

Turkish Journal of Pediatric Disease

Türkiye Çocuk Hastalıkları Dergisi

Official Journal of Ankara Bilkent City Hospital, Children's Hospital
Ankara Bilkent Şehir Hastanesi, Çocuk Hastanesi Yayını



ANKARA BİLKENT ŞEHİR HASTANESİ
ÇOCUK HASTANESİ

Editor Editör	İbrahim İlker ÇETİN, Ankara, Turkey		
Associate Editors Yardımcı Editörler	Neriman SARI, Ankara, Turkey Müjdem Nur AZILI, Ankara, Turkey		
Section Editors Bölüm Editörleri	Gülsüm İclal BAYHAN, Ankara, Turkey Umut Selda BAYRAKCI, Ankara, Turkey E.Bahar B. PEKÇİCİ, Ankara, Turkey Güzin ÇİNEL, Ankara, Turkey Banu ÇELİKEL ACAR, Ankara, Turkey Ayşegül Neşe ÇİTAK KURT, Ankara, Turkey Bahar ÇUHACI ÇAKIR, Ankara, Turkey Esra ÇÖP, Ankara, Turkey	Suna EMİR, Ankara, Turkey Serhat EMEKSİZ, Ankara, Turkey Fatih GÜRBÜZ, Ankara, Turkey Şamil HIZLI, Ankara, Turkey Çiğdem Seher KASAPKARA, Ankara, Turkey Ayşe Esin KİBAR GÜL, Ankara, Turkey Esra KILIÇ, Ankara, Turkey İlknur KÜLHAŞ ÇELİK, Konya, Turkey	Ayşe METİN, Ankara, Turkey Akgün ORAL, İzmir, Turkey N. Yaşar ÖZBEK, Ankara, Turkey Saliha ŞENEL, Ankara, Turkey Demet TAŞ, Ankara, Turkey H. Tuğrul TIRYAKI, Ankara, Turkey Sevim ÜNAL, Ankara, Turkey H. İbrahim YAKUT, Ankara, Turkey
National Advisory Board Ulusal Danışma Kurulu	Ayşe AKSOY, Samsun, Turkey Begüm ATASAY, Ankara, Turkey Beril AYDIN, Ankara, Turkey Fatma AYDIN, Ankara, Turkey Deniz Çağdaş AYVAZ, Ankara, Turkey Mehmet Fatih AZİK, Muğla, Turkey Dilek AZKUR, Kırıkkale, Turkey Alkan BAL, Manisa, Turkey Ahmet Yağmur BAŞ, Ankara, Turkey Ali BAYKAN, Kayseri, Turkey Abdullah BEREKET, İstanbul, Turkey Aysun BİDECI, Ankara, Turkey Ayhan BİLGİÇ, Konya, Turkey Leyla BİLGİN, İstanbul, Turkey Zeynep BİRSİN ÖZÇAKAR, Ankara, Turkey Ceyhan BOZKURT, İstanbul, Turkey Gökçe CELEP, Amasya, Turkey Serdar CEYLANER, Ankara, Turkey Aykut ÇAĞLAR, Aydın, Turkey Murat ÇAKIR, Trabzon, Turkey Atilla ÇAYIR, Erzurum, Turkey Pelin ÇELİK, Ankara, Turkey Semra ÇETİNKAYA, Ankara, Turkey Mahmut ÇOKER, İzmir, Turkey Ayhan CÖNGÖLOĞLU, Ankara, Turkey Feyza DARENDELİLER, İstanbul, Turkey Selim DEREÇİ, Ankara, Turkey Suzi DEMİRBAĞ, Ankara, Turkey Orhan DERMAN, Ankara, Turkey Emine DİBEK MISIRLIOĞLU, Ankara, Turkey Ener Çağrı DİNLEYİCİ, Ankara, Turkey Figen DOĞU, Ankara, Turkey	Murat ELEVLI, İstanbul, Turkey Nagehan E. ORDUKAYA, Ankara, Turkey Ömer ERDEVE, Ankara, Turkey İlknur EROL, Adana, Turkey Pelin ERTAN, Manisa, Turkey Mehmet ERTEM, Ankara, Turkey İhsan ESEN, Elazığ, Turkey Fatih Süheyl EZGÜ, Ankara, Turkey Zeynep Gökçe G. AYDIN, Trabzon, Turkey Ayfer GÖZÜ PİRİNÇCIOĞLU, Diyarbakır, Turkey Elif GÜLER, Antalya, Turkey Fulya GÜLERMAN, Kırıkkale, Turkey Metin GÜNDÜZ, Konya, Turkey Mehmet GÜNDÜZ, Ankara, Turkey Koray HARMANCI, Eskişehir, Turkey Ayşe KAMAN, Ankara, Turkey Gözde KANMAZ KUTMAN, Ankara, Turkey Ateş KARA, Ankara, Turkey Can Demir KARACAN, Ankara, Turkey Cüneyt KARAGÖL, Ankara, Turkey Tevfik KARAGÖZ, Ankara, Turkey Nazmi Mutlu KARAKAŞ, Ankara, Turkey Esra KARAKUŞ, Ankara, Turkey İbrahim KARAMAN, Ankara, Turkey İbrahim KARNAK, Ankara, Turkey Aytekin KAYMAKÇI, İstanbul, Turkey Murat KIZILGÜN, Ankara, Turkey Abdullah KOCABAŞ, Antalya, Turkey Ülker KOÇAK, Ankara, Turkey Mehmet KÖSE, Kayseri, Turkey Serdar KULA, Ankara, Turkey Zarife KULOĞLU, Ankara, Turkey	Selim KURTOĞLU, Kayseri, Turkey Tezer KUTLUK, Ankara, Turkey Mehmet Özgür KUZDAN, İstanbul, Turkey Engin MELEK, Adana, Turkey Mehmet Burhan OFLAZ, Konya, Turkey Mehmet Hanifi OKUR, Diyarbakır, Turkey Fahri OVALI, İstanbul, Turkey Elif ÖZMERT, Ankara, Turkey Hasan ÖNAL, İstanbul, Turkey Serhan ÖZCAN, Kayseri, Turkey Çağlar ÖDEK, Bursa, Turkey Behzat ÖZKAN, İzmir, Turkey Derya ÖZYÖRÜK, Ankara, Turkey Serpil SANCAR, Bursa, Turkey Ayşe SERDAROĞLU, Ankara, Turkey Betül SİYAH BİLGİN, Ankara, Turkey Gülser ŞENSES DİNÇ, Ankara, Turkey Ayşe TANA ASLAN, Ankara, Turkey Medine Aysin TAŞAR, Ankara, Turkey Cüneyt TAYMAN, Ankara, Turkey Ceyda TUNA KIRSAÇLIOĞLU, Ankara, Turkey Özden TURAN, Ankara, Turkey Canan TÜRKİYILMAZ, Ankara, Turkey Engin TUTAR, İstanbul, Turkey Leyla TÜMER, Ankara, Turkey Tayfun UÇAR, Ankara, Turkey F.Duygu UÇKAN ÇETİNKAYA, Ankara, Turkey Mutlu UYSAL YAZICI, Ankara, Turkey Emine VEZİR, Ankara, Turkey Aydın YAĞMURLU, Ankara, Turkey Hüsnüye Neşe YARALI, Ankara, Turkey Abdullah YILDIZ, İstanbul, Turkey
International Advisory Board Uluslararası Danışma Kurulu	Alastair Baker, London, UK Pelin CENGİZ, Madison, USA Enes COŞKUN, London, UK Aarif O. EIFAN, London, UK Refika ERSU, Ottawa, Canada Pinar G. BALÇIKOĞLU, North Carolina, USA	Jaak JAEKEN, Leuven, Belgium ChesterJ. KOH, Texas, USA Allahverdi MUSAYEV, Baku, Azerbaijan Prasad MATHEW, New Mexico, USA Artur MAZUR, Rzeszow, Poland Maria C. MONGE, Texas, USA	Alp NUMANOĞLU, Cape Town, South Africa Ashwin PIMPALWAR, Wisconsin, USA James E. SWAIN, New York, USA Süleyman Tolga YAVUZ, Bonn, Germany
Consultant in Biostatistics Biyostatistik Danışmanı	Ersoy ÇİVELEK	Yavuz SANISOĞLU	
English Consultant İngilizce Danışmanı	Zeynep GÖKER	Aslınur ÖZKAYA PARLAKAY	
Publication Secretary Yayın Sekreterliği	Emel KAYMAZ	(tchdergisi@gmail.com)	



Turkish Journal of Pediatric Disease

Türkiye Çocuk Hastalıkları Dergisi

ANKARA BİLKENT ŞEHİR HASTANESİ
ÇOCUK HASTANESİ

Owner on Behalf of the Ankara Bilkent City Hospital Children's Hospital Ankara Bilkent Şehir Hastanesi Çocuk Hastanesi Adına Sahibi	Emrah ŞENEL Ankara Bilkent City Hospital Children's Hospital, Turkey
Publishing Manager/Yazı İşleri Müdürü	Metin YİĞİT Ankara Bilkent City Hospital Children's Hospital, Turkey
Head Office/Yönetim Ofisi	Ankara Bilkent City Hospital Children's Hospital, Turkey Tel: +90 (312) 552 60 00 / 401506
Editor/Editör	İbrahim İlker ÇETİN Ankara Bilkent City Hospital Children's Hospital, Turkey
Press Office/Baskı Ofisi	Üçüncü Kitap® is a brand of Remres Research Advertising Consulting Software Trade Limited Company Kavaklıdere Mah. Güfte Cad. No:12/4 Kızılay, Çankaya, Ankara, Türkiye Tel: +90 (312) 419 01 53
Publication Type/Yayın Türü	Common periodical / Yaygın süreli Published four issues per year: January, March, May, July, September, November Yılda altı kez yayımlanır: Ocak, Mart, Mayıs, Temmuz, Eylül, Kasım
Publishing Frequency/Yayın Aralığı	Bimonthly / 2 Ayda Bir
Publication Language/Yayın Dili	English
This journal printed on acid-free paper Dergimiz asitsiz kağıda basılmaktadır	Printing Date / Basım Tarihi : 26. 05. 2023



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.



Turkish Journal of Pediatric Disease is indexed in Turkish Medical Index of TUBITAK/ULAKBİM, EBSCOhost Research Databases, CINAHL and Turkey Citation Index.

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

The paper used to print this journal conforms to ISO 9706: 1994 standard (Requirements for Permanence).
 The National Library of Medicine suggests that biomedical publications be printed on acid-free paper (alkaline paper).

Bu dergide kullanılan kağıt ISO 9706: 1994 standardına ("Requirements for Permanence") uygundur.
 National Library of Medicine biyomedikal yayınlarda asitsiz kağıt (acid-free paper/alkalin kağıt) kullanılmasını önermektedir.

ENVIRONMENTAL INFORMATION / ÇEVRE BİLGİSİ

The company that manufactures the paper used in this journal has an ISO 14001 environmental management certificate. The company obtains all wood fiber in a sustainable manner. The forests and plantations of the company are certified. The water used in production is purified and used after recovery. Heavy metals or film are not used for the publication of this journal. The fluids used for developing the aluminum printing templates are purified. The templates are recycled. The inks used for printing do not contain toxic heavy metals.

This journal can be recycled. Please dispose of it in recycling containers.

