT

Objective: The exact cause of idiopathic facial paralysis (Bell's palsy) is not clear. The objective of our study was to investigate the relationship between certain hemogram parameters and the clinical prognosis in pediatric patients with facial paralysis.

Material and Methods: The files of patients with Bell's palsy under the age of 18 who applied to our hospital were evaluated retrospectively. Leukocyte, neutrophil, lymphocyte, platelet count, red cell distribution width, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and monocyte to lymphocyte ratio were compared between patients with Bell's palsy and the control group. Information about their last health status recorded.

Results: A total of seventeen children with Bell's palsy and 17 control groups were included in the study. There were 7 boys (41.20%) and 10 girls (58.70%) in each group, the mean age was 11.80±4.40 (minimum 3.0-maximum 17.9) years. While the median neutrophil-lymphocyte ratio was 1.25 (0.41-7.63) in patients with Bell's palsy and 1.40 (0.42-2.52) in the control group, the median mean platelet volume level was 9.30 fL (8.20-12.30) in patients with Bell's palsy and 9.95 fL (9.30-11.70) in the control group, and the median red cell distribution width level was 12.75 % (11.50-26.30) in patients with Bell's palsy and 12.70% (12.10-26.30) in the control group. None of them were statistically significant. There were six patients with Bell's palsy with low mean platelet volume levels and no patients with low mean platelet volume levels in the control group (p=0.007). There was a positive correlation between the neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and monocyte-lymphocyte ratio and the recovery time of patients with Bell's palsy.

Conclusion: Bell's palsy may show a better prognosis in girls. High neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and monocyte-lymphocyte ratio may be indicators of delayed recovery, inflammation, and microvascular ischemia in Bell's palsy.

Key Words: Bell's palsy, Child, Blood Cell Count, Inflammation

ÖZ

Amaç: İdiopatik fasiyal paralizinin (Bell paralizisi) kesin sebebi belli değildir. Çalışmamızda fasiyal paralizi tanılı çocuk hastalarda, bazı hemogram parametreleri ile klinik prognoz arasında ilişki olup olmadığının araştırılması amaçlandı.

Gereç ve Yöntemler: Hastanemize başvuran 18 yaş altındaki Bell paralizi tanılı hasta dosyaları retrospektif değerlendirildi. Lökosit, nötrofil, lenfosit, trombosit sayısı, kırmızı hücre dağılım genişliği, nötrofil lenfosit oranı, trombosit lenfosit oranı ve monosit lenfosit oranı, Bell paralizili hastalar ile kontrol grubu arasında karşılaştırıldı. Son sağlık durumlarıyla ilgili bilgiler kaydedildi.

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Bulgular: Toplam on yedi Bell paralizi tanılı çocuk ve 17 kontrol grubu çalışmaya dahil edildi. Her bir grupta 7 erkek (%41.20), 10 kız (%58.70) vardı, yaş ortalaması 11.80±4.40 (minimum 3.00-maximum 17.90) yıldı. Bell paralizili hastalarda nötrofil lenfosit oranı medyanı 1.25 (0.41-7.63) iken kontrol grubunda nötrofil lenfosit oranı 1.40 (0.42-2.52), medyan ortalama trombosit hacim düzeyi Bell paralizili hastalarda 9.30 fL (8.20-12.30), kontrol grubunda 9.95 fL (9.30-11.70); medyan kırmızı hücre dağılım genişliği, Bell paralizili hastalarda 12.75 % (11.50-26.30) ve kontrol grubunda 12.70 % (12.10-26.30)'du. İstatistiksel olarak hiçbiri anlamlı değildi. Ortalama trombosit hacim düşüklüğü olan altı Bell paralizili hasta vardı, kontrol grubunda ortalama trombosit hacmi düşüklüğü olan kişi yoktu (p=0.007). Bell paralizili hastaların iyileşme süresi ile nötrofil lenfosit oranı, trombosit lenfosit oranı, monosit lenfosit oranı arasında pozitif korelasyon vardı.

Sonuç: Bell paralizisi kızlarda daha iyi prognoz gösterebilir. Nötrofil lenfosit oranı, trombosit lenfosit oranı ve monosit lenfosit oranı yüksekliği Bell paralizisinde iyileşmede gecikme, inflamasyon ve mikrovasküler iskeminin bir göstergesi olabilir.

Anahtar Sözcükler: Bell Paralizisi, Çocuk, Tam Kan Sayımı, İnflamasyon

INTRODUCTION

The facial nerve consists of motor and sensory fibers and runs through a long and narrow bony canal. For this reason, it is the cranial nerve whose function is most frequently impaired compared to other nerves. Central facial paralysis occurs with injuries to the facial nerve nucleus. Peripheral facial paralysis occurs after injuries to the facial nerve nucleus (1).

Facial nerve palsy can have many causes, such as congenital, idiopathic (Bell's palsy), infectious, trauma, metabolic causes, malignant diseases, neurological and autoimmune syndromes, and toxic conditions (1,2). Idiopathic facial paralysis (Bell's palsy) is the most common acute mononeuropathy (3). Bell's palsy (BP) is thought to develop as a result of vascular ischemia, autoimmunity, or viral inflammation of the neural sheath, a sudden temperature change after prolonged exposure to extreme cold or heat of the face, or reactivation of the Herpes virus. However, the exact cause is still unclear (1,3,4). BP is the most common cause of acute onset and unilateral facial paralysis in children (65-70%) (1,4,5). Bell's palsy is the most common cause of facial paralysis in our country (78-80%) (6). BP may be seen at any age. BP often resolves completely, but moderate-to-severe facial asymmetry may persist in approximately one-quarter of patients (4).

The diagnosis of facial paralysis is primarily made by anamnesis and physical examination. Laboratory tests and imaging methods are not routinely required in all cases (1). Systemic steroid use in treatment can reduce the risk of late sequelae such as autonomic disorders and contractures (5,7). Methods such as eye ointment, artificial tears, eye closure (corneal protection with a moisture-retaining eye shield at night), antiviral therapy in severe cases (intense pain, Herpes, or Zoster suspicion), and microsurgery in cases of residual facial weakness and incomplete healing can be used (5). A good physical examination and evaluation for etiology are important. It has been reported that when corticosteroid is started in the first three days, it is significant in terms of complete recovery and that hemogram parameters should be checked before starting the steroid (1).

Neutrophil-lymphocyte ratio (NLR) can give an idea about inflammation. The high neutrophil-to-lymphocyte ratio is associated with different malignancies, infectious diseases, metabolic syndrome, cardiovascular diseases, and other inflammatory diseases (8,9). It has been suggested in some studies that the neutrophil-lymphocyte ratio in peripheral blood may be a marker in determining the prognosis of facial paralysis (10, 11). Mean platelet volume (MPV) and red cell distribution width (RDW), platelet-lymphocyte ratio (PLR), and monocyte-lymphocyte ratio (MLR) are among the markers that can be used in general inflammatory and peripheral thrombotic diseases in the literature. Its relationship with BP has been investigated in some studies (2,3,12).

In our study, it was aimed to retrospectively examine the pediatric patients with Bell's paralysis who applied to our hospital within five years, to evaluate the results of the examination (hemogram parameters, imaging findings, if any), and to determine the relationship between the recovery time and the test results.

MATERIALS and METHODS

The study was approved by Erzincan Binali Yıldırım University Clinical Research Ethics Committee (decision no. 32/11 taken at session no. 32 on 16 October 2018). This study was conducted in accordance with the Declaration of Helsinki. The records of patients diagnosed with facial paralysis and Bell's palsy in our hospital between 2013 and 2018 were evaluated retrospectively and cross-sectionally.

Patients under the age of 18 with a diagnosis of Bell's palsy were included in the study. Patients who don't want to be examined, patients with a diagnosis of congenital facial paralysis, patients with an underlying neurological disease, patients with previous drug use, heart disease, kidney disease, etc., those with a diagnosis of acute or chronic disease, or those with a known history of systemic disease were not included in the study. Biochemistry, PT/APTT, hemograms, and other parameters, as well as the brain imaging reports of the patients included in the study, were recorded. Those with abnormal biochemistry, PT/APTT parameters, and abnormal brain imaging (bleeding, stroke, tumor, etc.) were excluded from the study. The phone number of the family of the patients who did not come for control recently was reached, and it was learned whether they had facial paralysis again, whether there were sequelae, and

in how many days the face shape improved. Brain imaging techniques and the results of the patients were recorded.

Examination values obtained for routine control purposes from pediatric patients of the same age and gender who did not have any disease in the records and who came to the general polyclinic for a healthy child examination were recorded in the system.

Laboratory reference ranges; WBC (leukocytes): 4-11x10^3 /L; Monocyte (%): 2-9; Neutrophil (%): 41-76; Lymphocyte (%): 25-50; Plt (platelet count): 150-450x10^3; MPV (mean platelet volume): 9-12 fL, Hb (Hemoglobin): 11.5-15 g/dL; Hematocrit (%): 34-45 RBC (erythrocyte): 4-5.3x1012/L: RDW (red cell distribution width): 11-14%; MCV (mean erythrocyte volume): 76-91 fL. The leukocyte, Hb, Htc, RBC, MCV, neutrophil, lymphocyte, and platelet counts, and RDW levels of the patients and control group were recorded. The lymphocyte-monocyte ratio (LMR) was calculated in the BP and control groups. It was statistically investigated whether there was a relationship between hemogram parameters and the clinical recovery process. According to MPV and RDW reference ranges, the mean or median value of NLR (1.40), MLR (0.19), LMO (5.80), and PLR (112.13) of the control group was considered normal and evaluated as high or normal.

Statistical analysis

While summarizing the data, categorical variables were presented as frequency and percentage and continuous variables as mean and standard deviation or median, minimum and maximum. The analysis of categorical variables was done by using the Fisher exact test. The conformity of the data to the normal distribution was tested with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used in the analysis of variables that did not fit the normal distribution. The independent samples t-test was used when testing the variables with a normal distribution. While determining the relationship between clinical recovery time and other variables, the Spearman correlation coefficient was used. For all statistical tests, a value of $p<0.050$ was considered statistically significant. IBM SPSS 20 (Armonk, NY: IBM Corp.) was used in the analysis of the data.

RESULTS

Seven males (41.20%) and 10 females (58.80%) totaled seventeen patients with BP, and 17 control groups of the same age and gender were included in the study. The mean age of the patients was 11.82±4.40 (minimum 3.0-maximum 17.9) years. The median clinical recovery time was 10 (3-90) days. The median clinical recovery time was 30 (10-90) days in boys and 7 (3-21) days in girls, and the clinical recovery time was longer in boys (p=0.032). The hemogram parameters (leukocyte count, platelet count, neutrophil-lymphocyte-monocyte percentage, RBC, Htc, Hb, MCV, RDW, MPV, NLR, MLR and PLR) of patients with Bell's palsy were similar to

Table I: Comparison of hemogram values of patients with Bell's palsy paralysis and the control group

	Control group	Patients with Bell's palsy	p
Leukocyte (10^9/L)*	7.10±1.47	8.47±3.16	0.125‡
RBC (10^{12}/L)*	5.14±0.52	5.06±0.40	0.606‡
Htc (%)*	41.80±4.30	41.86±3.63	0.961‡
Hb (gr/dl)*	13.90±1.46	14.15±1.34	0.610‡
MCV (fL)*	81.21±2.91	82.75±3.43	0.182‡
Plt (10^3/µl)*	296.18±59.46	304.81±85.92	0.744‡
Monocyte (%)*	7.74±1.85	7.22±1.55	0.719‡
Lymphocyte (%)*	39.41±9.29	40.46±11.54	0.778‡
Neutrophil (%)*	50.32±8.78	52.13±15.44	0.684‡
RDW (%)†	12.70 (12.1-26.3)	12.75 (11.5-26.3)	0.867§
MPV (fL)†	9.95 (9.3-11.7)	9.30 (8.2-12.3)	0.073§
MLR†	0.19 (0.07-0.31)	0.17 (0.10-0.66)	0.468§
LMR*	5.80±2.85	5.88±2.22	0.931‡
NLR†	1.40 (0.42-2.52)	1.25 (0.41-7.63)	0.669§
PLR*	112.13±37.22	128.23±86.03	0.484‡