Bu dergide kullanılan kağıdın üreticisi olan şirket ISO 14001 çevre yönetim sertifikasına sahiptir. Üretici şirket tüm odun elyafını sürdürülebilir şekilde temin etmektedir. Şirketin ormanları ve plantasyonları sertifikalıdır. Üretimde kullanılan su atılarak dönüşümlü kullanılmaktadır. Bu derginin basımında ağır metaller ve film kullanılmamaktadır. Alüminyum basım kalıplarının banyo edilmesinde kullanılan sıvılar arıtılmaktadır. Kalıplar geri dönüştürülmektedir. Basımda kullanılan mürekkepler zehirli ağır metaller içermemektedir.

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



AIMS and SCOPE / AMAÇ ve KAPSAM

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 pediatric surgery, dentistry, public health, genetics, psychiatry 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.

Turkish Journal of Pediatric Disease is indexed in Turkish Medical Index of Tübitak / Ulakbim, EBSCOhost Research Databases and Turkey Citation Index.

Journal is published on acid free paper.

Subscription

Turkish Journal of Pediatric Disease is delivered free of charge to library of Medical Faculties, Departments of Pediatrics in Universities and Research Hospitals and also to researchers involved in pediatrics. Full text of the articles are available on <http://dergipark.org.tr/tchd>. For subscription please visit <http://dergipark.org.tr/tchd>.

Scientific and ethical responsibility

When submitting a manuscript to the Turkish Journal of Pediatric Disease, authors should accept to assign the copyright of their manuscript to the Turkish Journal of Pediatric Disease. If authors rejected for publication, the copyright of the manuscript will be assigned back to the authors. The Turkish Journal of Pediatric Disease requires each submission to be accompanied by a Copyright Transfer and Acknowledgement of Authorship Form (available for download at <https://dergipark.org.tr/en/pub/tchd>). When using previously published content including figures, tables, or any other material in both of the print and electronic formats, authors must obtain permission from the copyright holder. Legal, financial and criminal liabilities in this regard belong to the author(s).

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 pedatrik cerrahi, dış hekimliği, halk sağlığı, genetik, çocuk ve ergen psikiyatrisi ve hemşirelik konularında makaleler yayınlanabilir. 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 Tübitak/Ulakbim Türk Tıp Dizini, EBSCOhost Research Databases ve Türkiye Atf Dizini tarafından indekslenmektedir.

Derimiz asitsiz kâğıda basılmaktadır.

Abonelik İşlemleri

Türkiye Çocuk Hastalıkları Dergisi Tıp Fakültesi olan Üniversite Kütüphanelerine, Çocuk Sağlığı ve Hastalıkları AD Başkanlıklarına, Sağlık Bakanlığı'na bağlı Eğitim ve Araştırma Hastanelerinin Başhekimliklerine ve konu ile ilgilenen bilim insanlarına ücretsiz olarak ulaştırılmaktadır. Yayınlanan makalelerin tam metinlerine <https://dergipark.org.tr/pub/tchd> adresinden ücretsiz olarak ulaşılabilir. Abonelik işlemleri için lütfen <https://dergipark.org.tr/pub/tchd> adresini ziyaret ediniz.

Yazarların Bilimsel ve Hukuki Sorumluluğu

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/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 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 pediatric surgery, dentistry, public health, genetics, psychiatrics and nursery could be published. The publication language of 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 original articles in each issue, taking into account the acceptance dates. If the articles sent to reviewers for evaluation are assessed as 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 researches 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.

All submissions are screened by a similarity detection software (iThenticate by CrossCheck).

In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, and data falsification/fabrication, the Editorial Board will follow and act in accordance with the COPE guidelines.

Each individual listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship should be based on the following 4 criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable of all aspects of the work in ensuring that questions related to the accuracy or the integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for the parts of the work he/she had done, an author should be able to identify which co-authors are responsible for the specific other parts of the work. In addition, authors should have confidence in the integrity of the contributions of their co-authors.

All those designated as authors should meet all of the four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all of the four criteria should be acknowledged in the title page of the manuscript.

The Turkish Journal of Pediatric Disease requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through <https://dergipark.org.tr/en/pub/tchd>) during the initial submission process in order to act appropriately on authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without a further review. As a part of the submission of the manuscript, the corresponding author should also send a short statement declaring that he/she accepts to undertake all of the responsibility for the authorship during the submission and review stages of the manuscript.

The Turkish Journal of Pediatric Disease requires and encourages the authors and the individuals who involved in the evaluation process of submitted manuscripts to disclose any existing or potential conflicts of interests, including financial, consultant, and institutional, that might lead to the potential bias or a conflict of interest. Any financial grants or other supports received for the submitted study from individuals or institutions should be disclosed to the Editorial Board. To disclose a potential conflict of interest, the ICMJE Potential Conflict of Interest Disclosure Form should be filled in and submitted by all of the contributing authors. Cases of the potential conflict of interest of the editors, authors, or reviewers are being resolved by the journal's Editorial Board within the scope of COPE and ICMJE guidelines.

The Editorial Board of the journal handles all of the appeal and complaint cases within the scope of COPE guidelines. In such cases, authors should get in direct contact with the editorial office to regard their appeals and complaints. When needed, an ombudsperson may be assigned to resolve cases that cannot be resolved internally. The Editor in Chief is the final authority in the decision-making process for all of the appeals and complaints.

When submitting a manuscript to the Turkish Journal of Pediatric Disease, authors should accept to assign the copyright of their manuscript to the Turkish Journal of Pediatric Disease. If authors rejected for publication, the copyright of the manuscript will be assigned back to the authors. The Turkish Journal of Pediatric Disease requires each submission to be accompanied by a Copyright Transfer and Acknowledgement of Authorship Form (available for download at <https://dergipark.org.tr/en/pub/tchd>). When using previously published content including figures, tables, or any other material in both of the

print and electronic formats, authors must obtain permission from the copyright holder. Legal, financial and criminal liabilities in this regard belong to the author(s).

Statistical analysis to support the conclusions are usually necessary. Statistical analyses must be conducted in accordance with the international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *Br Med J* 1983; 7; 1489-93). Information about the statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified certainly.

Statements or opinions expressed in the manuscripts published in the Turkish Journal of Pediatric Disease reflect the views of the author(s) and not the opinions of the editors, the editorial board, or the publisher; the editors, the editorial board, and the publisher disclaim any responsibility or liability for such materials. The final responsibility in regard to the published content rests with the authors.

MANUSCRIPT PREPARATION

The manuscripts should be prepared in accordance with the ICMJE-Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in May 2022 - <http://www.icmje.org/recommendations>).

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

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at

www.dergipark.org.tr/en/journal/2846/submission/step/manuscript/new. Manuscripts submitted via any other medium will not be evaluated.

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.

Authors are required to submit the following:

Copyright Transfer and Acknowledgement of Authorship Form and ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all of the contributing authors) during the initial submission. These forms are available for downloading at www.dergipark.org.tr/en/pub/tchd.

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 Turkey, 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 Turkey, 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: up to 40

Original articles should include; English title, English structured abstract (structured as, English key words. If the article is in Turkish, Turkish title and English title, Turkish structured summary and English summary (structured as Purpose, Material and Method, Conclusion and Discussion), Turkish and English keywords are required.

for most readers, reading the abstract first, is critically important. Moreover, various electronic databases integrate only abstracts into their index, so important findings should be presented in the abstract.

The other sections of the manuscript should include Introduction, Materials and Methods, Results, Discussion, Acknowledgement (if required) and References. All sections of the manuscripts 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 Turkey, 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.

Case reports should include; English title, English abstract and English key words. For manuscripts sent by authors in Turkey, a Turkish title, Turkish abstract and Turkish key words are also required.

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 Turkey, 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, Panatex 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 the text as superscripts 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 "et al." 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 pollen-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. *Environ 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). Access 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 polymorphism 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.

CHANGE OF AUTHORSHIP AND WITHDRAWAL REQUEST

Change of Authoship

Any request to change the author list after submission, such as a change in the order of the authors or the deletion or the addition of author names, is subject to the Editorial Board's approval. To obtain this approval, please find and complete the change of authorship form on the Journal's website and send it to the Journal's office. This form should include the following information: The reason for the change of authorship signatures of all authors (including the new and/or removed author)

Please note, if you are adding or removing author/authors, a new copyright transfer form signed by all authors should also be sent to the editorial office after the Editorial Board approves the change of the authorship.

Withdrawal Policy

Turkish Journal of Pediatric Disease is committed to provide high quality articles and uphold the publication ethics to advance the intellectual agenda of science. We expect our authors to comply mbestly with the practice in publication ethics as well as in the quality of their articles.

Withdrawal of a manuscript will be permitted only for the most compelling and unavoidable reasons. For the withdrawal of a manuscript, authors need to submit an "Article withdrawal Form", signed by all of the authors mentioning the reason for withdrawing to the Editorial Office. The form is available at the web page of the journal. Authors must not assume that their manuscript has been withdrawn until they have received appropriate notification to this effect from the editorial office.

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, dış 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 Dergisi'nde yayınlanmak üzere kabul edilmiş makaleler kabul tarihleri dikkate alınarak her sayıda en az 10 orijinal 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-Method bölümünde belirtilmelidir. Hastaların anonimliklerini dikkatlice korumak yazarların sorumluluğundadır. Hastaların kimliğini ortaya çıkarabilecek fotoğraflar için, hasta veya yasal temsilcisi tarafından imzalanmış bütünlük eklenmelidir.

Tüm başvurular intihal araştırılması için yazılımsal olarak (iThenticate by CrossCheck) taranır.

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 kopyanın içeriğini bilimsel olarak etkileyecek ve ileriye götüreceği 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 katkılarına bütünlüğüne güvenmelidir.

Yazar olarak atanmaların 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 şartlarını 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 Kuruluna 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. Gerekliğinde, 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 belirtilen 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.

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.

CONSORT	Randomize 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

Dergiyeye 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 tarafından önerilen Potansiyel Çıkar Çatışması Bildirim Formu ilk 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 verilerek 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 değer 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 kurumlara karşılık gelen bir üst simge numarası izlemelidir. Tüm yazarlar için isim soy isim, e-posta adresi, telefon ve faks numaraları dahili iletişim bilgileri verilmelidir. Ayrıca yazı ile ilgili olarak yapılacak 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 yazılar 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 gerçekleştirilmeli ve açıklayıcı olmalıdır.

Referanslar: En çok 40.

Orijinal makaleler; İngilizce başlık, İngilizce yapılandırılmış özet (yapılandırılmış, İngilizce anahtar kelimeler. Yazı Türkiye'de bulunan bir merkez tarafından gönderilmişse Türkçe başlık, Türkçe yapılandırılmış özet (Amaç, Gereç ve Yöntem, Sonuç ve Tartışma olarak yapılandırılmıştır) ve Türkçe anahtar kelimeler de gereklidir.

Çoğu okuyucu ilk olarak başlık ve özeti okuduğu için bu bölümler kritik öneme sahiptir. Ayrıca, çeşitli elektronik veritabanları yazıların sadece özetlerini indeksledikleri için özetle önemli bulgular sunulmalıdır.

Makalenin diğer bölümleri Giriş, Gereç ve Yöntemler, Sonuçlar, Tartışma, Teşekkür (gerekirse) ve Kaynaklar'dan oluşmalıdır. Makalelerin 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 sınırı yok ancak tam olarak gerçekleştirilmeli ve açıklayıcı olmalıdır.