*:mean±SD, †:*median (minimum-maximum)*, ‡: *Independent Samples T-test*, §:*Mann Whitney U Test*, ***RBC :*** *Red Blood Cell*, ***Htc:*** *Hematocrit;* ***Hb:*** *Hemoglobin*, ***MCV :*** *Mean Red Cell Volume*, ***Plt:*** *Platelet*, ***RDW:*** *Red Cell Distribution Width*, ***MPV:*** *Mean Platelet Volume*, ***MLR:*** *Monocyte to lymphocyte ratio*, ***LMR:*** *Lymphocyte-monocyte Ratio*, ***NLR:*** *Neutrophil-lymphocyte Ratio*, ***PLR:*** *Platelet-lymphocyte Ratio*

Table II. Comparison of inflammatory parameters of patients with Bell's palsy and control group

	Control group	Patients with Bell's palsy	p*	Correlation with clinical recovery time †
RDW				
Normal	15 (88.20)	13 (76.50)	0.656	r=0.204
High	2 (11.80)	4 (23.50)		p=0.598
MPV				
Normal	17 (100.00)	10 (58.80)	0.007	r= 0.140
Low	0 (0.00)	6 (41.20)		p=0.720
PLR				
Normal (<112.13)	9 (52.90)	8 (47.10)	1.000	r=0.897
High (>112.13)	8 (47.10)	9 (52.90)		p=0.001
MLR				
Normal (<0.19)	9 (52.90)	9 (52.90)	1.000	r=0.709
High (>0.19)	8 (47.10)	8 (47.10)		p=0.032
LMR				
Normal (>5.80)	6 (35.30)	6 (35.30)	1.000	r=-0.709
Low (<5.80)	11 (64.70)	11 (64.70)		p=0.032
NLR				
Normal (<1.40)	8 (47.10)	10 (58.80)	0.732	r=0.785
High (>1.40)	9 (52.90)	7 (41.20)		p=0.012

:** *Fisher's exact test*, †:*Spearman correlation*, ***RDW: *Red Cell Distribution Width;* ***MPV:*** *Mean Platelet Volume*, ***PLR:*** *Platelet-lymphocyte Ratio*, ***MLR:*** *Monocyte to lymphocyte ratio*, ***LMR:*** *Lymphocyte-monocyte Ratio,****NLR:*** *Neutrophil-lymphocyte Ratio*

those of the control group (Table I). There was a strong positive correlation between the number of days in which the face shape improved clinically and NLR (r=0.785, p=0.012), MLR (r=0.709, p=0.032), and PLR (r=0.897, p=0.001). In patients diagnosed with BP, the percentage of low MPV levels was higher than the percentage in the control group (p=0.007). The number of patients with elevated PLR and MLR in the patient and control groups was similar (Table II). Brain MRI alone was performed in 8 patients; only computerized brain tomography was performed in 4 patients, and both computerized brain tomography and brain MRI were performed in three patients, and imaging was not performed in two patients. Brain imaging was normal in all patients who underwent imaging. Oral steroid therapy, eye medications, and eye closure during sleep were initiated in all patients when they were applied.

DISCUSSION

Bell's palsy is idiopathic. The estimated incidence of Bell's palsy is 20-30:100.000 (13). Bell's palsy occurs with similar incidence in men and women. It has been reported that the prognosis of male patients with Bell's palsy is worse than that of female patients, and that progesterone in women accelerates peripheral nerve repair; therefore, peripheral nerve damage in women recovers faster than in men (5,11). Our number of male and female patients was similar. Our female patients healed in a shorter time, while the boys generally recovered later.

Whole blood analysis is an inexpensive assay that reflects the clinical condition of the patient. High neutrophil counts may be associated with inflammation, and a low lymphocyte count may be associated with increased stress (14). It has been reported that mean NLR and neutrophil values in adult and pediatric patients with BP are significantly higher than in healthy controls (2,3,10,11,15-17). Bucak et al. (10), in their study of 54 people in which they examined the relationship between NLR and progression in Bell's palsy, stated that NLR increased with the severity of inflammation and that NLR was higher in adult patients who did not respond to treatment. In the study of Wasano et al. (11) in 468 people, it was stated that NLR was higher in adult patients who did not respond to treatment. The severity of inflammation caused by viral infection has been associated with the prognosis of facial paralysis. In the study of Kum et al. (17), in which 656 patients were included, NLR was found to be higher in the Bell palsy group. Özler et al. (16) reported that NLR measurements in patients with BP correlated with the prognosis of the disease. There is no consensus in the literature about the correlation between NLR and the degree of disease (14). Some studies have reported that NLR is higher in BP, but NLR does not correlate with the severity of the disease (15,18). In our study, NLR was similar in the patient and control groups. There was a strong positive correlation between clinical recovery time and NLR.

Lymphocytes direct immune system activity. Some of the monocytes inhibit inflammation and immune reactions and promote damage repair (3). Yamamoto et al. (3) reported in their study that a low lymphocyte-monocyte ratio (LMR) is a negative prognostic marker in BP. In our study, MLR and LMR were similar in the patient and control groups. There was a strong positive correlation between clinical recovery time and MLR and a strong negative correlation between clinical recovery time and LMR. This may give an idea about tissue damage repair, inflammation severity, and recovery time.

Platelets play a major role in hemostasis and have important functions in inflammatory functions (19). In acute inflammatory conditions, platelet count increases due to some vasoactive peptides secreted in the vascular area (2). PLR has been reported as a poor prognosis marker in coronal vascular diseases, and hepatobiliary and gynecological malignancies (20). It has been suggested that circulatory disorders of the facial nerve resulting from inflammation, microcirculatory thromboembolism, and microvascular ischemia may play a role in the etiology of BP (2, 20). Therefore, the PLR level was measured to analyze the risk of thromboembolism in the microcirculation. It has been shown that there is a correlation between high PLR and BP, and it has been suggested that microvascular ischemia plays a role in BP (18, 20). Contrary to this view, many studies have reported that PLR does not increase BP (2,14,21). In our study, PLR was not found to be higher than the control group in our patients with BP. However, there was a positive correlation between clinical recovery time and PLR. This may be a finding that supports microvascular ischemia.

MPV is a parameter that shows the circulating platelet volume (14). It has been suggested that young platelets are larger in volume, but also more granular and have more adhesion molecules, which may predispose them to prothrombic events (2,22). Biochemical agents and cytokines emerging in inflammation may trigger the release of more young platelets into the circulation. Therefore, MPV may be elevated in microvascular thrombotic events (2,22). It has also been reported that MPV can be used as a negative acute phase reactant in chronic diseases (such as rheumatoid arthritis, and FMF) (23). MPV levels and BP has been investigated, but no correlation has been found (2,14, 17,21). It has been theorized that BP may be an inflammatory condition rather than a microvascular event (17). In our study, similar to the literature, MPV levels were similar in the BP and control groups. However, the number of patients with low MPV levels was high. Supporting the literature, it can be thought that MPV in BP may be a negative acute phase reactant and may be an indicator of inflammation.

Red blood cell distribution width (RDW) represents heterogeneity in the size and volume of circulating erythrocytes (24). RDW is an inflammatory biomarker increased in anemia, oxidative stress, microvascular thrombotic events, and inflammation (2,24). It has been suggested that RDW levels may also increase as a result of increased erythropoiesis due to inflammatory changes

(2,25,26). It has been reported that high RDW is associated with poor clinical outcomes in some diseases (2). Horibe et al. (26) showed that RDW was higher in Bell palsy patients who did not recover than in those who did. They suggested that RDW could be a useful prognostic biomarker for BP. However, in different studies, it has been reported that there is no significant increase in RDW levels in patients with BP (2,14,21). In our study, there was no significant increase in RDW levels in our patients diagnosed with BP compared to the control group. There was no correlation between recovery time and RDW.

The limitations of our study are that it is retrospective and the number of cases is small.

The strengths of our study are long-term follow-up and investigation of the relationship between admission hemogram parameters and recovery time.

CONCLUSION

In this study, there is a positive correlation between NLR, PLR, MLR, and clinical recovery day in pediatric patients with Bell's palsy. This supports the involvement of inflammation and microvascular ischemia in the etiology of Bell's palsy. Bell's palsy has a better prognosis in girls. Prospective studies with a high number of cases are needed.

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The Efficacy of Pre-Treatment Proton Pump Inhibitors in the Eradication of *Helicobacter pylori*

Helicobacter pylori Eradikasyonunda Tedavi Öncesi Proton Pompa İnhibitörlerinin Etkinliği

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ABSTRACT

Objective: Proton pump inhibitors significantly reduce *Helicobacter pylori* colonization and provide recovery in its activity and inflammation. We investigated; the effects of eradication initiated 28 days after proton pump inhibitor treatment and eradication initiated simultaneously with proton pump inhibitor treatment, on treatment success rates of *Helicobacter pylori*.

Material and Methods: The study took place at our tertiary care hospital, where 42 patients in the study group were given oral lansoprazole treatment for 28 days followed by eradication treatment and 41 patients in the control group were given both treatments simultaneously. Eradication success was monitored using *Helicobacter pylori* polyclonal antigen stool tests.

Results: A total of 83 participants, aged between 8 and 18 years, tested positive for *Helicobacter pylori*. The mean age of the participants was 15.14 ± 2.01 years. The *Helicobacter pylori* cure rate was found to be 92.9% in the study group and 92.7% in the control group. There were no significant differences observed between the two groups in terms of eradicating *Helicobacter pylori* (p=0.976).

Conclusion: We found no significant differences in *Helicobacter pylori* treatment success rates with modified proton pump inhibitor usage in children.

Key Words: Esophagogastroduodenoscopy, Helicobacter pylori, Proton pump inhibitors, Treatment

ÖZ

Amaç: Proton pompa inhibitörleri *Helicobacter pylori* kolonizasyonunu önemli ölçüde azaltarak aktivitesinde ve inflamasyonda azalma sağlar. Proton pompası inhibitörü tedavisinden 28 gün sonra başlatılan eradikasyonun ve proton pompası inhibitörü tedavisiyle eş zamanlı başlatılan eradikasyonun *Helicobacter pylori* tedavi başarı oranlarına etkisini araştırdık.

Gereç ve Yöntemler: Araştırma, üçüncü basamak tedavi merkezi olan hastanemizde gerçekleştirildi; burada çalışma grubundaki 42 hastaya 28 gün boyunca oral lansoprazol tedavisi ve ardından eradikasyon tedavisi verildi, kontrol grubundaki 41 hastaya ise her iki tedavi aynı anda verildi. Eradikasyon başarısı *Helicobacter pylori* poliklonal antijen dışkı testi kullanılarak değerlendirildi.

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Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. This research protocol was thoroughly examined and authorized by the Scientific Research Ethics Committee of Gülhane Training and Research Hospital, with approval number 2021-345 on September 23rd, 2021.

Contribution of the Authors / Yazarların katkısı*: *ÖZKEÇECİ CF: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***BALAMTEKİN N:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***ARSLAN M:*** Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***BAŞARAN EG:*** Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

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Bulgular: Çalışmamıza yaşları 8 ile 18 arasında değişen ve *Helicobacter pylori* pozitif olan toplam 83 katılımcı dahil edildi. Katılımcıların ortalama yaşı 15.14±2.01'di. Helicobacter pylori iyileşme oranı çalışma grubunda %92.9, kontrol grubunda ise %92.7 olarak bulundu. *Helicobacter pylori*'nin eradikasyonu açısından iki grup arasında anlamlı bir fark gözlenmedi (p=0.976).

Sonuç: Çocuklarda modifiye proton pompa inhibitörü kullanımı ile *Helicobacter pylori* tedavisi başarı oranlarında anlamlı bir fark bulunamadı.

Anahtar Sözcükler: Özofagogastroduodenoskopi, *Helicobakter pylori*, Proton pompa inhibitörleri, Tedavi

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a type of bacteria that has a spiral shape and is gram-negative and microaerophilic. It's prevalence varies depending on geographical location. It is found in more than 85% of people in areas with low socioeconomic status, and 30-40% of people in areas with high socioeconomic status (1). *H. pylori* is associated with gastrointestinal (GI) diseases, such as peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and adenocarcinoma, as well as other diseases like growth and developmental retardation, iron-refractory iron deficiency anemia, and idiopathic thrombocytopenic purpura (2).

Based on the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines, to diagnose *H. pylori* in children, a positive culture or the presence of *H. pylori* gastritis in a biopsy, as well as another positive test like a rapid urease test or polymerase chain reaction (PCR), is required (3).

The treatment for *H. pylori* typically involves proton pump inhibitors (PPIs), such as lansoprazole or esomeprazole, along with amoxicillin and clarithromycin, or PPIs, amoxicillin, and metronidazole (3). However, antibiotic resistance has become a problem, so new treatment protocols with different antibiotics have been developed for successful eradication (4,5). It is known that *H. pylori* has developed high resistance rates against conventional treatments in some populations, including Turkey (6-8). Therefore, the updated *H. pylori* guideline of ESPGHAN recommends using either a high dose of amoxicillin or the quadruple therapy protocol containing bismuth in health centers where antibiotic susceptibility tests are not available (3).

The mechanism behind the repression of *H. pylori* and the changes in gastric inflammation are not yet entirely clear. However, it is believed that changes in gastric pH caused by PPIs prevent *H. pylori* from growing and surviving (9). Acid suppression therapy performed with PPIs is known to change the anatomic distribution and strength of *H. pylori* in patients with gastritis (10). PPIs reduce the intensity of *H. pylori* in both the antrum and corpus, which can help to alleviate gastritis activity and chronic inflammation (11). PPIs affects the density and distribution of *H. pylori* (3,10). We still do not know if the timing of PPIs treatment has an impact on *H. pylori* eradication.

This study aims to investigate whether applying antibiotic treatment after 28 days of using PPIs increases or decreases treatment success in *H. pylori* eradication treatment.

MATERIALS and METHODS

Our study aimed to include pediatric patients between the ages of 8 and 18, who visited the pediatric gastroenterology outpatient clinic at Gülhane Research and Training Hospital between January 2022 and July 2022 and were diagnosed with *H. pylori* infection after undergoing upper GI endoscopy. Prior to the procedure, all patients and their parents signed an informed consent form. The reason for selecting children at or over the age of 8 was that the treatment protocol for those below the age of 8 differs based on treatment guidelines. The patients diagnosed with *H. pylori* are treated under the guidelines of the ESPGHAN (3).

An experienced pediatric gastroenterologist performed all upper gastrointestinal (GI) endoscopies using an Olympus® gastroscope that had an outer diameter of 9.2 mm. The endoscopies were conducted in the operating room while the patient was under deep sedation. Biopsy samples were obtained from the recommended sites during the procedure, following the guidelines provided by the ESPGHAN (3). A single pathologist analyzed the biopsy samples based on the Sydney System, which assesses chronic inflammation, activity, atrophy, intestinal metaplasia, and the presence or absence of *H. pylori* (12).

The study involved 83 patients who were diagnosed with *H. pylori* and tested positive for it using the polyclonal antigen stool test, rapid urease test, and biopsy materials. Patients with dyspeptic complaints underwent the polyclonal antigen stool test first, followed by the other two tests using biopsy materials obtained during endoscopy, to confirm the histopathological diagnosis of *H. pylori*. Once the diagnosis was confirmed, the planned treatments were initiated. All the patients attended their follow-up sessions regularly, and none of them were excluded from the study. The patients were assigned a number using a web-based computer system and included in the study according to the order they applied to the outpatient clinic for the evaluation of pathology results. Forty-two patients were assigned to the study group, where they were given lansoprazole (1 mg/kg/day) for four weeks. A 4-week pretreatment period was scheduled for the study group based on a previous adult study demonstrating the effectiveness of PPIs in improving elimination success (13). Bismuth base therapy was prescribed to all patients due to common amoxicillin and clarithromycin resistance. From the first day of the fifth week after the biopsy was performed, they were given tetracycline (25-50 mg/kg/

day), bismuth (<10 years of age: 4x262 mg, >10 years of age: 4x524 mg), and metronidazole (30 mg/kg/day) for two weeks. Forty-one patients were assigned to the control group (standard timing group), where they were given antibiotic eradication treatment by being given lansoprazole (1 mg/kg/day, orally), tetracycline (25-50 mg/kg/day), bismuth (<10 years of age: 4x262 mg, >10 years of age: 4x524 mg), and metronidazole (30 mg/kg/day) simultaneously for two weeks. Afterward, the treatment was completed. The eradication treatments were initiated at the doses mentioned in the ESPGHAN guideline (3). After eight weeks of cessation of eradication, the response to the *H. pylori* eradication treatment was evaluated using the *H. pylori* polyclonal antigen stool test, which is a non-invasive method recommended in the ESPGHAN guideline to assess the success of eradication. The patients were not given written information about possible drug side effects but were asked if they experienced any issues during their treatment that could lead to complaints.

This research protocol was thoroughly examined and authorized by the Scientific Research Ethics Committee of Gülhane Training and Research Hospital, with approval number 2021-345 on September 23rd, 2021. The research was conducted in compliance with the principles outlined in the Helsinki Declaration.

Statistical analysis

The data were processed and analyzed with the Statistical Package for the Social Sciences (SPSS) for Windows 21.0 package software. In the presentation of the descriptive statistics, frequency and percentages are used for the discrete variables, while mean ± standard deviation (SD) values are used for the continuous variables. Pearson's chi-squared (χ^2) test was used in comparing the discrete variables, while the Crosstabs procedure was used in comparing two different variables in the study and control groups. The correlation between the variables was evaluated with the Spearman's correlation coefficient. $p<0.050$ was acknowledged as statistically significant.

A power analysis was conducted to determine the necessary sample size for the study. The G*Power 3.1 program was used to calculate the statistical power of the test. Based on a similar study published by Janssen et al. (14), where the odds ratio of eradication rates was 0.201, and the actual α was 0.020. To achieve a statistical power of at least 80%, the study required a minimum of 70 participants, with 35 people in each group, at a significance level of 5%. Fortunately, we could include more participants than the minimum number required.

RESULTS

The study involved 83 patients aged between 8 to 18 years who had been diagnosed with *H. pylori* through histopathology (Figure 1). None of the patients had been admitted to the hospital before due to dyspepsia. Out of the 83 patients, 54 (65.1%) were female and 29 (34.9%) were male. Heartburn (74.7%), abdominal pain (67.5%), nausea (30.1%), eructation (8.4%), loss of appetite (6%), and bad breath (2.4%) were the most common symptoms that led to upper GI endoscopy. All patients had antral gastritis or pangastritis, but none of them had a peptic ulcer as confirmed by the endoscopy results (Table I). All patients were given *H. pylori* eradication treatment, and 92.8% of them (77 patients) were successfully treated (Table II). However, six patients who did not respond to the treatment still had the same complaints after it. The parents confirmed that all patients had taken their medications as prescribed, on time and in full. None of the patients developed any side effects from the treatment, and the treatment process was not terminated for any reason. The biopsy materials obtained

Table I: Upper gastrointestinal endoscopy results of the participants

Endoscopy result	Total*	Study group*	Control group*
Antral gastritis Antral gastritis + Esophagitis	35 (42.2) 1 (1.2)	12 (28.6)	24 (58.5)
Pangastritis Pangastritis + biliary reflux	42 (50.6) 5 (6)	30 (71.4)	17 (41.5)
Total	83	42	41

***:** *n(%)*

Table II: Efficacy of treatment modalities on cure rates

Treatment	Result*			p*
	Cure	Positive	Total	
Study group	39 (92.9)	3 (7.1)	42	0.976
Control group	38 (92.7)	3 (7.3)	41	
Total	77 (92.8)	6 (7.2)	83	

***** *Pearson's chi-squared (χ^2) test*

Table III: The correlation of the eradication results to the activity, colonization, and inflammation of *Helicobacter pylori*

	Result	
	Correlation	p*
H. pylori activity	0.054	0.627
H. pylori inflammation	0.088	0.429
H. pylori colonization	0.173	0.118

***Spearman's correlation*

Table IV: Results accompanying or not accompanying esophagitis, pangastritis, and biliary reflux

Endoscopy result	Cured Ones*	Positive*	χ^2	p
Antral Gastritis	32 (91.4)	3 (8.6)	0.116	0.734
Pangastritis	40 (95.2)	2 (4.8)	0.116	0.734
Antral gastritis + Esophagitis	1 (100)	0 (0)	0.079	0.779
Pangastritis + biliary reflux	4 (80)	1 (20)	1.294	0.255

***:** *n(%),* ***χ^2:** *Pearson's chi-squared test*

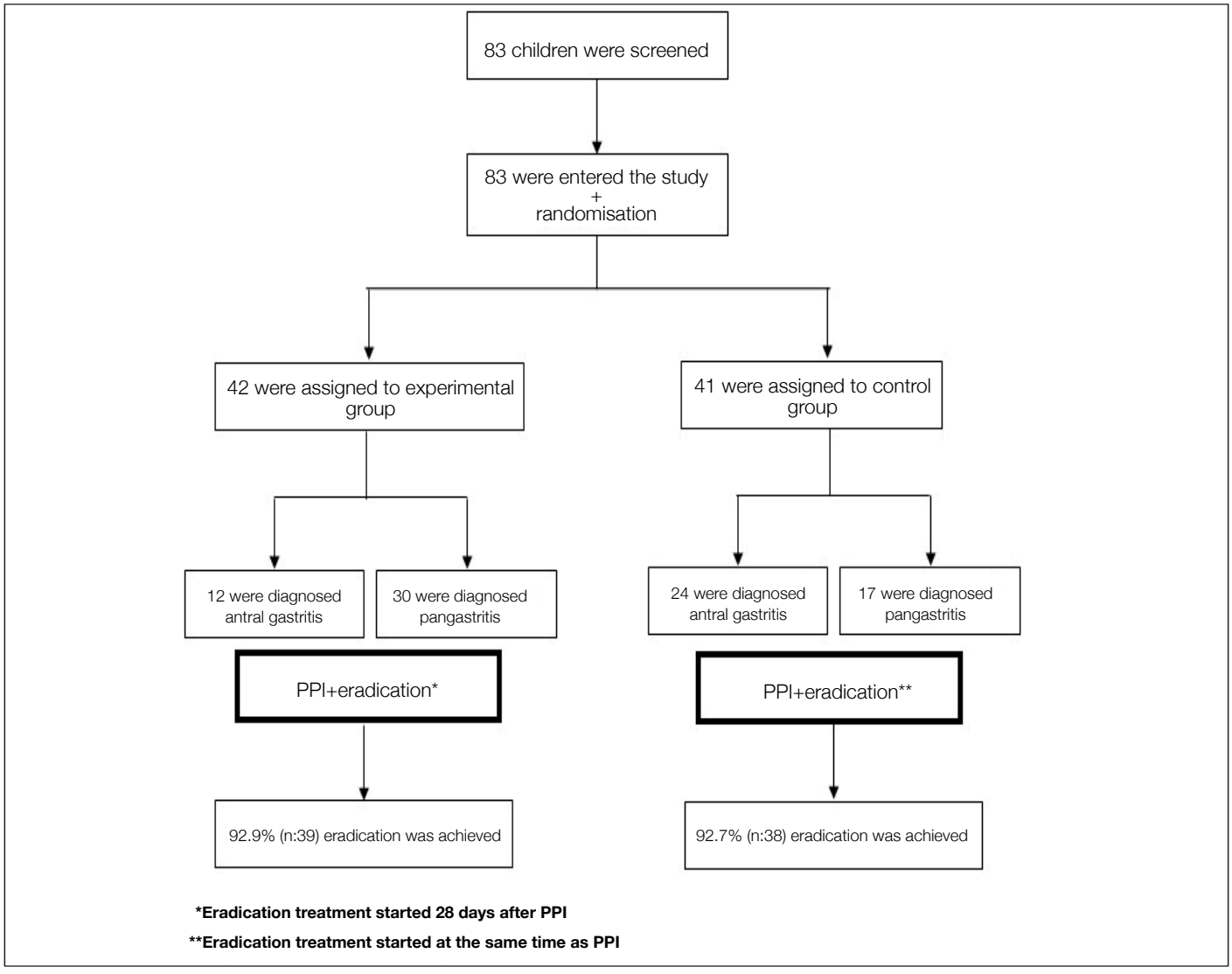

Figure 1: Determination of eradication ratio study group and control group.

during endoscopy were analyzed and evaluated based on the advanced Sydney System, and there was no statistically significant correlation between the activity, inflammation rate, and colonization intensity of *H. pylori* and the success of the eradication process (Table III). The success of eradication was not correlated with only antral gastritis or pangastritis, or the presence of esophagitis or biliary reflux along with antral gastritis or pangastritis (Table IV).