Referanslar: 80'e kadar

Derleme makaleleri, tıptaki belirli konuların kapsamlı olarak gözden geçirildiği, konunun tarihsel gelişimini, mevcut bilinenleri, araştırma ihtiyacı olan alanları içeren yazılardır. 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

Dergiyeye 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

References: En fazla 15

Editöre mektup daha önce yayınlanmış bir makalenin önemli bölümlerini, gözden kaçan yönlerini veya eksik bölümlerini tartışır. Dergi kapsamında okurların dikkatini çekebilecek konularda, özellikle eğitici vakalarda yer alan yazılarda editöre mektup şeklinde de gönderilebilir. Okuyucular ayrıca yayınlanan yazılar hakkındaki yorumlarını editöre mektup şeklinde sunabilirler. Bir özet ve Anahtar Kelimeler dahil edilmemelidir. Tablo, şekil, görüntü içerebilir. Metin alt başlıkları içermemelidir. Yorum yapılan makaleye bu yazının içinde uygun şekilde atıfta bulunulmalıdır.

Editöre mektuplar; İngilizce başlık. Türkiye'de bulunan bir merkez tarafından gönderilmişse editör mektubu için Türkçe bir başlık da gerekmektedir.

Çalışma Metodları:

Türkiye Çocuk Hastalıkları Dergisi araştırmanın şeffaflığını artırmak ve devam etmekte olan araştırmalar hakkında ilgili kişileri bilgilendirmek için çalışma metodları yayınlamaktadır. Çalışma metodlarının yayın karar editör tarafından verilmektedir. Pilot çalışmaların veya fizibilite çalışmalarının metodları genellikle yayınlanmamaktadır.

Çalışma metodları yazıları, çalışmanın hipotezi, gerekçesi ve metodolojisi hakkında ayrıntılı bir açıklama sunan SPIRIT yönergelerine uymalıdır. Tüm çalışmalar için etik kurul onayı alınmış olmalıdır. Klinik araştırmalar için tüm protokoller, araştırma kayıt numarasını ve kayıt tarihi verilmelidir.

Tablolar

Tablolar, referans listeden sonra ana belgeye dahil edilmelidir ana metin içine yerleştirilmemelidir. Ana metinde atıfta buldukları 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: *, †, ‡, §, ||, ¶, **, ††, ‡‡.

Şekiller ve şekil alt yazıları

Şekiller, grafikler ve fotoğraflar, gönderim sistemi aracılığıyla ayrı dosyalar (TIFF veya JPEG formatında) olarak gönderilmelidir. Dosyalar bir Word belgesine veya ana metne yerleştirilmemelidir. Şekil alt birimleri olduğunda, alt birimler tek bir görüntü oluşturacak şekilde birleştirilmemelidir, her alt birim, başvuru sistemi aracılığıyla ayrı ayrı yüklenmelidir. Resimlerin üzerine etiketleme (örneğin a,d,c,d gibi) yapılmamalıdır. Şekil alt yazılarını desteklemek için görüntülerde kalın ve ince oklar, ok uçları, yıldızlar, yıldız işaretleri ve benzeri işaretler kullanılabilir. Görüntülerde bir bireyi veya kurumu gösterebilecek her türlü bilgi kör edilmelidir. Gönderilen her bir şeklin çözünürlüğü en az 300 DPI olmalıdır. Değerlendirme sürecinde gecikmeleri önlemek için, gönderilen tüm şekiller net ve büyük boyutlu olmalıdır (en küçük boyutlar: 100 x 100 mm). Şekil açıklamaları ana metnin sonunda metindeki sıraya göre ayrı ayrı listelenmelidir.

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

Ana metinde bir ilaç, ürün, donanım veya yazılım programından bahsedildiğinde, ürünün adı, ürünün üreticisi ve şehri ve şirketin ülkesini (ABD'de ise eyalet dahil) içeren ürün bilgileri, parantez içinde aşağıdaki biçimde sağlanmalıdır: The skin prick tests were

performed using a multi-prick test device (Quantitest, Panatrex Inc, Placentia, California, USA)

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 kaçınılmalıdır. 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 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:ilk ve son sayfa numarası.

Örnek: Benson M, Reinholdt J, Cardell LO. Allergen-reactive antibodies are found in nasal fluids from patients with birch pollen-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):ilk 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. Kaçınıcı 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. Kaçınıcı 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 yazar 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. Aaccessed 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."

Düzeltilme istenmesi aşaması:

Bir makalenin hakemler tarafından istenen değişiklikler yapılmış kopyası gönderilirken yazar, hakemler tarafından istenen her açıklama/düzeltilmeye cevap vermekle yükümlüdür. Yazarlar hakemlerin düzeltme/açıklama isteklerini her isteğin ardından

olacak şekilde madde madde açıklmalı, düzeltilmiş kopyaya yazılacak metin bu açıklamanın altına eklemelidir. Düzeltilme 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 otomatik olarak düşürülecektir ve tekrar başvuru yapılması gerekecektir. Eğer yazarlar ek zaman talep ediyorlarsa bu taleplerini ilk 30 günlük süre sona ermeden önce dergiye iletmelidir.

Kabul edilen yazılar dilbilgisi ve noktalama işaretleri yönünden kontrol edilir. Kabul süreci ve düzenleme işlemleri tamamlandıktan sonra yazı son onay için yazara gönderilir ve yazar tarafından son defa onaylanması istenir. Bu işlem bittikten sonra yazı dergi web sayfasında cilt ve sayfa numarası verilmeden DOI verilerek yayınlanır.

Yazar Listesi/Sırası Değişimi

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 yayını etliğini korumayı taahhüt etmektedir. Yazarlardan, yayını etğinde 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 karşılır.

CONTENTS / İÇİNDEKİLER*Original Articles**Özgün Araştırmalar*

- 175** **The Importance of Regular and Ongoing Training For Congenital CMV in Countries Without Routine Screening: A Survey Among Pediatricians**
Rutin Tarama Yapılmayan Ülkelerde Konjenital CMV İçin Düzenli ve Sürekli Eğitimin Önemi: Pediatristler Arasında Bir Anket
Saliha KANIK YÜKSEK
- 182** **Comparison of Ambulance Usage Characteristics in Children Between the Pre-Pandemic and Pandemic Periods in Turkey**
Türkiye’de Pandemi Öncesi ve Pandemi Dönemi Arasında Çocukların Ambulans Kullanım Özelliklerinin Karşılaştırılması
Eyüp SARI, İshak SAN, Burak BEKGÖZ, Halise AKCA
- 187** **The Efficacy of Erythrocyte Transfusion in Very Low Birth Weight Infants with Premature Anemia**
Prematüre Anemisi Olan Çok Düşük Doğum Ağırlıklı Bebeklere Eritrosit Transfüzyonunun Etkisi
Aybuke YAZICI, Betül SIYAH BILGIN, Ahmet Serkan ÖZCAN, Sevim ÜNAL
- 194** **Determinants of Low Disease Activity and Remission in Pediatric Systemic Lupus Erythematosus Patients**
Pediatrik Sistemik Lupus Eritematosus Hastalarında Düşük Hastalık Aktivitesi ve Remisyonun Belirleyicileri
Melike Mehveş KAPLAN, Vildan GÜNGÖRER, Elif CELİKEL, Zahide EKİCİ TEKİN, Tuba KURT, Nilüfer TEKGÖZ, Müge SEZER, Cüneyt KARAGÖL, Serkan COŞKUN, Nimet ÖNER, Merve Cansu POLAT, Fatma Şemsa ÇAYCI, Banu ÇELİKEL ACAR
- 201** **Why Do Mothers Use Or Not Use Walkers For Their Babies?**
Anneler Bebekleri İçin Niçin Yürüteç Kullanıyorlar veya Kullanmıyorlar?
Tülin ÇATAKLI, Hüsniye YÜCEL
- 207** **Clinical and Sociodemographic Characteristics of Patients Hospitalized in A Child and Adolescent Psychiatry Inpatient Unit**
Bir Çocuk ve Ergen Yataklı Psikiyatri Servisinde Tedavi Gören Hastaların Klinik ve Sosyodemografik Özellikleri
Merve ONAT, Elif AKÇAY, Ayşegül DEMİR, Ümran Gül AYVALIK BAYDUR, Zeynep GÖKER, Gülser ŞENSES DİNÇ, Esra ÇÖP

- 214** **Evaluation of Lefflunomide Treatment in Patients with Juvenile Idiopathic Arthritis: A Single Center Experience**
Jüvenil İdiopatik Artritli Hastalarda Leflunomid Tedavisinin Değerlendirilmesi: Tek Merkez Deneyimi
Elif ARSLANOĞLU AYDIN, Semanur ÖZDEL, İlknur BAĞRUL, Nesibe Gökce KOCAMAZ, Esra BAĞLAN, Şerife TUNCEZ, Mehmet BÜLBÜL
- 219** **Assessment of Risk Factors for Obesity in Children Aged 6-17 Years Where Obesity Reaches Peak**
Obezitenin Zirve Yaptığı 6-17 Yaş Aralığındaki Çocuklarda Obezite Gelişiminde Rol Oynayan Risk Faktörlerinin Değerlendirilmesi: Tek Merkez Deneyimi
Onur KAŞLI, Ayşe Derya BULUŞ, Mesut KOÇAK, Uğur Ufuk IŞIN
- 227** **Evaluation of Chronic Cough Etiologies in Children**
Çocuklarda Kronik Öksürük Sebeplerinin Değerlendirilmesi
Özge YILMAZ TOPAL
- 233** **Comparison of Language Development, Emotional and Behavioral Problems, Parental Attitude Characteristics, Parental Stress Level and Related Factors in Preschool Period, Between Preterm and Term-Born Children**
Preterm ve Term Doğan Çocuklarda Dil Gelişimi, Duygusal ve Davranışsal Sorunlar, Ebeveyn Tutum Özellikleri, Ebeveyn Stres Düzeyi ve İlişkili Faktörlerin Okul Öncesi Dönemde Karşılaştırılması
Barış GÜLLER, Erbu YARCI, Ferhat YAYLACI
- 243** **Determination of the Relationship Between Self-Esteem and Social Anxiety in Adolescents with Burns**
Yanığı Olan Adölesanlarda Benlik Saygısı ile Sosyal Anksiyete Arasındaki İlişkinin Belirlenmesi
Derya SULUHAN, Ecem SAĞIROĞLU, Sabri DEMİR, Dilek YILDIZ, Merve ONAT, Emrah ŞENEL

Case Reports

Olgu Sunumları

250

A Novel Double Homozygous BTD Gene Mutation in A Case of Profound Biotinidase Deficiency

Ağır Biotinidaz Eksikliği Olgusunda Yeni Çift Homozigot BTD Gen Mutasyonu

Kübra DEVECİ, Halil Tuna AKAR, Yılmaz YILDIZ, R. Köksal ÖZGÜL

253

Unusual Surgical Treatment Option For An Uncommon Disease: Ureterocutaneostomy in an Emphysematous Pyelonephritis Patient

Nadir Bir Hastalık İçin Olağandışı Cerrahi Tedavi Seçeneği: Amfizematöz Piyelonefritli Hastada Üreterokutanostomi

Günay EKBERLİ, Sevgin TANER, Nevzat Can SENER

The Importance of Regular and Ongoing Training for Congenital CMV in Countries without Routine Screening: A Survey among Pediatricians

Rutin Tarama Yapılmayan Ülkelerde Konjenital CMV İçin Düzenli ve Sürekli Eğitimin Önemi: Pediatristler Arasında Bir Anket

Saliha KANIK YÜKSEK

University of Health Sciences, Ankara City Hospital, Department of Pediatric Infectious Diseases, Ankara, Turkey



ABSTRACT

Objective: Although CMV is the most common congenital infection, studies on how its importance is understood by healthcare professionals are limited. This research aims to assess awareness and knowledge of pediatricians regarding congenital CMV infection (cCMVi).