DISCUSSION

To successfully eradicate *H. pylori*, it is crucial to complete the treatment as prescribed and on time. Patients and their families should be informed about the potential side effects of the medications and educated about the treatment process. Extending the treatment plan from 7-10 days to 14 days could increase the likelihood of success (3,15). Additionally, other factors can affect the success of the treatment. In this study, we analyzed the success rates of eradication treatment for patients who tested positive for *H. pylori*. We compared the outcomes of patients who took lansoprazole at the same time as the treatment to those who took it after using lansoprazole for 28 days.

There have been various reasons reported for the failure of treatment for *H. pylori*. Some of these include the patient not following the treatment as instructed, resistance to antibiotics, and excessive bacterial load (3,16). However, it is unfortunate that antibiotic susceptibility tests are often expensive and not available in many health centers. At our institution, we use histopathological and rapid urease tests to check for positive results. Based on the test results, we diagnose the patient and recommend the same treatment as advised in the guideline (3).

PPIs are an essential component of every *H. pylori* eradication therapy, as they increase the success rate of the treatment by creating a suitable pH level for the antibiotics used to eradicate the bacteria. Although they have a weak eradication potential

on their own, PPIs contribute positively to the success of the treatment by creating a synergistic effect when used in combination with antibiotics (9). PPIs can be highly effective when taken at the right times, even in high doses when gastric acid levels are high, or when taken once every 12 hours instead of 24 hours (15). Jeong Gong et al. (10) have reported that PPIs treatment significantly reduces colonization in the antrum and leads to significant recovery in terms of *H. pylori* activity and inflammation. According to Labenz et al., (17) *H. pylori* cannot increase its colonization when gastric acid levels are low and is rendered susceptible to amoxicillin and clarithromycin with acid suppression, resulting in an increased treatment success rate. In contrast to previous studies that focused on the aftermath of the treatment, we examined the correlation between the activation, inflammation degree, and colonization intensity of *H. pylori* in the pre-treatment period and the eradication success results. Our findings indicate that there is no statistically significant correlation between these factors and the success of the treatment. In our pursuit to improve the success of *H. pylori* treatment, we examined changes in treatment outcomes by altering PPIs usage. Our findings showed that the treatment success rate was 92.7% (n=38) in the study group and 92.9% (n=39) in the control group. Therefore, we concluded that there was no statistically significant difference between the two treatment modalities (p=0.976). Similarly, a meta-analysis conducted by Kuang et al. (18) also found that pre-treatment use of PPIs did not impact the success of *H. pylori* eradication. Celebi et al.(19) reported that a lansoprazole-based regimen is more influenced by CYP2C19 in comparison to esomeprazole and rabeprazole. They found that esomeprazole had the highest success rate in achieving an intragastric pH value higher than 4 (19). In our study, we chosed to use lansoprazole for both the study and control groups due to easier access. We set the lansoprazole treatment as 1 mg/kg/day for both groups to avoid any variations. Therefore, we attribute the eradication success rate in our study to the antibiotherapy rather than lansoprazole. While PPIs can reduce *H pylori*'s density and quickly alleviate dyspeptic complaints in adult studies, we believe that altering the treatment time or increasing the dosage may not be significant in terms of eradicating the bacteria in children. None of our patients in the study group experienced an increase in complaints while taking lansoprazole. Complaints regressed in all patients in both study and control groups while taking lansoprazole.

Although Sydney scoring is an important method for evaluating inflammation severity, *H. pylori* colonization intensity, and atrophy presence through microscopic analysis, our study found that microscopic findings did not significantly affect the eradication rate (12). Szőke et al. (20) also found that biliary reflux did not intensify endoscopy results or lead to pre-malignant lesions in *H. pylori*-positive patients. Similarly, Agin et al. (21) reported that biliary reflux did not affect the presence or intensity of *H. pylori*. Our studies showed that biliary reflux, which occurs with antral gastritis or pangastritis, did not significantly impact *H. pylori* eradication treatment success. While we recognize that the compared scenarios are different, we observed that biliary reflux does not positively contribute to *H. pylori* intensity nor have a negative effect on *H. pylori* eradication.

It's important to note a few limitations in this study. Firstly, due to the way the biopsy samples were grouped as "antrum-corpus", it was not possible to make an anatomical comparison. Secondly, gender discrimination was not made due to the limited number of patients compared to adults. Lastly, all patients received bismuth-containing treatment as there was no detection of antibiotic resistance in our hospital.

Our research has revealed that administering PPIs either before or concurrently with antibiotics to pediatric patients aged 8-18 years may not have a significant impact on eradicating *H. pylori*, despite PPI's known influence on *H. pylori* colonization. These findings differ from those observed in adult patients. Further comprehensive research is necessary to gain a deeper understanding of this issue.

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Sleep Behavior of Children Born Preterm and Its Relationship with Parental Sleep Quality

Prematüre Çocukların Uyku Davranışları ve Ebeveyn Uyku Kalitesi ile İlişkisi

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ABSTRACT

Objective: We aimed to evaluate the sleep characteristics of children born preterm and the relationship between these characteristics and parental sleep quality.

Material and Methods: In this cross-sectional study, the parents of children born preterm were administered the Child Sleep Habits Questionnaire (CSHQ) and Pittsburgh Sleep Quality Index (PSQI).

Results: The study included 89 children born preterm with a current mean age of 38.7±55 months. According to the CSHQ, 95.5% of children had a sleep disorder. According to the PSQI, 48.9% of the mothers, 35.3% of the fathers had poor sleep quality. Maternal and paternal total PSQI scores were significantly correlated (r=0.373, p=0.030). In regression analysis of factors that may affect total CSHQ score, sleep disorder was found to be associated with low maternal education, hemiplegia, no smoking in the home (p=0.001, p<0.001and p<0.001 respectively). When factors that may affect total PSQI score were examined by regression analysis, the odds of poor sleep quality were 5.5 times higher in mothers with a high education level, 4 times higher in mothers with a history of multiple pregnancy (p=0.006 and p=0.027).

Conclusion: Our study revealed a high rate of sleep disorder in children with a history of preterm birth and high rates of poor sleep quality among their parents.

Key Words: Behaviors, Child, Parental, Premature, Sleep

ÖZ

Amaç: Prematüre doğan çocukların uyku özelliklerini ve bu özellikler ile ebeveyn uyku kalitesi arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu kesitsel çalışmada prematüre doğan çocukların ebeveynlerine Çocuk Uyku Alışkanlıkları Anketi (ÇUAA) ve Pittsburgh Uyku Kalitesi İndeksi (PUKİ) uygulandı.

Bulgular: Çalışmaya mevcut yaş ortalaması 38.7±55 ay olan preterm doğan 89 çocuk dahil edildi. ÇUAA'ya göre çocukların %95.5'inde uyku bozukluğu vardı. PUKİ'ye göre annelerin %48.9'u, babaların ise %35.3'ünün uyku kalitesi kötüydü. Anne ile babanın toplam PUKİ puanları arasında anlamlı korelasyon vardı (r=0.373, p=0.030). Toplam ÇUAA puanını etkileyebilecek faktörlerin regresyon analizinde uyku bozukluğunun anne eğitiminin düşük olması, hemipleji, evde sigara içilmemesi ile ilişkili olduğu belirlendi (sırasıyla p=0.001, p<0.001, p<0.001). Toplam PUKİ puanını etkileyebilecek faktörler regresyon analizi ile incelendiğinde, uyku kalitesinin kötü olma ihtimali eğitim düzeyi yüksek olan annelerde 5.5 kat, çoğul gebelik öyküsü olan annelerde 4 kat daha yüksekti (p=0.006 ve p=0.027).

Sonuç: Çalışmamız, preterm doğum öyküsü olan çocuklarda yüksek oranda uyku bozukluğu olduğunu ve ebeveynlerinde yüksek oranda uyku kalitesinin kötü olduğunu ortaya koydu.

Anahtar Sözcükler: Davranış, Çocuk, Ebeveyn, Prematüre, Uyku

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INTRODUCTION

Sleep problems are common in children, reported at rates of 20-30% (1). The prevalence of prematurity, defined as birth before 37 weeks of gestation, is reported to be approximately 10-12% (2,3). There are few studies and limited data on the sleep behaviors of children born preterm and their effects on the sleep quality of their parents (4-6). In this study, we aimed to evaluate the sleep behaviors of children with a history of prematurity and the relationship between these behaviors and their parents' sleep quality.

MATERIALS and METHODS

In this observational, cross-sectional study, the Children's Sleep Habits Questionnaire (CSHQ) and Pittsburgh Sleep Quality Index (PSQI) were administered between January and June 2023 to the parents of children with a history of preterm birth at Ali Kemal Belviranlı Maternity and Children's Hospital or Konya City Hospital (7-11).

The parents of children between 2 months and 18 years of age who were being followed up in the pediatric neurology outpatient clinic of Ali Kemal Belviranlı Maternity and Children's Hospital and Konya City Hospital for a history of prematurity were included in the study after providing written informed consent. Any children or parents unwilling to participate in the study were excluded.

Demographic and clinical data were collected from patient files, and sleep-related data were collected by administering a survey to the parents in the pediatric neurology outpatient clinic or sending the survey home to be completed and returned. Both parents of each child included in the study were asked to complete the sleep questionnaires. The response rate was 98.9% among the mothers (n=88) and 38.2% for the fathers (n=34).

Data Collection Tools

Children's Sleep Habits Questionnaire: The CSHQ was developed by Owens et al. (7) to investigate children's sleep behaviors and sleep-related problems. The scale consists of 8 subscales (sleep anxiety, bedtime resistance, delayed sleep onset, sleep duration, night awakenings, parasomnias, sleep-disordered breathing, and daytime sleepiness) with a total of 33 items. Parents complete the scale retrospectively based on their child's sleep habits over the previous week. Most items in the scale are coded by the frequency of the behavior as usually (3 = 5-7 times/week), sometimes (2 = 2-4 times/week), or rarely (1=0-1 times/week). Six items (1,2,3,10,11, and 26) are reverse coded and two items (32 and 33) are coded as 0 = not sleepy, 1 = very sleepy, and 2 = falls asleep. Total scores above the cut-off (41 points) are regarded as indicative of clinically significant sleep disorder. The CSHQ also includes 3 open-ended questions about the child's usual bedtime, total sleep time, and time spent awake at night (7). The CSHQ questionnaire has been demonstrated to be valid and reliable for children aged 2 months to 18 years (7-9). The Cronbach's alpha value of the CSHQ was reported as 0.78 (7,8).

Pittsburgh Sleep Quality Index: The PSQI is a self-report measure consisting of 7 subscales (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction) with 19 items. A total score higher than 5 indicates poor sleep quality and was shown to have a diagnostic sensitivity of 89.6% and specificity of 86.5% (10,11). The Cronbach's alpha value of the PSQI was reported as 0.83 (10).

In addition to these assessments, sociodemographic characteristics such as age, sex, parental consanguinity, presence of siblings, parental education level, family structure (nuclear/extended), daily media use, and clinical data such as gestational age at birth, physical examination findings, and neurological development were recorded on a patient information form.

For statistical comparison, children born at a gestational age of 34 to 37 weeks were grouped as late preterm, and those born before 34 weeks of gestation were grouped as early preterm (12-14).

The study received ethics committee approval from Karatay University (date: 30.12.2022, meeting no: 12, decision no: 2022/029).

Statistical Analysis:

The data were analyzed using IBM Statistical Package for the Social Sciences, version 23.0 (SPSS Inc., Armonk, NY, IBM Corp., USA) The Shapiro-Wilk and Kolmogorov-Smirnov tests were used as normal distribution tests. Mann-Whitney U test was used for pairwise comparisons of quantitative data that were not normally distributed. Chi-square test, Yates correction, and Fisher's exact test were used to compare categorical variables between the groups. Robust regression analysis was used to examine the variables affecting children's sleep scores, as the dependent variable did not show a normal distribution. Binary logistic regression analysis was used to examine risk factors associated with maternal and paternal sleep disturbance. Significance was accepted at $p<0.050$.

RESULTS

The study included 89 children (57.3% girls) with a mean age of 38.7±55 months. Their clinical features are summarized in Table I. The mean sleep durations were 9.8±2.6 hours for the children, 7.4±1.7 hours for mothers, and 7.5±1.2 hours for fathers, and 95.5% of the children had sleep disorder according to the CSHQ cut-off value. Most of the children went to sleep between 22:00 and 22:59 (41.6%) and woke up between 07:00

Table I: Demographic and Clinical Characteristics

Characteristic	
Parental consanguineity *	13 (14.6)
Parents are married*	83 (93.3)
Maternal education level (high school or lower)*	70 (78.7)
Paternal education level (high school or lower)*	73 (82.0)
Maternal employment status (working)*	10 (11.2)
Paternal employment status (working)*	85 (95.5)
Smoking in the home*	38 (42.7)
Nuclear family*	75 (84.3)
Early preterm*	63 (70.8)
Asphyxiation*	5 (5.6)
Multiple pregnancy*	16 (18.0)
In vitro fertilization*	8 (9)
Advanced maternal age at birth (>35)*	9 (10.1)
Prenatal problem*	40 (45)
Mode of delivery (cesarean section)*	76 (85.4)
Parent-child shared bedroom*	74 (83.1)
History of intrauterine growth restrictio*	7 (7.9)
Microcephaly*	8 (9)
Malnutrition*	8 (9)
Short stature*	6 (6.7)
Normal prognosis*	37 (41.6)
Developmental delay*	23 (25.8)
Gross motor delay*	18 (20.2)
Fine motor delay*	14 (15.7)
Cognitive delay*	6 (6.7)
Language-related delay*	16 (18)
Social or individual/self-care delay*	8 (9)
History of seizure*	8 (9)
History of jaundice*	39 (43.8)
Retinopathy of prematurity*	8 (9)
Patent ductus arteriosus*	1 (1.1)
Atrial septal defect*	2 (2.2)
Ventricular septal defect*	3 (3.4)
History of neonatal pneumonia*	31 (34.8)
Abnormality on brain MRI*	16 (18)
PVL on brain MRI*	8 (9)
EEG abnormality (focal)*	2 (2.2)
Concomitant psychopathology*	4 (4.5)
Presence of hemiplegia*	6 (6.7)
Epilepsy*	4 (4.5)
Length of stay in neonatal intensive care unit (days)†	21.5 ± 27.1
Breastfeeding duration (months) †	8.0 ± 6.9
Daily media usage (hours) †	1.6 ± 2.7

:** *n(%),* **†:** *mean±SD,* ***EEG: *Electroencephalography,* ***PVL:*** *Periventricular leukomalacia*

and 07:59 (40.4%). Based on the PSQI cut-off value (>5), sleep quality was poor in 48.9% of the mothers and 35.3% of the fathers. Compared to the late preterm group, children in the early preterm group had a higher rate of sleep disorder (98.4%) and rates of poor sleep quality were higher in their mothers (49.2%) and fathers (37%) according to total PSQI score. Both mothers and fathers most frequently went to sleep between 23:00 and 23:59 (36.4% and 32.4%, respectively) and woke up between 07:00 and 07:59 (33% and 38.2%, respectively). The children's sleep behaviors and their parents' sleep quality are summarized in Table II.

According to Spearman correlation analysis, total CSHQ score was not significantly correlated with the total PSQI scores of mothers or fathers, whereas a statistically significant correlation was observed between parents' total PSQI scores (r=0.373, p=0.033).

The regression analysis of factors that may be associated with the children's total CSHQ scores and maternal and paternal total PSQI scores included the sociodemographic and clinical characteristics shown in Table I. In robust regression analysis of factors affecting total CSHQ scores, the generated regression model was found to be statistically significant (F=2.992; p<0.001). The results of the model indicated that sleep scores were 3.8 points higher in girls than boys (p=0.004). Sleep scores were also associated with parental education, with scores 6.8 points higher for children with a maternal education level of high school or below compared to university or higher (p=0.001) and 5.5 points lower for children with a paternal education level of high school or below compared to university or higher (p=0.006). Total sleep scores were 5.8 points lower in the children of working mothers compared to not working mothers (p=0.004) and 6.3 points lower for those with smoking in the home compared to those without (p<0.001). Conception by in vitro fertilization (IVF) was associated with a 9.2-point decrease in total sleep score (p=0.002), whereas prenatal problems were associated with a 3.7-point increase in total sleep score (p=0.005). In terms of development, total sleep scores were 6.6 points lower in children with current short stature compared to those of normal height (p=0.009), 6.5 points lower in children with gross motor delays compared to those without (p=0.006), and 4.9 points higher in children with language-related delays compared to those without (p=0.034). The total sleep score of those with a history of neonatal pneumonia was 3.8 points higher than those with no history of neonatal pneumonia (p=0.010) and 12.9 points higher in children with hemiplegia than in those without hemiplegia (p<0.001). With the established model, independent variables explained 68.5% of the dependent variable. In particular, we observed a relationship between sleep disorder and low maternal education, hemiplegia, and no smoking in the home (Table III).

When the factors that may affect maternal PSQI total score were examined by univariate binary logistic regression analysis,

Table II: Characteristics of the Sleep Behaviors of Children and Sleep Quality of Parents

	Early Preterm*	Late Preterm*	Entire population*
Children's Sleep Habits (CSHQ)			
Duration of Night Wakings (min)	20.1±25.3	13.5±11.7	18.2±22.4
Total Sleep Time (hours)	9.6±2.5	10.1±2.8	9.8±2.6
Total CSHQ Sleep Score	50.6±5.1	50.1±6.7	50.5±5.6
CSHQ Subscale Scores			
Daytime Sleepiness	12.2±2.1	11.9±2.7	12.1±2.3
Sleep-Disordered Breathing	3.6±1	3.7±0.9	3.6±1
Parasomnias	8.9±1.6	9.1±2.1	8.9±1.8
Night Wakings	5.6±1.3	5.7±1.4	5.6±1.4
Sleep Anxiety	6.6±1.2	7.4±2.4	6.8±1.6
Sleep Duration	3.6±0.9	4.1±1.2	3.7±1
Sleep Onset Delay	1.6±0.6	1.4±0.6	1.6±0.6
Bedtime Resistance	9.6±2.7	11.2±3	10±2.9
Parental Sleep Quality (PSQI)			
Sleep onset delay (min)			
Mother	14.6±17.3	26.2±29.8	17.9±22
Father	17.2±15.4	12.1±8.6	16.2±14.3
Nighttime sleep duration (h)			
Mother	7.5±1.7	7.2±2	7.4±1.7
Father	7.5±1.3	7.4±0.7	7.5±1.2
Total PSQI score			
Mother	5±2.6	6.1±4.1	5.3±3.1
Father	4±2	3.1±1.8	3.8±2
PSQI Subscale Scores			
Subjective Sleep Quality			
Mother	0.9±0.7	1.2±0.9	1±0.8
Father	0.9±0.5	0.9±0.7	0.9±0.6
Sleep Delay			
Mother	0.9±0.8	1.2±0.9	1±0.9
Father	0.7±0.9	0.3±0.8	0.7±0.9
Sleep Duration			
Mother	0.8±0.9	0.9±1.2	0.9±1
Father	0.3±0.6	0.1±0.4	0.3±0.5
Habitual Sleep Efficiency			
Mother	0.3±0.8	0.8±1.3	0.5±1
Father	0.2±0.4	0±0	0.1±0.3
Sleep Disturbances			
Mother	1.3±0.6	1.2±0.7	1.3±0.6
Father	1.1±0.3	1.1±0.7	1.1±0.4
Use of Sleep Medication			
Mother	0.1±0.3	0±0	0.1±0.3
Father	0±0	0±0	0±0
Daytime Dysfunction			
Mother	0.5±0.6	0.7±0.9	0.5±0.7
Father	0.7±0.9	0.7±1	0.7±0.9

***:** *mean±SD*

we determined the odds of poor sleep quality were 5.5 times (1/0.182) higher in mothers with high education level (university or higher) than in mothers with low education level (high school or lower) (p=0.006). In addition, mothers with multiple pregnancy had a 4-fold higher risk of poor sleep quality than those without (p=0.027) (Table III).

When factors that may affect paternal PSQI total score were examined by univariate binary logistic regression analysis, none of the possible risk factors were found to be significantly associated with sleep quality.

DISCUSSION

In our study, 95.5% of the children had poor sleep habits according to the CSHQ. According to the PSQI, 48.9% of the mothers and 35.3% of the fathers had poor sleep quality. Regression analysis of factors that may affect total CSHQ score showed that sleep disorder was found to be associated with low maternal education, hemiplegia, and no smoking in the home. Regression analysis of factors that may affect total PSQI score showed that the odds of poor sleep quality were 5.5 times higher in mothers with a high education level and 4

Table III: Regression analysis results of factors associated with CSHQ (Robust regression) and PSQI (Logistic regression) Scores

Variables	Estimate	SE	p	95% CI	
				Lower	Upper
Children's CSHQ Total Sleep Score					
Sex *	3.778	1.269	0.004	1.231	6.326
Maternal education level†	6.827	2.009	0.001	2.794	10.859
Paternal education level†	-5.508	1.921	0.006	-9.364	-1.653
Maternal employment status ‡	-5.770	1.929	0.004	-9.642	-1.897
Smoking in the home §	-6.265	1.571	<0.001	-9.419	-3.111
Conception by in vitro fertilization§	-9.213	2.741	0.002	-14.716	-3.710
Prenatal problem§	3.661	1.232	0.005	1.188	6.135
Current height‖	-6.566	2.422	0.009	-11.429	-1.703
Gross motor delay§	-6.531	2.270	0.006	-11.088	-1.974
Language-related delay §	4.876	2.241	0.034	0.377	9.375
History of neonatal pneumonia§	3.832	1.435	0.010	0.952	6.713
Presence of hemiplegia§	12.748	3.339	<0.001	6.044	19.452
Maternal PSQI Total Sleep Quality Score					
Maternal education level†	0.182	0.614	0.006	0.055	0.606
Multiple pregnancy§	3.968	0.624	0.027	1.167	13.493

0= Female 1= Male, †0 = high school or below, 1 = university or higher, ‡0= working 1= not working, §0=yes 1=no, ‖0= short or long 1= normal* ***Estimate:* *β1 values for Robust regression and OR values for Logistic regression,* ***CSHQ:*** *Children's Sleep Habits Questionnaire,* ***PSQI:*** *Pittsburgh Sleep Quality Index,* ***SE:*** *Standart Error,* ***CI:*** *Confidence interval*

times higher in mothers with a history of multiple pregnancy. Our study revealed a high rate of poor sleep habits in children with a history of preterm birth and a high rate of poor sleep quality in their parents.

Developments in neonatal intensive care have led to an increase in the proportion of surviving preterm infants, the number of which is steadily increasing according to the World Health Organization (15). In our sample, approximately 70% of the children were early preterm, 41.6% had a normal prognosis, gross motor delay was the most common type of developmental delay (20.2%), and 6.7% developed hemiplegia. The most common cardiac pathology was ventricular septal defect (3.4%), while the rates of patent ductus arteriosus (PDA), retinopathy of prematurity (ROP), and epilepsy were 1.1%, 9%, and 4.5%, respectively. Although the prevalence of PDA is reported to be over 50% in preterm infants ≤28 weeks gestational age, this rate was 1.1% in our sample of mostly early preterm infants at a mean age of approximately 3 years, suggesting that PDAs close by 3 years of age (16). Furthermore, compared to a reported ROP rate of 27% in a study to 115 preterm infants, a lower proportion of patients in our study had ROP (9%), suggesting improved in the neonatal unit (17). Based on a study reporting the incidence of epilepsy as 102 per 100 000 in children up to 12 months of age, 50 per 100 000 in childhood, and 20 per 100 000 in adolescence, the 4.5% rate of epilepsy in our study supports existing evidence that epilepsy is more common in preterm children (18,19). Our findings of hemiplegia in 6.7%, developmental delay (most commonly gross motor delay) in 25.8%, and cognitive delay in 6.7% of the children in our study are also consistent with literature data indicating increased cerebral palsy and cognitive delay in preterm children (20-26).