Material and Methods: The target group of the study was pediatricians in Turkey. A 26-item anonymous questionnaire was developed, and implemented online. Participants were grouped by their professional seniority: Group-I, pediatric residents; Group-II, pediatricians; Group-III, specialists in any sub-branches of pediatrics; Group-IV, associate professors/professors in pediatrics.

Results: The questionnaire was completed by 434 respondents. The mean duration of practice was 11.95 ± 7.3 (1-40) years for professionals, and 31.14 ± 13.1 (1-60) months for pediatric residents. Of the participants, 85.9% knew that cCMVi screening is not applied in Turkey and 89.4% had previously followed a patient with suspected cCMVi. Incorrect answers regarding transmission routes and diagnosis methods were significantly more preferred by pediatricians other than residents. Correct answer rates about most common clinical presentation, imaging modalities, common disease-related sequelae, and treatment were generally quite low.

Conclusion: The responses revealed a lack of knowledge and awareness about cCMVi in Turkey among pediatricians, especially in professionals rather than residents. It is important to provide regular and ongoing training about cCMVi in countries where screening is not implemented.

Key Words: Awareness, Congenital Cytomegalovirus infection, Knowledge, Pediatrician, Screening

ÖZ

Amaç: CMV en sık görülen konjenital enfeksiyon olmasına rağmen öneminin sağlık profesyonelleri tarafından nasıl anlaşıldığına dair çalışmalar sınırlıdır. Bu araştırma, çocuk doktorlarının konjenital CMV enfeksiyonu (kCMVe) konusundaki bilgi ve farkındalıklarını değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Çalışmanın hedef grubu Türkiye'deki çocuk doktorlarıydı. Yirmi altı maddelik anonim bir anket geliştirildi ve çevrimiçi olarak uygulandı. Katılımcılar mesleki kıdemlerine göre gruplandırıldı: Grup-I, pediatri asistanları; Grup-II, çocuk doktorları; Grup-III, pediatri'nin herhangi bir yan dal uzmanları; Grup-IV, pediatri doçent/profesörleri.

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

0000-0002-2538-2872 : KANIK YÜKSEK S

Ethics Committee Approval / Etik Kurul Onayı: This study was conducted in accordance with the Helsinki Declaration Principles. Ethical approval for the study was obtained from Ankara City Hospital Local Ethics Committee (No: E2-21-942).

Contribution of the Authors / Yazarların katkısı: KANIK YÜKSEK S: 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.

How to cite / Atıf yazım şekli : Kanik Yüksek S. The Importance of Regular and Ongoing Training for Congenital CMV in Countries without Routine Screening: A Survey among Pediatricians. Turkish J Pediatr Dis 2023;17:175-181.

Correspondence Address / Yazışma Adresi:

Saliha KANIK YÜKSEK
University of Health Sciences, Ankara City Hospital,
Department of Pediatric Infectious Diseases, Ankara, Turkey
E-posta: salihakanic@gmail.com

Received / Geliş tarihi : 20.09.2022

Accepted / Kabul tarihi : 04.11.2022

Online published : 09.12.2022

Elektronik yayın tarihi

DOI:10.12956/tchd.1177657

Bulgular: Anket 434 kişi tarafından doldurulmuştur. Ortalama çalışma süresi pediatri asistanları dışındakiler için 11.95 ± 7.3 (1-40) yıl, pediatri asistanları için 31.14 ± 13.1 (1-60) aydı. Katılımcıların %85.9' u Türkiye'de kCMVe taramasının uygulanmadığını biliyordu ve %89.4'ü daha önce kCMVe şüphesi olan bir hastayı takip etmişti. Bulaş yolları ve tanı yöntemleri ile ilgili yanlış cevaplar asistanlar dışındaki pediatristler tarafından anlamlı olarak daha fazla tercih edilmiştir. En yaygın klinik prezentasyon, görüntüleme modaliteleri, yaygın hastalıkla ilgili sekeller ve tedavi hakkında doğru cevap oranları genel olarak oldukça düşüktü.

Sonuç: Yanıtlar, Türkiye'de pediatristler arasında, özellikle asistanlardan ziyade diğer pediatristler arasında kCMVe hakkında bilgi ve farkındalık eksikliği olduğunu ortaya koydu. Taramanın uygulanmadığı ülkelerde kCMVe hakkında düzenli ve sürekli eğitim verilmesi önemlidir.

Anahtar Sözcükler: Farkındalık, Konjenital Sitomegalovirüs enfeksiyonu, Bilgi, Çocuk doktoru, Tarama

INTRODUCTION

Congenital Cytomegalovirus infection (cCMVi) is the most common congenital infection worldwide, and is considered to be the most frequent cause of infectious neurological handicaps (1, 2). cCMVi rates vary according to the CMV seroprevalence of the areas; cCMVi rates are between 1-5% in regions with high CMV seroprevalence, and the rate is lower in regions with low CMV seroprevalence as 0.4-2% (3, 4). About 90% of infected infants have no symptoms at birth and early in life, but approximately 10-15% of these infants develop persistent and serious disorders that may have lifelong effects, such as deafness, cognitive and motor impairment, seizures, and microcephaly (1, 5). Among infants with symptomatic cCMVi, treatment with some antiviral drugs showed promising results. They are now used more frequently since they seem safe, although the duration of treatment is uncertain (6, 7). Medical treatment remains the only possibility for this infection, which does not have a chance to be protected with any vaccine yet. Unlike symptomatic disease, there are currently no treatment recommendations or guidelines for asymptomatic cCMVi (7). In newborns and infants who are asymptomatic or without visible signs of disease, cCMVi goes undiagnosed. Screening programmes for pregnant women and newborns are controversial and still being discussed (3, 4). Especially in countries where screening programs are not implemented, it is even more important for healthcare professionals to recognize this congenital infection, which has long-term effects. However, there are limited reports to reveal the level of knowledge of medical professionals about cCMVi and to allow the necessary improvements and interventions to be made (8-13).

According to the limited studies, the seroprevalence of CMV in Turkey is between 94.9%-96.4% in pregnant women (14, 15). Turkey has a high seroprevalence for CMV with these rates, however, the actual frequency for cCMVi is unknown. Considering that newborns are not screened for cCMVi in Turkey, the awareness and knowledge of clinicians on this issue gains more importance in order to diagnose cCMVi in early period and initiate treatment on time when necessary. The objective of this study was to determine the awareness and knowledge of pediatricians about cCMVi, who frequently encounter infants with possible cCMVi.

MATERIALS and METHODS

Pediatricians working in the hospitals of Turkey were chosen as the target group of the study. Physicians who had completed their education in the pediatrics or any of its sub-branches or who were still in the education process and volunteered to participate in the survey were included in the study. Participants were grouped according to their professional seniority, and comparisons were made over these groups: Group I, residents in pediatrics; Group II, pediatricians; Group III, specialists in any sub-branches of pediatrics; Group IV, associate professors/professors in pediatrics. A 26-item anonymous questionnaire on cCMVi, which takes 20 min to complete, was developed, and implemented online. The questionnaire was designed with GoogleForm, and the link of the questionnaire was sent by e-mail and Whatsapp application in pediatrician groups of hospitals, from 1 October 2021 to 1 January 2022. The response period was closed after 3 months. Ethical approval for the study was obtained from Ankara City Hospital Local Ethics Committee (No: E2-21-942).

At the top of the questionnaire, a preliminary information was given to the participants explaining the purpose of the study and stating that the participation was on a voluntary basis. In the first part of the questionnaire, questions about demographic variables including age, gender, career duration, professional field, and professional seniority were asked to responders. The remaining part of the questionnaire consisted of multiple-choice questions in which only one or more than one option could be ticked. The contents of the questions were whether cCMVi screening is performed in Turkey, probability of encountering a patient with suspected cCMVi, the transmission routes of CMV and cCMVi, symptoms and clinical findings, clinical presentation forms, laboratory tests and imaging methods required for diagnosis, the postnatal time for the definitive diagnosis, the indications and duration for cCMVi treatment, antivirals that can be used in the treatment, expected benefit from treatment, and cCMVi-related sequelae.

Power calculation to determine the sample size was not performed for this descriptive survey. Statistical analyzes were performed using SPSS v25.0 (IBM Corp., Armonk, New York, USA) statistical package on the total participants reached during the previously determined three-month study period. The results were expressed as mean±standard deviation,

median and range (smallest value–largest value), and number (%) depending on whether the data were parametric or not. Categorical variables were compared by chi-square or Fisher exact tests, and were summarized with frequencies. All tests were 2-sided with a significance level of 0.05.

RESULTS

The questionnaire was completed by 434 respondents. Of them, 74% (n = 321) were female. The median age of participants was 35 (24-70) years. The distribution of participants by groups was as follows: 104 (24%) participants in group I, 167 (38.5%) participants in group II, 119 (27.4%) participants in group III and 44 (10.1%) participants in group IV. The mean duration of practice was 11.95±7.3 (1-40) years for professionals other than residents, and 31.14±13.1 (1-60) months for residents.

Three hundred and eighty-eight (89.4%) participants stated that they had followed up any patient with suspected cCMVi before. Three hundred and seventy-three participants (85.9%) answered that cCMVi screening is being implemented in Turkey, while 46 (10.6%) participants marked as “not being implemented”, and 15 (3.5%) participants did not have any idea. The best-known routes of transmission for CMV were intrauterine transmission (91.2%), blood transfusion (89.6%) and solid organ transplantation (82.9%). However, some participants were unaware of the exact route of CMV transmission with

their response of air-borne transmission (49.3%). Additionally, kissing (55.8%), close contact (51.6%), breast feeding (54.4%), changing diapers (53.7%), sexual intercourse (42.2%), and CMV-contaminated food (19.4%) were given as answers to this multiple-choice question. The rate of those who marked at incorrect option was 47.9% (n = 208), and was significantly higher in group II (p = 0.007). Answers to the question about the possible transmission route of cCMVi in a newborn baby were as follows: intrauterine transmission (68.7%), contact with maternal secretions during delivery (31.6%), breast milk (13.6%), kissing by an infected individual (6.9%), all options (27.9%), and have not an idea (1.2%). Incorrect marking to the option of “contact with maternal secretions during delivery” was significantly higher in group II (p = 0.02) and group III (p = 0.022), but there was no difference between the groups for incorrect answers to the other options. The answers of the question about most common maternal CMVi form during pregnancy, are respectively; primary CMVi 74.4% (n = 323), recurrent CMVi 13.6% (n = 59), and no idea 12% (n = 52). The responses and significance levels regarding the symptoms and findings of cCMVi in a newborn infant are summarized in Table I. Answers to the question about the most common clinical presentation of cCMVi by the groups were shown in Figure I.

The answers given to the question about the most appropriate sample for the diagnosis in newborns were “blood” 69.4%, “urine” 48%, “saliva” 10.4%, “breast milk” 1.6%, all options 5.8%, and no idea 2%. While group II did not select urine as the

Table I: The responses and significance levels regarding the symptoms and clinical findings of cCMVi according to the groups.