In general, this study found a sleep disorder in 95.5% of a sample of preterm children at a mean age of approximately 3 years, 57% of whom were girls. According to the literature which reports sleep disorders in 20-30% of children, sleep disorder is significantly more common in preterm children, especially in those born early preterm (98.4%) (1). In addition, although parental sleep quality did not correlate with child sleep disorder, the parental sleep quality scores were correlated with each other. Moreover the rates of poor sleep quality were higher in the mothers (48.9%) and fathers (35.3%) of early preterm children. Finally, significant factors associated with sleep disorder in children born preterm were low maternal education, hemiplegia, and no smoking in the home, whereas high education level and history of multiple pregnancy were factors associated with poor maternal sleep quality.

The preterm children in our study had sleep and wake times consistent with those in the literature, but their mean CSHQ total sleep score of 50.5±5.6 was high compared with other studies evaluating the sleep characteristics of preterm children using the CSHQ (4-6, 27). When the CSHQ scores in our study were compared with those in previous studies, the scores for bedtime resistance, sleep anxiety, parasomnias, and daytime sleepiness scores were lower; the scores for sleep onset delay and sleep duration were similar, and the scores for nocturnal awakenings and sleep-disordered breathing scores were higher than those in the literature (6, 27). Accordingly, our study emphasizes that overall sleep disorders may be more common in preterm children and that higher CSHQ scores may be associated with more frequent nighttime awakenings and sleep-disordered breathing. Compared with previous studies in which sleep disturbances were reported in 20-60% of children and 71-89% of preterm children, the higher percentage of

sleep disorder (95.5%) in our study may be related to the small sample size (1,6,27,28).

The mean sleep duration of the preterm children in our study was 9.8±2.6 hours, which is shorter than the mean sleep duration reported in the literature for both term and preterm children (5).

In the literature, gastroesophageal reflux, vomiting, loud snoring, difficulty breathing, sleeping in the parents' room, maternal smoking, gestational age at birth, and number of siblings are the main clinical conditions identified as associated with sleep disorder in children according to the CSHQ (6). When we evaluated the effects of the clinical conditions in Table I on sleep disorder according to the CSHQ by regression analysis, we found a relationship between sleep disorder and low maternal education, presence of hemiplegia, and the absence of smoking in the home. Although there are not many studies in the literature examining factors associated with sleep disorders in preterm infants, we believe that maternal education and early detection and intervention of hemiplegia are important in terms of preventing sleep disorders in children born preterm. However, because the relationship between sleep problems and low maternal education, the presence of hemiplegia, and no smoking in the home may be related to our small sample size, studies in larger populations are needed to further clarify these relationships.

In our study, the mean nighttime sleep duration was 7.4±1.7 hours for mothers and 7.5±1.2 hours for fathers, which is longer than the 6.4±1.7 hours reported in the literature for the mothers of children born preterm (4). When the sleep quality of the parents was evaluated according to the PSQI cut-off point, poor sleep quality was detected in 48.9% of the mothers and 35.3% of the fathers, with higher rates in the early preterm group (49.2% and 37%, respectively) compared to the late preterm group. The total PSQI score was 5.3±3.1 for mothers and 3.8±2 for fathers, indicating better sleep quality compared with literature data reporting a total PSQI score of 7.9±3.6 for mothers of children born preterm. Parents in our study most frequently reported falling asleep between 23:00 and 23:59 (36.4% of mothers, 32.4% of fathers) and waking up between 07:00 and 07:59 (33% of mothers, 38.2% of fathers). These findings are consistent with reports in the literature that mothers go to sleep at 23:28 and wake up on average at 07:20 (4, 29).

When the sleep quality subscale scores of the parents of children born preterm were compared with the literature, we noted that mothers had lower subjective sleep quality, sleep delay, sleep duration, habitual sleep efficiency, use of sleep medication, and daytime dysfunction scores and higher sleep disturbance scores than in the literature, whereas fathers had lower scores on all subscales than in the literature (5).

Accordingly, although the rate of poor sleep quality was generally high among mothers and fathers of children born preterm in our study, compared to the PSQI total and subscale scores reported in the literature for the mothers of preterm children, our sample had better parental sleep quality, but sleep disturbances were more common among the mothers in our study than in the literature (4). Correlation analysis in our study revealed a significant relationship between maternal and paternal PSQI total scores (r=0.373, p=0.033), indicating that the sleep quality of mothers and fathers is correlated.

The results of our univariate binary logistic regression analysis showed that the odds of poor sleep quality according to the maternal PSQI total sleep quality score was 5.5 times higher in mothers with a university education or higher compared to those with a high school education or lower (p=0.006) and 4 times higher in mothers with multiple pregnancies compared to those without (p=0.027) (Table III).

Little is known about the sleep of mothers and fathers of preterm infants, because there are not many studies on this subject in the literature. The mothers and fathers of preterm infants in our study had sleep and wake schedules consistent with the literature, but our study provides novel findings in terms of the correlation in the sleep quality of mothers and fathers, the higher sleep disturbance scores in the mothers of preterm children, and the association between multiple pregnancy and high maternal education level and increased risk of poor maternal sleep quality.

Our study had a cross-sectional design and evaluated the 3-year clinical history, current sleep behavior, and parental sleep status of children born preterm, an area in which data are scarce in the available literature. However, the small number of participants and the absence of control group are limitations of our study. Nevertheless, we believe that determining sleep behaviors, characteristics, and quality in preterm children and their parents is important in defining and resolving sleep-related health problems in this growing population.

CONCLUSION

Our study revealed a high rate of sleep disorder in children with a history of preterm birth (especially early preterm) and a high rate of poor sleep quality in their parents. These findings highlight the relationship between preterm birth and children's and parents' sleep and demonstrate the need for more comprehensive studies in this area.

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Educational Needs of Pediatric Surgery Residents

Çocuk Cerrahisi Araştırma Görevlilerinin Eğitim İhtiyacı

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ABSTRACT

Objective: Surgical education and training play a critical role for surgeons to develop their professional skills and provide the best care to their patients. A survey was conducted to determine the education needs of surgery residents, especially in specialized fields such as pediatric surgery. The aim of this study was to determine the educational needs of pediatric surgery residents and to contribute to the development of educational programs for these needs.

Material and Methods: The study was conducted with a questionnaire designed to determine the demographic data and educational needs of pediatric surgery residents working in city hospitals in Ankara. The questionnaire questions covered topics such as surgical decision making, communication, leadership, professionalism, surgical ethics, surgical simulation, scientific research and patient management.

Results: Residents were 39% female who participated in the questionnaire and their graduation included Ankara, Istanbul and Izmir. The most needed areas of education among residents were identified as scientific research (87%), surgical simulation (74%) and leadership (43%). Other important needs included surgical decision making, communication, professionalism and surgical ethics.

Conclusion: Increasing surgical simulation and scientific research training in surgical training programs will play an important role in improving the professional competencies of research assistants and the quality of patient care. Future studies may evaluate the generalizability of these findings with larger samples. In conclusion, more targeted and comprehensive approaches should be adopted in pediatric surgery education.

Key Words: Clinical Skills, Decision making, Postgraduate education

ÖZ

Amaç: Cerrahi eğitim, hekimlerin mesleki becerilerini geliştirmeleri ve hastalarına en iyi bakımı sunabilmeleri için kritik bir rol oynamaktadır. Özellikle çocuk cerrahisi gibi özelleşmiş alanlarda, araştırma görevlisi hekimlerin eğitim ihtiyaçlarını belirlemek amacıyla bir anket çalışması yapılmıştır. Bu çalışmanın amacı, çocuk cerrahisi araştırma görevlilerinin eğitim ihtiyaçlarını belirlemek ve bu ihtiyaçlara yönelik eğitim programlarının geliştirilmesine katkı sağlamaktır.

Gereç ve Yöntemler: Çalışma, Ankara'da bulunan şehir hastanelerinde görev yapan çocuk cerrahisi araştırma görevlisi olan 23 katılımcının demografik verileri ve eğitim ihtiyaçlarını belirlemek üzere tasarlanmış bir anket ile gerçekleştirilmiştir. Anket soruları, cerrahi karar verme, iletişim, liderlik, profesyonellik, cerrahi etik, cerrahi simülasyon, bilimsel araştırma ve hasta yönetimi gibi konuları kapsamaktadır.

Bulgular: Ankete katılanların %39'u kadındı ve mezun oldukları üniversiteler arasında Ankara, İstanbul ve İzmir yer almaktadır. Araştırma görevlileri arasında en çok ihtiyaç duyulan eğitim alanları bilimsel araştırma (%87), cerrahi simülasyon (%74) ve liderlik (%43) olarak belirlenmiştir. Diğer önemli ihtiyaçlar arasında cerrahi karar verme, iletişim, profesyonellik ve cerrahi etik yer almaktadır.

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Sonuç: Çalışma ile cerrahi eğitim programlarında yer alan cerrahi simülasyon ve bilimsel araştırma eğitimlerinin artırılması, araştırma görevlilerinin mesleki yetkinliklerini ve hasta bakım kalitesini artırmada önemli bir rol oynayacaktır. Gelecekteki araştırmalar, daha geniş örneklemlerle bu bulguların genellenebilirliğini değerlendirebilir. Sonuç olarak, çocuk cerrahisi eğitiminde daha hedeflenmiş ve kapsamlı yaklaşımlar benimsenmelidir.

Anahtar Sözcükler: Klinik beceriler, Karar verme, Mezuniyet sonrası eğitim

INTRODUCTION

Surgical training is crucial for surgeons to develop their professional skills and provide the best care to their patients (1). In a specialized field such as pediatric surgery, the education that resident surgeons will receive should include both basic principles and practical skills (2). However, there is controversy about the extent to which current educational programs meet the needs of resident surgeons.

Research on the limitations of surgical education and what needs to be improved reveals that resident surgeons encounter various difficulties during their residency (3-4). These difficulties include surgical decision-making, effective communication, leadership skills, professionalism, surgical ethics, simulation-based training, patient management and scientific writing (3-7).

This study aimed to present the results of a questionnaire designed to better understand the educational needs of pediatric surgery residents. The questionnaire questions included topics such as surgical decision making, communication, leadership, professionalism, surgical ethics, surgical simulation, scientific writing and patient management. The results will provide important information for reshaping surgical educational programs and improving the technical and non-technical skills of resident surgeons.

MATERIALS and METHODS

This study is a cross-sectional study to describe the educational needs of pediatric surgery residents. Pediatric surgery residents in city hospitals in Ankara participated in the study. There are a total of 38 resident surgeons working in city hospitals. Of these, 23 participated in the study. The selection of participants was based on volunteerism.

Data were collected through a designed questionnaire. The questionnaire included two sections to determine the demographic information and educational needs of the participants. In the demographic section, the participants were asked questions such as gender, age, university of graduation, year of graduation, duration of general practitioner experience and year of residency. The educational needs section included questions on topics such as surgical decision making, communication, leadership, professionalism, surgical ethics, surgical simulation, scientific writing and patient management, and finally the other section.

The questionnaire was prepared electronically and sent to the participants via e-mail. Participants were given two weeks to complete the questionnaire and reminders were sent during this period. It took approximately 4 minutes to complete the questionnaire.

The collected data were analyzed using IBM Statistical Package for the Social Sciences, version 25.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). While demographic data were analyzed with frequency and percentage distributions, mean and standard deviation were calculated for the analysis of questions related to training needs. In addition, chi-square test was used to compare the educational needs between different demographic groups.

RESULTS

The questionnaire was sent to 30 people and 23 answered the questionnaire. Nine of the participants (39%) were female. Among the medical faculties from which the participants graduated, 11 (48%) graduated from medical faculties located in Ankara, Istanbul and Izmir. They worked as general practitioners for an average of 1.2 years before becoming residents.

Participants' responses regarding their educational needs:

- Surgical Decision Making: 9 participants (39%)
- Communication: 8 participants (35%)
- Team Work: 4 participants (17%)
- Leadership: 10 participants (43%)
- Professionalism: 7 participants (30%)
- Surgical Ethics: 8 participants (35%)
- Surgical Simulation: 17 participants (74%)
- Patient Management: 7 participants (30%)
- Scientific Research: 20 participants (87%)

According to the questionnaire results, scientific research (87%), surgical simulation (74%) and leadership (43%) were identified as the most needed training areas for pediatric surgery residents. These results indicate that pediatric surgery training programs should be improved in these areas.

The distribution of educational needs according to the year of residency is shown in Table I. The need for teamwork training was found to be significantly higher among third year residents (p=0.021). There was no significant difference in other educational needs according to the year of residency. However, the need for scientific research and surgical simulation training was highly expressed by resident surgeons of all years.

The distribution of training needs according to gender is shown in Table II. It was found that female residents felt a higher

Table I: Educational needs by resident year

	1st year (n=2)	2nd year (n=9)	3rd year (n=4)	4th year (n=3)	5th year (n=5)	p
Surgical Decision Making	2	3	2	1	1	>0.205
Communication	2	4	0	1	1	>0.105
Teamwork	0	1	3	0	0	0.021
Leadership	2	4	2	1	1	>0.119
Professionalism	2	3	0	1	1	>0.179
Surgical Ethics	1	5	0	1	1	>0.194
Surgical Simulation	2	5	2	3	4	>0.725
Patient Management	0	5	0	1	1	>0.201
Scientific Research	2	7	4	2	5	>0.492
Other	-	-	-	-	-	-

Table II: Educational needs by gender

	Female	Male	p
Surgical Decision Making	8	1	<0.001
Communication	6	2	0.010
Teamwork	3	1	>0.050
Leadership	8	2	<0.001
Professionalism	6	1	0.002
Surgical Ethics	5	3	>0.110
Surgical Simulation	7	10	>0.565
Patient Management	4	3	>0.239
Scientific Research	8	12	>0.668
Other	-	-	-

need for educational needs than male residents in areas such as surgical decision making, communication, leadership and professionalism. On the other hand, no significant difference was found between genders in areas such as teamwork, surgical ethics, surgical simulation, patient management and scientific research. Especially surgical simulation and scientific research education are highly important for both genders.

These findings suggest that the educational needs of pediatric surgery residents should be addressed comprehensively. Particularly, the development of basic principles, technical and non-technical skills such as scientific research and surgical simulation will play a critical role in improving the professional competence of resident surgeons.

DISCUSSION

This study was conducted to determine the educational needs of pediatric surgery residents. The findings, when compared with the existing literature, suggest that there are deficiencies in certain areas of surgical education.

According to the questionnaire results, scientific research (87%) and surgical simulation (74%) were found to be the most needed educational areas for pediatric surgery residents. In the literature, surgical simulation training has been shown to be effective in improving residents' practical skills and reducing surgical complications (8-12). Similarly, education in scientific research is critical for the advancement of surgeons in their careers and the development of innovative surgical techniques (6).

Leadership (43%) and communication (35%) skills were also mentioned as important educational needs. Effective leadership and communication in surgical teams are of great importance for patient safety and team cohesion (13-15). These results suggest that surgical programs should include modules to develop leadership and communication skills.

Professionalism (30%) and surgical ethics (35%) were also mentioned as important educational areas by the residents. These results emphasize that surgeons should be equipped not only with technical skills, but also with ethical and professional behaviors that are included in non-technical skills (13, 16-20).

This study has some limitations. First, the questionnaire only included pediatric surgery residents in city hospitals in Ankara and therefore the results cannot be generalized to pediatric surgery fellows in Turkey. Second, the sample size of the questionnaire is small and this may limit the representativeness of the results.

Future research could be conducted with larger samples and participants from different regions. In addition, longitudinal studies evaluating the effects of specific educational modules such as surgical simulation and scientific research could be conducted.

CONCLUSION

This study revealed that scientific research, surgical simulation and leadership are the most needed educational areas for pediatric surgery residents. It emphasizes that surgical training programs should be improved in these areas. Establishment of surgical simulation laboratories and encouragement of scientific research projects are recommended to increase the professional competencies of residents. In conclusion, more targeted and comprehensive approaches should be adopted in pediatric surgery education.

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How to Wean: A Case Report of Abrupt Weaning and Acute Dystonia

Emzirmeyi Sonlandırma Nasıl Olmalı: Ani Sütten Kesme ve Akut Distoni Olgu Sunumu

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ABSTRACT

World Health Organization (WHO) recommends exclusive breastfeeding for the first 6 months, followed by continued breastfeeding with complementary foods until 2 years of age or beyond. Despite these recommendations, there is limited research on the timing and methods of breastfeeding cessation, with abrupt weaning potentially causing unforeseen consequences.

This report describes a case involving a 33-month-old girl who experienced acute dystonic reaction following the abrupt cessation of breastfeeding. It was learned that medication containing chlorpheniramine was given to the child to alleviate the uneasiness that developed due to abrupt cessation of breastfeeding. Patient's symptoms were consistent with an acute dystonic reaction due to medication side effects, which improved with successful medical intervention.

Breastfeeding initiation, continuation, and cessation influence the mental and physical health of the mother-baby pair. Abrupt weaning can pose challenges. While there are no strict guidelines for weaning, gradual weaning is generally considered a more comfortable approach for both mother and baby.

To safeguard the well-being of the mother-baby pair, healthcare professionals should inform mothers about the discontinuation of breastfeeding and support a gradual weaning process. The presented case highlights the importance of careful consideration and professional guidance during the weaning process to prevent adverse outcomes.

Key Words: Breastfeeding, Dystonia, Weaning

ÖZ

Dünya Sağlık Örgütü (DSÖ), ilk 6 ay boyunca yalnızca anne sütüyle beslenmeyi, ardından 2 yaş veya sonrasına kadar tamamlayıcı besinlerle birlikte emzirmeye devam edilmesini önermektedir. Bu önerilere rağmen, emzirmeyi bırakmanın zamanlaması ve yöntemleri konusunda sınırlı araştırma bulunmaktadır ve emzirmeyi aniden kesmenin öngörülemeyen sonuçlara yol açma potansiyeli vardır.

Bu raporda, akut distonik reaksiyon gelişen 33 aylık bir kız çocuğunu içeren bir olgu anlatılmaktadır. Emzirmenin aniden kesilmesi nedeniyle çocukta gelişen huzursuzluğu hafifletmek için klorfeniramin içeren ilaç verildiği öğrenildi. Hastanın semptomları ilaç yan etkilerine bağlı gelişen akut distonik reaksiyonla uyumluydu ve başarılı tıbbi müdahale ile düzeldi.

Emzirmenin başlatılması, sürdürülmesi ve durdurulması anne-bebek çiftinin ruhsal ve fiziksel sağlığını etkilemektedir. Emzirmenin aniden sonlandırılması hem anne hem bebek için zorluklar yaratabilir. Emzirmenin sonlandırılmasına yönelik kesin kurallar bulunmamakla birlikte, kademeli olarak sütten kesmenin genellikle hem anne hem de bebek için daha iyi bir yaklaşım olduğu düşünülmektedir.

Anne-bebek çiftinin refahını korumak için sağlık profesyonelleri anneleri emzirmenin sonlandırılması konusunda bilgilendirmeli ve kademeli sütten kesme sürecini desteklemelidir. Sunulan vaka, olumsuz sonuçları önlemek için sütten kesme sürecinde dikkatli değerlendirmenin ve profesyonel rehberliğin önemini vurgulamaktadır.

Anahtar Kelimeler: Anne sütü, Distoni, Emzirmeyi sonlandırma

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INTRODUCTION

World Health Organization (WHO) recommends exclusive breastfeeding for the first 6 months of life, and thereafter, breastfeeding should be continued with appropriate complementary foods until 2 years of age or beyond (1). With its unique and bioactive composition, human milk contributes to both maternal and infant health. Breastfeeding is known to decrease the risk of breast and ovarian cancer especially in mothers who breastfeed their infants longer than a year. In terms of child health, in addition to early benefits such as a protection from infections; breastfeeding also decreases risk of chronic conditions including obesity, asthma, childhood leukemias, and inflammatory bowel diseases (2).

It is recommended to initiate breastfeeding as soon as possible after birth, and guidelines under the Baby-Friendly Hospital Initiative provide recommendations for an adequate start and continuation of breastfeeding (3). It is known that humans breastfeed their babies for a very long time, at least until they are two years old. An archaeological study spanning the 2200s BCE investigating duration of breastfeeding revealed that breastfeeding was typically discontinued around the age of two (4). However, research on exactly when and how breastfeeding should be discontinued and short- and long-term effects of such decisions is limited. Mothers may want to discontinue breastfeeding for various reasons, including the thought that breastfeeding period is sufficient, health issues, returning to work or the child waking up frequently at night (5,6). Although current recommendations suggest gradual weaning, studies show that mothers often choose to wean their babies abruptly by altering the taste of breast milk with application of bitter tasting substances to the breasts, or by changing appearance of the breast with items like paint, lipstick, etc. to frighten the infant (5,6).

Acute dystonic reaction is a neurologic condition characterized by involuntary muscle contractions, primarily involving the muscles of the head and neck, often encountered as a side effect of some medications. It can be accompanied by oculogyric crisis. Diagnosis can be made with physical examination and history. Cases of acute dystonic reactions have been reported in children following the use of various medications including chlorpheniramine (7).

In this report, we aimed to assess the possible effects of abrupt discontinuation of breastfeeding on the infant and the coping strategies of the mother. The case describes an acute dystonic reaction due to medication given to the baby to relieve the restlessness and agitation resulting from the sudden cessation of breastfeeding. It is aimed to emphasize the importance of breastfeeding cessation.

CASE REPORT

A 33-month-old girl, who began experiencing weakness, blank stares, muscle contractions, and restlessness the day before, was brought to pediatric emergency department.

Her medical history included birth at 38 weeks of gestation, with a weight of 2800 grams through normal spontaneous vaginal delivery. She did not require hospitalization after birth and attended routine check-ups. All screenings were conducted timely, and her immunizations were up to date. Additionally, she adequately received vitamin D and iron prophylaxis. She had no history of chronic illnesses or hospitalization. Her 43 year-old mother and 45 year-old father were healthy with the education level of elementary school graduation.

Physical examination revealed an oriented and cooperative infant in moderate general condition with normal body temperature. Respiratory, cardiovascular and gastrointestinal system examinations were normal. Dystonia in the upper and lower extremities, neck, and oculogyric crisis in the eyes were observed. There were no signs of meningeal irritation. As the physical examination findings were consistent with acute dystonia, a detailed medication history was obtained. It was revealed that the mother abruptly discontinued breastfeeding the patient yesterday by applying tomato paste to the breasts. To relieve the child's excessive restlesneess, she reported giving a total 560 mg of paracetamol and 2 mg of chlorpheniramine maleate in two different suspension forms she already had at home in the last 24 hours. Laboratory findings including complete blood count with differential, urea, creatinine, liver function tests, and electrolytes were within normal limits.

With the diagnosis of drug-induced acute dystonic reaction, the patient was administered 2 mg of biperiden intramuscularly. Gradual decrease in symptoms was observed in half an hour.

After dystonic reaction was treated successfully, mother was educated extensively about weaning. Gradual natural weaning was recommended and practical personalized suggestions were provided. Patient was discharged without any further complications. At the outpatient clinic follow-up one week later, mother reported continuing breastfeeding and she planned gradual discontinuation.

DISCUSSION

Initiation, continuation, and cessation of breastfeeding may impact both mental and physical health of the mother-baby dyad. Support from healthcare professionals in these areas will help mother-baby dyads overcome these challenging periods easily and resolve any encountered issues.

Cessation of breastfeeding can take place abruptly or gradually through natural weaning. Breastfeeding may need to be abruptly discontinued due to acute health issues affecting either mother

or baby. Additionally, studies show that that breastfeeding can be abruptly stopped with mother's decision even in planned or parent-led weaning (8). In a study conducted in our country, participants, the majority of whom were elementary school graduates, were found to commonly stop breastfeeding by applying substances such as tomato paste, pepper, lemon, etc., to the breast (5). In another study involving pyhsician mothers, it was observed that more than half of the mothers terminated breastfeeding gradually by talking to and persuading their children. However, even among physician mothers, almost one-third of participants weaned abruptly by placing or applying something to the breasts with the aim of changing the taste of milk or altering the appearance of the breasts (6).

There are no strict guidelines on how breastfeeding should be discontinued. However, it is generally stated that a gradual weaning would be more comfortable for both the mother and the baby. In gradual weaning, likelihood of encountering issues like blocked ducts or mastitis is lower. The recommended approach for gradual weaning is to drop one feeding at a time by skipping the most acceptable breastfeeding session for the mother-baby dyad and introducing a food alternative if needed. There is no definitive recommendation on which breastfeeding session to start with. It is recommended to choose the breastfeeding session that is most convenient for mother to skip when initiating the weaning process. By gradually reducing one breastfeeding session at a time, weaning from breastfeeding should be achieved over time (9).