Symptoms and findings*	Group I†	Group II†	Group III†	Group IV†	Total†	p
Asymptomatic	62 (59.6)	103 (61.7)	70 (58.9)	17 (38.6)	252 (58.1)	0.049
Rash	78 (75)	139 (83.2)	105 (88.2)	44 (100)	336 (84.3)	0.001
Fever	65 (62.5)	109 (65.2)	88 (73.9)	27 (61.4)	289 (66.6)	0.226
Organomegaly	79 (75.9)	148 (88.7)	106 (89)	42 (95.5)	375 (86.4)	0.003
Microcephaly	102 (98)	164 (98.2)	116 (97.5)	43 (97.7)	425 (97.9)	0.977
Diarrhea	44 (42.3)	69 (41.3)	59 (49.6)	18 (41)	190 (43.8)	0.517
Extremity anomaly	53 (51)	65 (39)	56 (47)	11 (25)	185 (42.6)	0.015
Seizure	84 (81)	130 (78)	92 (77.3)	34 (77.2)	340 (78.3)	0.921
Chorioretinitis	68 (65.4)	99 (59.3)	79 (66.4)	31 (70.5)	277 (63.8)	0.427
Intestinal anomaly	7 (6.7)	7 (4.2)	8 (6.7)	5 (11.4)	27 (6.2)	0.352
Cardiac anomaly	20 (19.2)	30 (18)	22 (18.5)	9 (20.5)	81 (18.7)	0.982
Cytopenia	55 (52.9)	80 (48)	69 (58)	29 (66)	233 (53.7)	0.122
Intracranial calcification	68 (65.4)	92 (55)	72 (60.5)	31 (70.5)	263 (60.6)	0.178
Urinary anomaly	4 (3.8)	1 (0.6)	2 (1.7)	0	7 (1.6)	0.166
High transaminases	54 (52)	86 (51.5)	77 (64.7)	27 (61.4)	244 (56.2)	0.098
Hyperbilirubinemia	40 (38.5)	57 (34.1)	59 (49.6)	21 (47.7)	177 (40.8)	0.046
Hearing loss	64 (61.5)	94 (56.3)	71 (59.6)	25 (56.9)	254 (58.5)	0.837
All options	33 (31.7)	61 (36.5)	39 (32.8)	11 (25)	144 (33.2)	0.517
No idea	0	1 (0.6)	0	1 (2.3)	2 (0.5)	0.236

*Only those who answered “yes” were listed, † n(%)

Table II: The answers given to the questions about treatment of cCMVi by the groups.

	Group I*	Group II*	Group III*	Group IV*	Total*	p
Is there any drug approved for treatment?						
Yes	89 (85.6)	154 (92.2)	110 (92.4)	37 (84.1)	390 (89.9)	0.138
No	6 (5.8)	10 (6)	5 (4.2)	4 (9.1)	25 (5.8)	
No idea	9 (8.7)	3 (1.8)	4 (3.4)	3 (6.8)	19 (4.4)	
Which drug(s) do you prefer for treatment?						
Cidofovir	1 (1)	3 (1.8)	0	2 (4.5)	6 (1.4)	0.086
Ganciclovir/valganciclovir	91 (87.5)	152 (91)	110 (92.4)	41 (93.2)	394 (90.8)	
Acyclovir/valacyclovir	2 (1.9)	2 (1.2)	1 (0.8)	0	5 (1.2)	
All options	2 (1.9)	8 (4.8)	5 (1.2)	1 (0.2)	16 (3.7)	
No idea	8 (7.7)	2 (1.2)	3 (2.5)	0	13 (3)	
What is the appropriate duration of treatment?						
Oral						0.201
3 weeks	2 (1.9)	4 (2.4)	5 (4.2)	2 (4.5)	13 (3)	
6 weeks	5 (4.8)	17 (10.2)	9 (7.6)	5 (11.4)	36 (8.3)	
3 months	7 (6.7)	26 (15.6)	11 (9.2)	8 (18.2)	52 (12)	
6 months	53 (51)	61 (36.5)	47 (39.5)	14 (31.8)	175 (40.3)	
12 months	2 (1.9)	9 (5.4)	8 (6.7)	3 (6.8)	22 (5.1)	
No idea	35 (33.7)	50 (29.9)	39 (32.8)	12 (27.3)	136 (31.3)	
Parenteral						0.761
3 weeks	24 (23.1)	40 (24)	32 (26.9)	12 (27.3)	108 (24.9)	
6 weeks	36 (34.6)	74 (44.3)	44 (37)	19 (43.2)	173 (39.9)	
3 months	5 (4.8)	8 (4.8)	7 (5.9)	2 (4.5)	22 (5.1)	
6 months	4 (3.8)	9 (5.4)	10 (8.4)	2 (4.5)	25 (5.8)	
12 months	1 (1)	1 (0.6)	0	0	2 (0.5)	
No idea	34 (32.7)	35 (21)	26 (21.8)	9 (20.5)	104 (24)	

*n(%)

Table III: The responses about the indications for initiating treatment, expectations from the treatment, and the most common disease-related sequelae.

	Group I*	Group II*	Group III*	Group IV*	Total*	p
Indications for initiating treatment						
All infants diagnosed with cCMVi	45 (43.3)	52 (31.1)	29 (24.4)	10 (22.7)	136 (31.3)	0.003
Infants with symptomatic cCMVi	49 (47.1)	88 (52.7)	64 (53.8)	28 (63.6)	229 (52.8)	
Infants with hearing loss	2 (1.9)	1 (0.6)	0	0	3 (0.7)	
Infants with chorioretinitis and neurological signs	2 (1.9)	23 (13.8)	20 (16.8)	6 (13.6)	51 (11.8)	
No idea	6 (5.8)	3 (1.8)	6 (5)	0	15 (3.5)	
Expectations from the treatment						
Negativity in CMV viremia	11 (10.6)	16 (9.6)	17 (14.3)	12 (27.3)	56 (12.9)	0.015
Preventing an asymptomatic infection from transformation to a symptomatic infection	14 (13.5)	19 (11.4)	13 (10.9)	6 (13.6)	52 (12)	0.713
Preventing CMV reactivations	12 (11.5)	18 (10.8)	13 (10.9)	4 (9.1)	47 (10.8)	0.978
Long-term improvement in audiological and neurodevelopmental findings	29 (27.9)	64 (38.3)	55 (46.2)	13 (29.5)	161 (37.1)	0.027
All options	45 (43.3)	61 (36.5)	41 (34.5)	16 (36.4)	163 (37.6)	0.565
No idea	8 (7.7)	13 (7.8)	5 (4.2)	5 (11.4)	31 (7.1)	0.410
Most common disease-related sequelae						
Neuromuscular problems	11 (10.6)	7 (4.2)	5 (4.2)	0	23 (5.3)	0.051
Loss of vision	7 (6.7)	10 (6)	9 (7.6)	4 (9.1)	30 (6.9)	
Hearing loss	62 (59.6)	118 (70.7)	73 (61.3)	32 (72.7)	285 (65.7)	
Intellectual disability and delay in psychomotor development	19 (18.3)	24 (14.4)	23 (19.3)	2 (4.5)	68 (15.7)	
Behavioral problems	1 (1)	0	0	0	1 (0.2)	
No idea	4 (3.8)	8 (4.8)	9 (7.6)	6 (13.6)	27 (6.2)	

*n(%)

most appropriate sample significantly ($p = 0.010$), there was no difference between groups in other sample choices. The order of preference for the laboratory test(s) to diagnose if cCMVi is suspected was as follows: polymerase chain reaction (PCR)

in blood from baby (72.4%), serological tests of blood from baby (54.4%), PCR in urine from baby (48.4%), PCR in breast milk (5.1%), serological tests of blood from mother (35.5%), all options (15.9%), and no idea (0.2%). Group IV preferred the

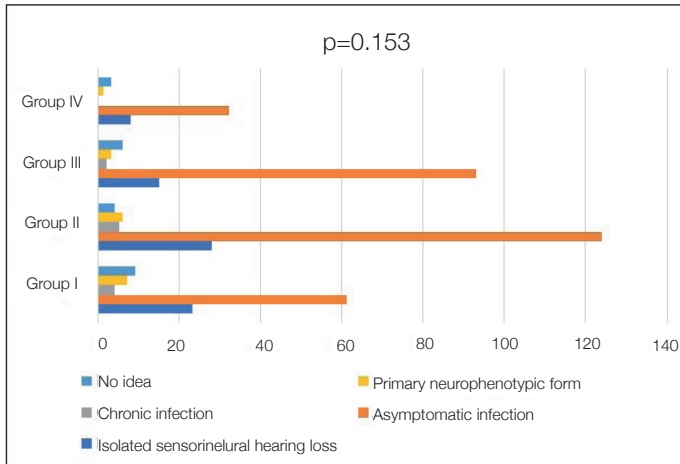


Figure I: Responses (n) about the most common clinical presentation of cCMVi by groups.

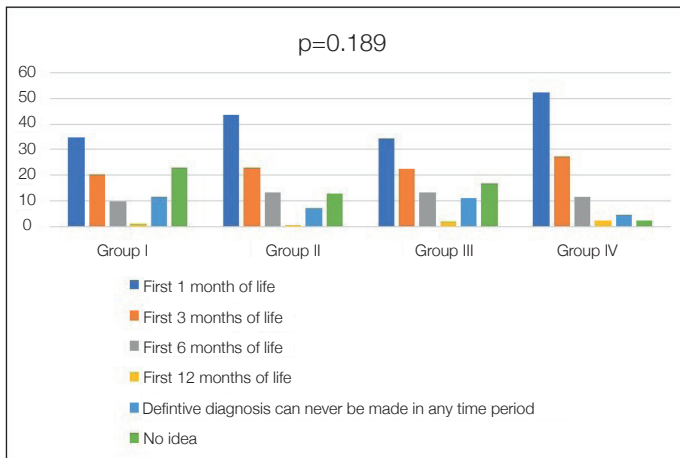


Figure II: Responses (%) of the groups about the period in which the diagnosis of cCMVi can be made definitively with the tests performed (Percentages are indicated separately for each group).

CMV PCR in urine for diagnosis significantly less ($p = 0.048$). However, there was not any difference between the groups for other test options. Preferences by the groups about the period in which the diagnosis of cCMVi can be made definitively with the tests performed were shown in Figure II.

Bone radiographic surveys (65.9%), echocardiography (30.9%), cranial imaging (23.7%), hearing test (21.4%), and eye examination (19.8%) options were preferred as unnecessary imaging methods or examinations during the diagnosis, respectively. Of the participants, 2.8% had no idea about this approach. Any statistical difference was not detected between the groups in terms of preferences ($p = 0.404$). The answers of the questions about treatment options and duration of treatment in oral and parenteral administration according to the groups and their significance levels were summarized in Table II. The responses reflecting the level of knowledge about the indications for initiating treatment, expectations from the treatment, and the most common disease-related sequelae were summarized in Table III.

DISCUSSION

Although cCMVi is the most common congenital infection, studies on how the importance of cCMVi, its transmission routes, clinical findings and treatment approaches are understood by healthcare professionals are limited (9-13, 16, 17). Awareness studies on medical professionals, who are more likely to encounter cCMVi patients such as pediatricians, obstetricians and audiologists, will enable to reveal level of knowledge about cCMVi and make necessary improvements and interventions. The knowledge and awareness about the cCMVi among pediatricians in Turkey was investigated in this study. This report is the first survey conducted among only pediatricians in this context, and several remarkable results were obtained. The vast majority (89.4%) of the responders stated that they had followed any patient with suspected cCMVi before. However, the responses revealed that there is a significant lack of knowledge about cCMVi, which is not parallel to the high rate of this cCMVi experience.