Australian Breastfeeding Association provides more practical recommendations to facilitate the process of weaning, especially in toddlers. Those recommendations include waking up before the toddler and preparing breakfast for toddlers who prefer to nurse as the first thing in the morning, to be able to skip that session. Limiting nursing such as nursing only at home or nursing after meals are thought to be effective. For toddlers who are nursed until they fall asleep or self-disengage from the breast, breastfeeding sessions can be shortened by distraction. Proposing a shorter breastfeeding session and suggesting distractions such as going to playground can help to gradually wean these toddlers. Avoiding clothing that facilitates the toddler's access to breastfeeding and not undressing in front of toddler during weaning period are also among these recommendations. Seeking support from close circles such as relatives or friends and allowing them to take care of the baby at times should be encouraged. Refusing the child when they want to breastfeed can be challenging for some mothers. In such cases, it is advised not to refuse breastfeeding when the child asks for, but to avoid offering breastfeeding when child is not interested (10).

In countries like ours, where breastfeeding is more common and relatively longer, most mothers should have the choice to make the decision to stop breastfeeding, and they need more practical recommendations on when and how to wean (11). In order to provide adequate support to these mothers and prevent adverse outcomes, which may even include dystonia as described in our case, more definitive and universal as well as local guidelines are needed.

CONCLUSION

Breastfeeding is not only a means of nourishment but also is a process that affects the mental well-being of the mother-baby dyad. Abrupt cessation of breastfeeding can be challenging for both mother and baby. In our case, the coping strategy of uncontrolled drug use during this process led to intoxication in the child and resulted in an acute dystonic reaction. To prevent harm to the mother-baby pair, mothers should be well educated about discontinuation of breastfeeding, and gradual weaning should be supported by all health care professionals. In addition, more studies are needed on weaning practices and their short- and long-term results which might help generation of more universal and practical guidelines on the subject.

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Zinc Spray for Treatment of Acrodermatitis Enteropathica

Akrodermatitis Enteropatika Tedavisinde Çinko Sprey

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ABSTRACT

Acrodermatitis enteropathica is a rare disorder caused by zinc deficiency. The classic triad of symptoms includes perioral dermatitis, diarrhea, and alopecia. A rare cause of the acquired form is zinc deficiency due to total parenteral nutrition. Diagnosis can be challenging due to nonspecific symptoms. This paper presents a case of acrodermatitis enteropathica in a 5-month-old infant who had been on total parenteral nutrition since birth. Unlike the literature, the patient's clinical improvement was observed with zinc spray and zinc cream treatment.

Key Words: Acrodermatitis enteropathica, Zinc deficiency, Zinc spray

ÖZ

Akrodermatitis enteropatika çinko eksikliğinin neden olduğu nadir görülen bir hastalıktır. Klasik triadı perioral dermatit, diyare ve alopesidir. Kazanılmış formunun nadir bir nedeni total parenteral beslenmeye bağlı eksik çinko alımıdır. Belirti ve bulguları spesifik olmadığı için tanı koymak zordur. Biz bu makalede doğduğundan beri total parenteral beslenen 5 aylık bir hastada gelişen akrodermatitis enteropatika olgusunun literatürden farklı olarak çinko sprey ve çinko krem tedavisi ile görülen klinik iyileşmesini sunuyoruz.

Anahtar Kelimeler: Akrodermatitis enteropatika, Çinko eksikliği, Çinko sprey

INTRODUCTION

Zinc, the body's second-most abundant trace element, is critical for tissue development, differentiation, and growth (1,2). Zinc deficiency presents as acrodermatitis enteropathica (AE), a condition marked by eczema, pustular lesions in perioral and acral regions, diarrhea, and alopecia (3). This deficiency can be inherited or acquired, with acquired cases stemming from inadequate dietary intake, malabsorption syndromes (e.g., celiac disease), and short bowel syndrome (4,5). This paper presents a case of acrodermatitis enteropathica arising from zinc deficiency in a patient with short bowel syndrome who relies on long-term total parenteral nutrition (TPN).

CASE REPORT

A female infant born at 36 weeks via cesarean section with a weight of 2540 grams to a 24-year-old mother was admitted to the neonatal intensive care unit (NICU) with a diagnosis of hypoxic-ischemic encephalopathy. Due to respiratory distress, the patient was intubated and placed on mechanical ventilation. Therapeutic hypothermia was initiated. After completing 72 hours of therapeutic hypothermia, the patient underwent surgery on the third day of hospitalization for perforated necrotizing enterocolitis. The patient had multiple perforations in the jejunum, terminal ileum, and transverse colon. Approximately 50 cm of necrotic bowel was resected, and a colostomy was created. Following surgery, the

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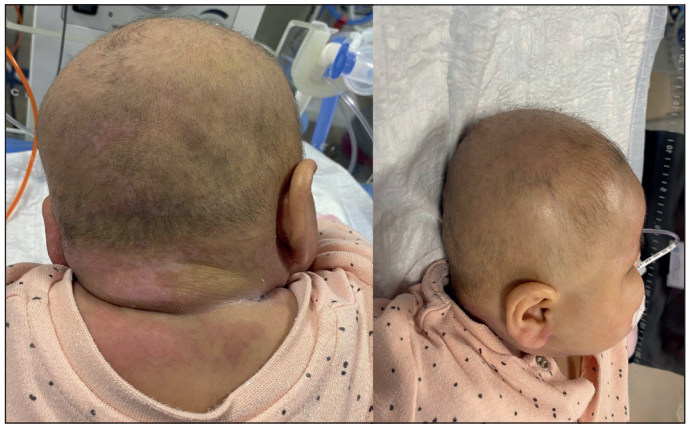

Figure 1: Diffuse hair loss due to zinc and trace element deficiency.

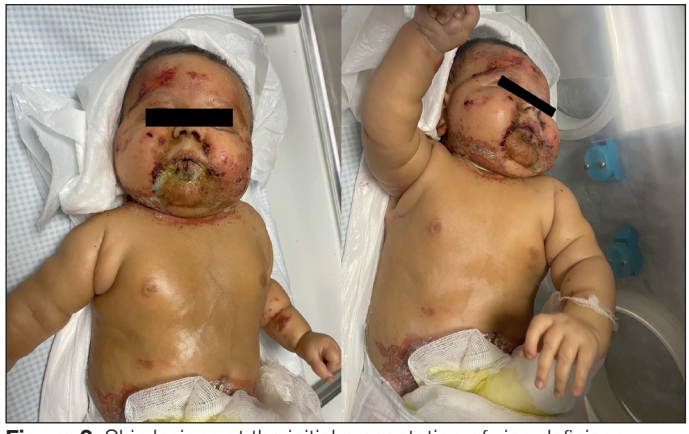

Figure 2: Skin lesions at the initial presentation of zinc deficiency.

patient developed short bowel syndrome and was initiated on TPN. Intermittent enteral feeding was attempted, but enteral feeding was never possible due to feeding intolerance and abdominal distension. The patient received TPN for 5 months. In the fourth month of follow-up, the patient developed perioral lesions and alopecia of the scalp (Figure 1). Physical examination revealed sharply demarcated, yellow-brown erythematous, scaly, erosive, and occasionally dirty yellow crusted lesions around the mouth, face, neck, arms, and genital area (Figure 2). Laboratory tests revealed leukocytes 10.51 x 10^3/uL, hemoglobin 10.1 g/dL, platelets 343 x 10^3/uL, albumin 3.4 g/dL, and alkaline phosphatase 33 U/L. Serum zinc level was 54.16 µg/dL (normal range 70-114 µg/dL). Acrodermatitis enteropathica secondary to zinc deficiency was suspected in our patient. Due to the unavailability of an intravenous form of zinc-containing trace element preparation in our country for the past year, it could not be added to TPN. Oral zinc suspension could not be administered to the patient with short bowel syndrome who was unable to tolerate enteral feeding. Therefore, the patient was given 1.1 mg zinc spray (Costus Root Spray, Nutraxin, Germany) twice a day intraorally and wound care was performed with zinc cream. Significant improvement in skin lesions was observed within a week of initiating treatment. The lesions completely regressed on the 15th day of treatment (Figure 3). The patient is currently being followed up in the NICU and continues to receive zinc therapy.

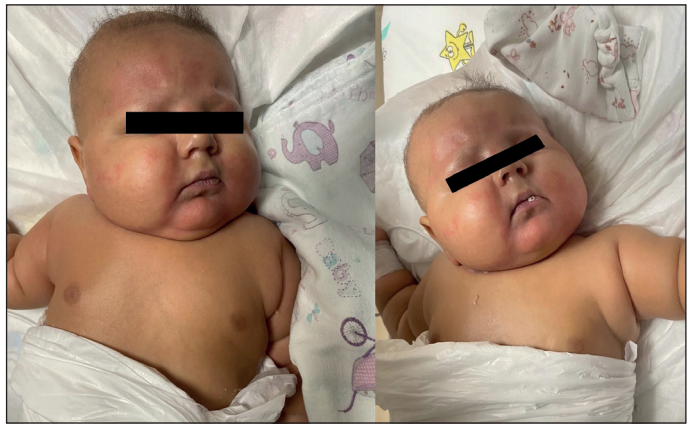

Figure 3: Improvement after zinc therapy.

DISCUSSION

Zinc is the third most abundant trace element in the human body, with the highest concentrations found in skeletal muscle, bone, and skin (6). Acrodermatitis enteropathica (AE) is a rare disorder characterized by dermatitis, diarrhea, and alopecia caused by zinc deficiency (7). The classic triad of symptoms is present in only about 20% of cases (8). The disease typically presents with erythematous, scaly, eczematous lesions in perioral, genital, and acral areas. If left untreated, the lesions may become erosive (9). Our patient also had erythematous, scaly, erosive lesions of yellowish-brown color around the mouth, neck, and genital area, as well as alopecia. Since she had diarrhea throughout her enteral feeding period, it was more likely associated with short bowel syndrome.

Inherited AE results from mutations in the SLC39A4 gene, which encodes the zinc transporter protein ZIP4 (5). The acquired form can be due to multiple causes, including inadequate intake, malabsorption syndromes, excessive intestinal loss, renal loss, and, rarely, iatrogenic zinc deficiency due to TPN (10). Patients on long-term TPN are at risk of trace element deficiencies (4). In our country, since trace elements and intravenous forms of zinc have not been added to TPN for the past year, careful attention should be paid to zinc deficiency in patients receiving TPN.

Zinc is a cofactor for numerous enzymes, including alkaline phosphatase and RNA polymerase (9). The diagnosis of acrodermatitis enteropathica is primarily based on clinical findings and confirmed by plasma zinc deficiency (10,11). Low alkaline phosphatase levels, a zinc-dependent enzyme, can also aid in diagnosis (8). Even if the serum zinc level is normal, clinical symptoms may be present if the zinc-bound form of albumin is low (9). Our patient was diagnosed with acquired zinc deficiency-related AE based on clinical findings, a serum zinc level of 54.16 µg/dL, and an alkaline phosphatase level of 33 U/L. After treatment, her alkaline phosphatase level was found to be 371 U/L. In patients suspected of zinc deficiency, low alkaline phosphatase levels can be a helpful diagnostic clue if zinc levels cannot be measured.

Zinc replacement is the standard treatment for AE stemming from dietary deficiency. Elemental zinc is often initiated at a dosage of 0.5-1 mg/kg/day. In acquired cases, response to zinc supplementation is typically rapid (12). Previous work in the literature demonstrates the use of oral or intravenous zinc to treat iatrogenic AE in patients receiving TPN (3,4,10). Our patient's inability to tolerate oral intake precluded the use of zinc suspension. Additionally, an intravenous zinc formulation was unavailable in our country for inclusion in the TPN regimen. In a departure from standard protocols, we administered zinc spray orally twice daily and applied zinc cream for wound care. The patient's lesions showed improvement on the 7th day of treatment and fully resolved by the 15th day.

In conclusion, careful monitoring for trace element deficiencies is essential in patients receiving TPN. This case highlights the potential effectiveness of topical zinc spray and cream formulations as alternative treatment options for individuals with zinc deficiency who cannot receive oral or intravenous replacement.

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