The well-known transmission routes of CMV by the participants were intrauterine transmission, blood transfusion and solid organ transplantation. Other possible transmission routes, such as kissing, close contact, breast feeding, changing diapers, sexual intercourse, and CMV-contaminated food were marked at lower rates. However air-borne transmission which is not a exact route of transmission, was marked at a rate that was not at all low. The rates of correct answers about the possible transmission route of cCMVi in a newborn were found to be quite low compared to the rates of the answers given to CMV transmission routes. It is important to know the possible transmission route of cCMVi in order to consider the cCMVi infection that may occur in the babies of women who are exposed to the risk of maternal infection during pregnancy and to examine the patient in this direction. It is also interesting that inappropriate answers were detected at a higher rate among professionals in group II and group III, rather than residents who are in education processes. This data may bring on the agenda the additional information programs on cCMVi after the pediatric education process. The risk of inutero transmission to the fetus is far higher with primary maternal infection than with recurrent infection (1). Three quarters of the participants in this study stated that the most common maternal CMVi form was primary maternal infection.

While most newborn infants with cCMVi are asymptomatic at birth, 10-15% of infants born symptomatically may have clinical signs and symptoms that affect many systems and organs, often including neurological abnormalities, petechiae, hepatosplenomegaly, and jaundice (1, 5). Of the participants, 58.1% marked that the infection could be asymptomatic, but the rate was considered low. Among the groups, group II marked this option with the highest rate (61.7%), while group IV marked this option at the lowest rate (38.6%, $p = 0.049$). It is worrying that this rate is not high; because some asymptomatic

newborns who cannot be diagnosed will develop long-term sequelae, and the ignorance of this fact by pediatricians may result in delayed diagnosis of possible sequelae that may occur after the neonatal period, since cCMVi screening is not performed in Turkey. Correct options marked in order of frequency were microcephaly, organomegaly, rash, seizure, fever, chorioretinitis, intracranial calcification, hearing loss, high transaminases, cytopenia, and hyperbilirubinemia. It was observed that the neurologic findings, which are often expected in symptomatic newborns, were frequently marked by the participants. However, it was remarkable that unexpected or rarely reported clinical manifestations such as extremity anomaly, intestinal anomaly, diarrhea, cardiac anomaly, and urinary anomaly were also chosen by some participants at a substantial rate. Frequent marking of unexpected clinical findings may result in unnecessary investigation of possible cCMVi cases by the physician and prolongation of diagnosis time. Nearly all respondents had an opinion on this question, with a third of professionals ticking “all options”. Infants with congenital CMV infection are classified according to the symptoms at the time of birth, and are divided into four groups according to this classification: asymptomatic, symptomatic, primary neurophenotype, and asymptomatic with isolated hearing loss (1). The most common clinical presentation is asymptomatic infection as mentioned above. Asymptomatic form was the most marked option by all groups of this study with no statistical difference, followed by the “isolated sensorineural hearing loss”. It is also interesting that the “chronic infection”, a form not included in the classification, is also marked by some professionals.

Clinical findings in the symptomatic neonate with cCMVi can be similar to those in other congenital infections (1, 5). Therefore, additional diagnostic procedures are required for definitive diagnosis. The diagnosis can be established by detection of the virus in body fluids within the first 3 weeks of life, and urine and saliva are the preferred specimens for diagnosis (1). Blood samples is not recommended as a first-line test because not all infected infants are viremic. Viral cultures and PCR are the preferred methods of testing. However, PCR is widely applied due to its high sensitivity and rapid results compared to culture (18). In this report, participants preferred “blood” sample most frequently, but less preferred “urine” and “saliva” samples, which are primarily recommended samples. Interestingly, pediatricians preferred urine significantly less than other groups. Although not primarily recommended, PCR and serological tests from blood were also the most preferred laboratory tests by the responders. Group IV professionals, the most qualified physician group, preferred the CMV PCR in urine for diagnosis significantly less than the others. In addition, although the “First 1 month of life” was preferred by most of the participants as the period in which the diagnosis of cCMVi can be made definitively, it was noticed that there was a lack of information about the period of diagnosis and a variety of answers. It is also very thought-provoking that almost a quarter

of the participants prefer cranial imaging, hearing test, and eye examination for unnecessary imaging methods for diagnosis. With these results, possible cases of cCMVi seems to be at risk of underdiagnosis due to not using the appropriate test samples and examination methods for definitive diagnosis by pediatricians.

Although there is more than one effective agents against CMV, treatment of cCMVi with intravenous ganciclovir or oral valganciclovir therapy has been shown to reduce the risk of long-term sequelae of hearing loss and neurodevelopmental delay in symptomatic newborns (6, 7). Although there are uncertainties regarding the duration of treatment, there is a trend to use 6 months of oral therapy and 6 weeks of parenteral therapy (1, 6, 7). In this study, 90% of the participants stated that there is an approved drug for cCMVi, and the level of knowledge about the use of ganciclovir/valganciclovir in treatment was found to be quite high in all groups and in total (87.5%-93.2%). However, the lack of knowledge about the duration of treatment approaches is remarkable. Although pediatric residents were the group that most accurately stated the oral 6-month treatment period, the rate (51%) was quite low even in this group, while the overall rate remained at 40%. The rate of those not express any opinion is relatively high with 31.3%. The lack of knowledge on the duration of parenteral treatment is also quite evident, the rate of those who chose 6 weeks (39.9%) was higher than those who chose the other options, however it was similar with the rate of those who chose 3 weeks (24.9%) or did not express an opinion (24%), and there was no prominent group. The indication for initiating cCMVi treatment is currently considered all newborns with symptomatic cCMVi (19). In this study, this indication was marked with a significantly higher rate by the participants ($p = 0.003$), but it was still found to be proportionally low (52.8%). In this study, this indication was marked with a significantly higher rate by the participants ($p = 0.003$), but it was still found to be proportionally low (52.8%), the highest rate of correct answers is in group IV professionals (63.6%). It is also significant that one third of the participants marked the option “All infants diagnosed with cCMVi”, and it is a misinformation that can cause problems in the approach. In the answers about the expectations from the treatment, the “Long-term improvement in audiological and neurodevelopmental findings” option was marked more than the other options, but it is quite low (37.1%). Group III professionals were significantly higher among those who marked this option ($p = 0.027$). Group IV professionals are significantly higher in those who marked “Negativity in CMV viremia” (27.3%, $p = 0.015$). It is noteworthy that the rate of those who chose the “All option” was similar to those who chose the correct option (37.1% vs. 37.6%), but no difference was found between the groups. These results suggest that the exact expectation from cCMVi treatment among pediatricians is not understood.

The answer to the question about the most common disease-related sequelae was “hearing loss” with the highest rate

(65.7%). Other options are marked low. It is important that pediatricians know the most common disease-related sequelae, because the main benefit expected from treatment is shaped by targeting the sequelae.

This study has some limitations. Completing the questionnaire may have been subject to response bias, as respondents who were unsure of their knowledge of cCMVi may refuse to respond. For this reason, the actual results may be lower than the results presented in this report. Additionally, the participant ratio could have been higher to better reflect the country in general. As a shortcoming, the time elapsed from the baseline training on cCMVi and the additional training received after completing the pediatric training were not questioned.

The most significant knowledge gaps identified in this study were in the areas of cCMVi transmission, clinical findings, diagnostic tests and methods, and treatment of cCMVi. Wrong answers are notable not only in the group of residents who are in the education process, but also in the groups that are in the advanced stages of the pediatrics profession. In fact, it has been observed that the level of knowledge of residents in pediatrics is better in some areas. This seems to indicate that further educational efforts about cCMVi should target all levels of the pediatric profession not only during assistant training. In countries where cCMVi screening is not available like Turkey, it would be realistic to support clinicians' training on cCMVi and to be repeated at intervals to keep the information up-to-date.

REFERENCES

- Pesch MH, Schleiss MR. Emerging Concepts in Congenital Cytomegalovirus. *Pediatrics* 2022;150:e2021055896.
- Dobbins GC, Patki A, Chen D, Tiwari HK, Hendrickson C, Britt WJ, et al. Association of CMV genomic mutations with symptomatic infection and hearing loss in congenital CMV infection. *BMC Infect Dis* 2019;19:1046.
- Leruez-Ville M, Ville Y. Is it time for routine prenatal serological screening for congenital cytomegalovirus? *Prenat Diagn* 2020;40:1671-80.
- Kabani N, Ross SA. Congenital Cytomegalovirus Infection. *J Infect Dis* 2020;221(Suppl 1):S9-14.
- Ross SA, Kimberlin D. Clinical outcome and the role of antivirals in congenital cytomegalovirus infection. *Antiviral Res* 2021;191:105083.
- Chiopris G, Veronese P, Cusenza F, Procaccianti M, Perrone S, Daccò V, et al. Congenital Cytomegalovirus Infection: Update on Diagnosis and Treatment. *Microorganisms* 2020;8:1516.
- Kimberlin DW, Jester PM, Sánchez PJ, Ahmed A, Arav-Boger R, Michaels MG, et al. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Valganciclovir for symptomatic congenital cytomegalovirus disease. *N Engl J Med* 2015;372:933-43.
- Hosseinzadeh Adli A, Karami C, Baghban Rahimi S, Mirarab A, Tabarraei A. What family doctors know about congenital CMV: a regional survey in Iran. *Ital J Pediatr* 2018;44:31.
- Korver AM, de Vries JJ, de Jong JW, Dekker FW, Vossen AC, Oudesluys-Murphy AM. Awareness of congenital cytomegalovirus among doctors in the Netherlands. *J Clin Virol* 2009;46:S11-5.
- Fellah T, Sibiude J, Vauloup-Fellous C, Cordier AG, Guitton S, Grangeot-Keros L, et al. Evolution of awareness and knowledge of congenital cytomegalovirus infection among health care providers in France between 2011 and 2018. *J Clin Virol* 2020;129:104335.
- Okahashi A, Kobayashi M, Okuyama K, Hiraishi N, Morioka I. Survey of physician knowledge of congenital cytomegalovirus infection and clinical practices in Japan: A web-based survey. *Medicine (Baltimore)* 2021;100:e27589.
- Pesch MH, Anderson C, Mowers E. Improving Obstetric Provider Congenital Cytomegalovirus Knowledge and Practices. *Infect Dis Obstet Gynecol* 2020;2020:8875494.
- Dedhia K, Tomlinson J, Murray N, Park A. Congenital Cytomegalovirus and Hearing Loss: A Pilot Cross-Sectional Survey of Otolaryngologists' and Pediatric Otolaryngologists' Knowledge. *OTO Open* 2019;3:2473974X19849874.
- Şahiner F. Konjenital Sitomegalovirüs Enfeksiyonlarının Tanı ve Yönetiminde Güncel Yaklaşımlar ve Türkiye'deki Durum [Current Approaches in the Diagnosis and Management of Congenital Cytomegalovirus Infections and the Situation in Turkey]. *Mikrobiyol Bul* 2020;54:171-90.
- Coppola T, Mangold JF, Cantrell S, Permar SR. Impact of Maternal Immunity on Congenital Cytomegalovirus Birth Prevalence and Infant Outcomes: A Systematic Review. *Vaccines (Basel)* 2019;7:129.
- Muldoon KM, Armstrong-Heimsoth A, Thomas J. Knowledge of congenital cytomegalovirus (cCMV) among physical and occupational therapists in the United States. *PLoS One* 2017;12:e0185635.
- Baer HR, McBride HE, Caviness AC, Demmler-Harrison GJ. Survey of congenital cytomegalovirus (cCMV) knowledge among medical students. *J Clin Virol* 2014;60:222-42.
- Nicloux M, Peterman L, Parodi M, Magny JF. Outcome and management of newborns with congenital cytomegalovirus infection. *Arch Pediatr* 2020 ;27:160-5.
- American Academy of Pediatrics. Cytomegalovirus infection. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, (eds). *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. American Academy of Pediatrics: Itasca; IL 2018:310.

Comparison of Ambulance Usage Characteristics in Children Between the Pre-Pandemic and Pandemic Periods in Turkey

Türkiye’de Pandemi Öncesi ve Pandemi Dönemi Arasında Çocukların Ambulans Kullanım Özelliklerinin Karşılaştırılması

Eyüp SARI¹, İshak SAN², Burak BEKGÖZ³, Halise AKÇA^{3,4}

¹Department of Pediatrics, University of Health Sciences, Ankara, Turkey

²Department of Emergency Medicine, University of Health Sciences, Ankara, Turkey

³Department of Emergency Medicine, Bilkent City Hospital, Ankara, Turkey

⁴Ankara Yıldırım Beyazıt University, Faculty of Medicine, Department of Pediatric Emergency Medicine, Ankara, Turkey



ABSTRACT

Objective: A pandemic is an epidemic of an infectious disease that has spread across a large region of the world and affects many people. In this study, it was aimed to evaluate the impact of the coronavirus disease 2019 (COVID-19) pandemic on ambulance use by pediatric patients in Ankara Province, Turkey.

Material and Methods: This retrospective study was conducted in the spring-summer of 2019 and 2020. The electronic medical records of pediatric patients who were transported to the hospital by ambulance were analyzed.

Results: It was determined that 49.6% of the 23,201 patients included in the study were transported during the pandemic period. Male gender was higher in both the pandemic and pre-pandemic periods, there was no difference in terms of average age. The rate of forensic cases and refugee patients increased, while that of emergency patients decreased. Both the arrival at the scene time and intervention time were prolonged. Medical cause was the most common cause of emergency calls in both years, however, it increased significantly in 2020. The decrease in cases of traffic accidents, suicides, and other accidents was statistically significant. In the pandemic period, total rate of COVID-19 infection and suspicion was 29.7%. Most of the patients had been referred to a public hospital.

Conclusion: It was found that most of the ambulances were used for transporting patients with minor illnesses that did not require immediate medical attention in pandemic period.

Key Words: Ambulance, Child, COVID-19 pandemic, Pediatric emergency medicine

ÖZ

Amaç: Pandemi, dünyanın geniş bir bölgesine yayılan ve birçok insanı etkileyen bulaşıcı hastalık salgınıdır. Bu çalışmada, Türkiye’nin Ankara ilinde, 2019 koronavirüs hastalığı (COVID-19) pandemisinin çocuk hastaların ambulans kullanımına etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif çalışmada 2019 ve 2020 yıllarının bahar-yaz aylarında ambulans ile hastaneye nakledilen çocuk hastaların elektronik tıbbi kayıtları incelendi.



0000-0003-3020-5632 : SARI E
0000-0002-9658-9010 : SAN I
0000-0002-4183-9633 : BEKGÖZ B
0000-0003-4990-5735 : AKÇA H

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. Ethics committee approval was obtained from the Ankara City Hospital Clinical Research Ethics Committee-1 under number E1-20-1160.

Contribution of the Authors / Yazarların katkısı: **SARI E:** 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 logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. **SAN I:** 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 logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. **BEKGÖZ B:** 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 H:** 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.

How to cite / Atıf yazım şekli : Sari E, San I, Bekgöz B and Akça H. Comparison of Ambulance Usage Characteristics in Children Between the Pre-Pandemic and Pandemic Periods in Turkey. Turkish J Pediatr Dis 2023;17:182-186.

Correspondence Address / Yazışma Adresi:

Halise AKÇA
Department of Pediatric Emergency Medicine,
Ankara Yıldırım Beyazıt University, Faculty of Medicine, Ankara, Turkey
E-posta: haliseakca@gmail.com

Received / Geliş tarihi : 13.10.2022

Accepted / Kabul tarihi : 15.12.2022

Online published : 28.12.2022

Elektronik yayın tarihi

DOI: 10.12956/tchd.1179829

Bulgular: Çalışmaya alınan 23201 hastanın %49.6'sının pandemi döneminde nakledildiği belirlendi. Erkek cinsiyet hem pandemi hem de pandemi öncesi dönemlerde daha yüksekti, yaş ortalamaları açısından fark yoktu. Pandemi döneminde adli vaka ve mülteci hasta oranı artarken, acil hasta oranı azaldı. Hem olay yerine gelme süresi hem de müdahale süresi uzadı. Medikal nedenler her iki yılda da en sık acil çağrı nedeniydi, ancak 2020'de önemli ölçüde arttı. Trafik kazası, özkıyım ve diğer kaza vakalarındaki azalma istatistiksel olarak anlamlıydı. Pandemi döneminde toplam kesin ve şüpheli COVID-19 enfeksiyonu oranı %29.7'di. Hastaların çoğu devlet hastanesine sevk edildi.

Sonuç: Pandemi döneminde ambulansların çoğunun acil tıbbi müdahale gerektirmeyen hafif hastalığı olan hastaları taşımak için kullanıldığı tespit edildi.

Anahtar Sözcükler: Ambulans, COVID-19 pandemisi, Çocuk, Çocuk Acil Tıp

INTRODUCTION

A pandemic is an epidemic of an infectious disease that spread over countries or continents. An epidemic anywhere in the world is now a threat to all countries due to easier transportation. Throughout human history, there have been several pandemics of plague, cholera, and influenza. On 11 March 2020, the World Health Organization announced the spread of coronavirus disease 2019 (COVID-19) as a pandemic (1). Non-pharmaceutical interventions against COVID-19 including but not limited to social distancing, hand hygiene, wearing of face masks and self-quarantine were used to control the spread of the disease all over the world. This helps decrease the risk of health services being overwhelmed and provides more time for a vaccine and treatment to be developed (2).

The first confirmed case in Turkey was detected on 11 March 2020, which was the same day that the pandemic was declared. On 16 March 2020, educational institutions, and day care centers were closed across the country. In addition, a curfew was imposed for those under 20 years of age, from 3 April to 10 June 2020. The curfew for adults was held on weekends, starting on 10–12 April 2020. The normalization process started in June (1). In accordance with the policy of 'stay at home' to prevent the spread of COVID-19, a restriction was made for hospital outpatient visits. However, easy access to the Pediatric Emergency Department was provided.

Emergency calls in Turkey are a public service, and anyone can request an ambulance for free. Due to the health policies of the country, suspected or confirmed COVID-19 patients were transported to the hospital by ambulance and isolated so that they would not infect other people around them. Emergency aid ambulances are vehicles that have a team, and technical and medical equipment that can make the necessary emergency medical intervention at the scene and in the ambulance (3). During the current pandemic, emergency medical services have faced unprecedented challenges when transporting highly infectious patients in enclosed spaces. The smallness of the patient cabin in ambulances, insufficient ventilation, and the air conditioning system are risk factors in terms of infection transmission. There have been studies examining the advantages of air and ground ambulances in the transportation of trauma patients (4). Although the contact time with the patient is shortened in air ambulances, there is closer contact in the closed environment. Being unprepared is not an option and thoughtful detailed planning is key.

In this study, we aimed to evaluate the impact of the COVID-19 pandemic on emergency medical services used by pediatric patients in Ankara Province, Turkey.

MATERIALS and METHODS

This study was a retrospective, observational comparative study, which was conducted at Ankara the capital city of Turkey Emergency Medical Services. Electronic medical records of patients aged <18 years old, who were transported by ground ambulance, were examined between 1 May and 31 July 2020, and compared with those in the same period of the previous year. The exclusion criteria for this study were patients being >18 years of age and using private ambulances. Sociodemographic and clinical information of the patients, triage status, presence of forensic case, emergency call date, reason for calling an ambulance, response and intervention times were recorded. Response times were measured from the time of receiving an emergency call to the time that an ambulance arrived at the patient's location. The intervention time consisted of the time from the response of the teams at the scene until the patient was taken to the ambulance. Ethics committee approval was obtained from the Ankara City Hospital Clinical Research Ethics Committee-1 under number E1-20-1160.

Statistical analysis: All data were analyzed using IBM SPSS Statistics for Windows 20.0. (Armonk, NY: IBM Corp). To summarize the baseline demographic and clinical features, the descriptive statistics of the patients were analyzed. Data were expressed as the mean \pm standard deviation for the quantitative variables or number and percentage for the categorical variables. Categorical variables were compared using the chi square test. Median values and ranges were used for ordinal scaled or quantitative parameters. The student t test was used to compare the normally distributed variables of the 2 groups. The Mann-Whitney U test was used to compare quantitative or ordinary scaled variables. To analyze the proportions accurately, the chi square or Fisher exact tests was used. Each of these tests was 2-sided. $p < 0.050$ was considered statistically significant.

RESULTS

During the study period, a total of 23.201 patients were transported by ambulance, comprising 50.4% in 2019 and

Table I: Demographical characteristics of the patients.

	2019 (n = 11704)	2020 (n = 11497)	p
Gender			
Male	6522 (55.7)	6237 (54.2)	0.024 ^a
Female	5182 (44.3)	5260 (45.8)	
Age (years)			
Mean ± standard deviation			
All	9.4 ± 6.3	9.4 ± 6.2	0.469 ^b
Male	9.3 ± 6.2	9.2 ± 6.1	0.600 ^b
Female	9.5 ± 6.4	9.7 ± 6.3	0.128 ^b
p	0.017 ^b	0.000 ^b	
Refugee patients	408 (3.5)	1067 (9.3)	<0.001 ^a
Forensic case (yes)	2040 (17.4)	1270 (11.0)	<0.001 ^a
Triage (red tag)	726 (6.2)	599 (5.2)	0.001 ^a

^a: Chi square test (n, %), ^b: independent samples t test (mean ± SD)

Table II: Emergency call, response at scene, and intervention times

Emergency calls	2019 (n = 11704)	2020 (n = 11497)	p
Month			
May	4141 (35.4)	3718 (32.3)	<0.001 ^a
June	3648 (31.2)	3812 (33.2)	0.001 ^a
July	3915 (33.5)	3967 (34.5)	0.093 ^a
Day			
Weekdays	8772 (74.9)	7984 (69.4)	<0.001 ^a
Weekend	2932 (25.1)	3513 (30.6)	
Hour			
00:00–07:59	1741 (14.9)	2046 (17.8)	<0.001 ^a
08:00–15:59	4817 (41.2)	4169 (36.3)	<0.001 ^a
16:00–23:59	5146 (44.0)	5282 (45.9)	0.003 ^a
Response at scene time (min/s) mean ± SD	6.64 ± 8.67	7.73 ± 7.99	<0.001 ^b
Intervention time (min/s) mean ± SD	13.85 ± 20.32	15.12 ± 12.26	<0.001 ^b

^a: Chi square test (n, %), ^b: independent samples t test (mean ± SD)

49.6% in 2020. Demographical characteristics of the patients are shown in Table I. Male gender was higher during both the pandemic and pre-pandemic periods, while there was no difference in terms of average age. The rate of refugee patients increased from 3.5% in 2019 to 9.3% in 2020 (p<0.001), and the increase in Syrian and Iraqi refugee children was remarkable. There was a statistically significant decrease between the pre-pandemic and pandemic periods in terms of forensic case frequency (p<0.001). The number of patients with higher acuity levels called red tag, tended to decrease (p= 0.001).

Emergency call, response at the scene, and intervention times are shown in Table II. The frequency of emergency calls tended to decrease in May and increase in June. There were more calls in the evenings and nighttime, and on weekends in 2020 than the previous year. Both the response at scene times and intervention times were prolonged (p<0.001).

Medical cause was the most common cause of emergency calls in both years; however, it increased significantly in 2020

Table II: Comparison of emergency call causes.

	2019 (n = 11704)	2020 (n = 11497)	p ^a
Call causes			
Medical	5342 (45.6)	8618 (75.0)	<0.001
Traffic accidents	1494 (12.8)	877 (7.6)	<0.001
Injuries	327 (2.8)	278 (2.4)	0.083
Suicides	132 (1.1)	60 (0.5)	<0.001
Other accidents	1842 (15.7)	1378 (12.0)	<0.001
Other causes	2567 (21.9)	265 (2.3)	<0.001

^a: Chi square test (n, %)

Table IV: Comparison of final symptoms/affected systems.

Symptoms/diagnosis	2019 (n = 11704)	2020 (n = 11497)	p ^a
Suspected infection of COVID-19	-	1867 (16.2)	-
Infected with COVID-19	-	1554 (13.5)	-
Fever	750 (6.4)	357 (3.1)	<0.001
Respiratory system	912 (7.8)	400 (3.5)	<0.001
Cardiovascular system	713 (6.1)	372 (3.2)	<0.001
Gastrointestinal system	1042 (8.9)	866 (7.5)	<0.001
Neurological system	774 (6.6)	568 (4.9)	<0.001
Hematological system	145 (1.2)	143 (1.2)	0.973
Psychiatric causes	717 (6.1)	457 (4.0)	<0.001
Traumatic causes	4585 (39.2)	3306 (28.8)	<0.001
Poisoning	450 (3.8)	300 (2.6)	<0.001
Other causes	1548 (13.2)	1266 (11.0)	<0.001
Arrest	68 (0.6)	41 (0.4)	0.012

^a: Chi square test (n, %)

(p<0.001). The reduction in traffic accidents and other accidents was statistically significant (p<0.001) (Table III). Although there was a numerical decrease in injuries, it was not statistically significant. The decrease in suicide cases in 2020 was also statistically significant (p = 0.001).

The final symptoms and system involvement of the patients after intervention is shown in Table IV. In the 2020 pandemic period, the total rate of COVID-19 infection and suspicion was 29.7%. It affected all systems significantly, except for the hematological system. The effects on the systems were all in a decreasing trend.

The health centers where the patients were referred to comprised 64.7% Public Hospitals and 15.5% University Hospitals in 2019, respectively, and 71.5% and 12.7% in 2020. Ankara City Hospital was the hospital with the highest number of patients in both the pandemic and pre-pandemic periods (3442 patients (29.9%) in 2020, 1556 patients (13.3%) in 2019).

DISCUSSION

In this study, whether there was any difference in the use of ground ambulances for pediatric patients during the pandemic

period was evaluated. The total number of ambulance usage did not change due to the density of Covid infection patients. The need for ambulance transportation for trauma and high acuity level patients decreased. Also, there were significant differences in the demographic information, diagnosis, and call characteristics of the patients.

The mean age of the patients was similar to the pre-pandemic period. This can be explained by the fact that COVID-19 infection can be seen at any age. The increasing number of cases on Saturday and Sunday may have been due to the parents having a curfew on the weekends.

According to the January 2019 data in Turkey, there were around 3.5 million Syrian and 142 thousand Iraqi refugees. The proportion of children under the age of 18 was about half of the population, for both Syrian and Iraqi refugees (5). Due to war, poverty, and household dynamics, the living standards of the refugees were decreasing (6). In their study about refugees, Budak et al. (7) reported that they are a group who are not aware of the seriousness of the pandemic, who do not have enough information about the pandemic, and do not have access to personal protective equipment (such as masks or gloves). In our study, the increased frequency of ambulance usage by refugees during the pandemic may have been due to unhygienic and crowded living conditions.

Forensic cases in the pediatric age group generally consist of poisoning, trauma, and suicide (8). The decreased number of forensic cases in our study can be explained by the decrease in traffic accidents and suicide cases. The decrease in suicide cases during the pandemic period may have been due to different reasons. School closure may have caused the elimination of poor school success, which may be one of the reasons for suicidal tendency. In addition, the opportunity to spend more time with their families because of the curfew may have contributed positively. A significant increase in unintentional home accidents was reported in children during the school holidays when they spent so much time at home (9). However, there was a significant decrease in the number of poisoning cases observed in the study. This situation can be explained by the presence of the parents at home because of the curfew.

The ambulance response time was affected by incorrect address notification, distance to the patient, weather and climate changes, closed roads, and traffic density (10). In the pandemic period, there has been a significant increase in the response times of ambulances at the scene. In fact, it would be expected that the reduced traffic density due to the part-time work program and the curfew would shorten this period. The transport team should don appropriate personal protective equipment outside of the home of the patient before transport (11). The prolongation of the intervention time during the pandemic period can be explained by infection protection

methods. In Turkey, when there is an emergency call by phone, a conversation takes place about COVID-19 infection and the ambulance team is alerted accordingly. First at the scene, a person from the ambulance team goes to the scene and performs pre-triage. If the patient has a suspicion of COVID-19 infection, the other members of the team perform intervention after wearing personal protective equipment. Therefore, it takes time for the team to start intervention for the patient.

It has been reported that pediatric patients are most often transported due to breathing difficulties, trauma, and seizure (12-15). In studies conducted in Turkey regarding the use of pediatric ambulances in the pre-pandemic period, the most common symptoms have been trauma, fever, convulsion, and poisoning (16). Katayama et al. (17) reported that child traffic accident rates have decreased during the pandemic period (17). It was found that traffic accidents and other accidents decreased during the pandemic period when compared to the pre-pandemic period. The fact that all of the training activities were suspended, and curfews were implemented may have been effective in this decrease. The absence of a significant decrease in the number of injuries can be explained by domestic accidents.

During the pandemic period, 29.7% of all of patients in this study were infected with COVID-19. The respiratory and gastrointestinal system are frequently affected in COVID-19 (18). In our study, the absence of an increase in symptoms in these systems can be explained by the evaluation of these patients in the suspicion of COVID-19 group. The rate of fever seemed to have decreased, since the fever symptom is generally considered in the suspected or diagnosed disease group. Since the follow-up and treatment of hematology patients continued during the pandemic period, they did not require ambulance transfer.

Among the hospitals where the patients were referred to, the rate of University Hospitals decreased, while the rate of Public Hospitals increased. Among the Public Hospitals, the health center that accepted the most patient was Ankara City Hospital. This situation can be explained by the physical suitability of City Hospitals and it being a Pandemic Hospital.

LIMITATIONS

This study was a retrospective, observational study, and there could be some unknown confounding factors due to the study type. The final diagnoses and prognoses in-hospital were unknown. The characteristics of other accidents were not given in detail. Therefore, the frequency of possible domestic accidents could not be determined. Private ambulance data could not be evaluated because only Ankara Provincial Health Directorate Emergency Medical Service data were used in the study. The beginning of the study period was not the same as the beginning of the pandemic in our country. It would be

more appropriate to start the study on March 11, when the first case was seen in our country. However, due to the availability of data, the study could only be started on 11 May.

CONCLUSION

The impact of the COVID-19 pandemic on the emergency medical service system was assessed, and it was found that most of the ambulances have been used for transporting patients with minor illnesses that did not require immediate medical attention. Future studies may include in-ambulance interventions and hospital procedures.

REFERENCES

1. T. C. Ministry of Health Covid-19 Guide. 29 June 2020. Available from: <https://covid19.saglik.gov.tr/>
2. Regmi K, Lwin CM. Impact of non-pharmaceutical interventions for reducing transmission of COVID-19: a systematic review and metaanalysis protocol. *BMJ Open* 2020;10:e041383.
3. Ambulances and Emergency Health Vehicles and Ambulance Services Regulation. Turkey Official Gazette. 07.12.2006; Issue: 26369.
4. Starnes AB, Oluborode B, Knoles C, Burns B, McGinnis H, Stewart K. Direct Air Versus Ground Transport Predictors for Rural Pediatric Trauma. *Air Med J* 2018;37:165-9.
5. Operational Portal Refugees Situations. 14 Oct 2020. Available from: <https://data2.unhcr.org/en/situations/syria/location/113>.
6. Gül SS, Türkmen E. Ulisa. Being Syrian Refugee Children in Turkey: Remaining Outside of Education, Falling Behind the Dreams. *Ulisa: Journal of International Studies* 2019;3:114-31.
7. Budak F, Bostan S. The Effects of Covid-19 Pandemic on Syrian Refugees in Turkey: The Case of Kilis. *Social Work in Public Health* 2020;35:579-89.
8. Korkmaz MF, Bostancı M, Tutaç M. An Evaluation of the Hospitalized Pediatric Forensic Cases at a Tertiary Hospital. *J Pediatr Emerg Intensive Care Med* 2019;6:140-5.
9. Al Rumhi A, Al Awisi H, Al Buwaiqi M, Al Rabaani S. Home Accidents among Children: A Retrospective Study at a Tertiary Care Center in Oman. *Oman Med J* 2020;35:e85.
10. Thornes JE, Fisher PA, Rayment-Bishop T, Smith C. Ambulance call-outs and response times in Birmingham and the impact of extreme weather and climate change. *Emerg Med J* 2014;31:220-8.
11. Yousuf B, Sujatha KS, Alfoudri H, Mansurov V. Transport of critically ill COVID-19 patients *Intensive Care Med* 2020;46:1663-4.
12. Lerner EB, Studnek JR, Fumo N, Banerjee A, Arapi I, Browne LR, et al. Multicenter Analysis of Transport Destinations for Pediatric Prehospital Patients. *Acad Emerg Med* 2019;26:510-6.
13. Overgaard MF, Heino A, Andersen SA, Thomas O, Holmén J, Mikkelsen S. Physician staffed emergency medical service for children: a retrospective population-based registry cohort study in Odense region, Southern Denmark. *BMJ Open* 2020;10:e037567.
14. Drayna PC, Browne LR, Guse CE, Brousseau DC, Lerner EB. Prehospital Pediatric Care: Opportunities for Training, Treatment, And Research. *Prehosp Emerg Care* 2015;19:441-7.
15. Mönür M, Gülen M, Avcı A, Satar S. Evaluation of patients admitted to pediatric emergency service by 112 ambulance. *Med J Bakirkoy* 2018;14:253-62.
16. Güngör A, Hanalioğlu D, Türk NE, Catak A. Evaluation of Patients Presenting to Pediatric Emergency Department using a Ground Ambulance. *J Pediatr Emerg Intensive Care Med* 2020;7:19-23.
17. Katayama Y, Kiyohara K, Kitamura T, Hayashida S, Shimazu T. Influence of the COVID-19 pandemic on an emergency medical service system: a population-based, descriptive study in Osaka, Japan. *Acute Med Surg* 2020;7:e534.
18. Tezer H, Demirdağ TB. Novel Coronavirus Disease (Covid-19) In Children. *Türk J Med Sci* 2020;50:592-603.

The Efficacy of Erythrocyte Transfusion in Very Low Birth Weight Infants with Premature Anemia

Prematüre Anemisi Olan Çok Düşük Doğum Ağırlıklı Bebeklere

Eritrosit Transfüzyonunun Etkisi

Aybüke YAZICI¹, Betül SİYAH BİLGİN¹, Ahmet Serkan ÖZCAN², Sevim ÜNAL¹

¹Department of Neonatology, Ankara City Hospital Ankara, Turkey

²Department of Child Health and Diseases, Ankara City Hospital, Ankara, Turkey

ABSTRACT

Objective: This study aimed to determine the clinical efficacy of erythrocyte transfusion (ET) in premature infants.

Material and Methods: Very low birth weight (VLBW) infants with gestational age (GA) < 32 weeks and/or birth weight (BW) <1500 g and hospitalized in neonatal intensive care unit (NICU) between 2012-2018 were retrospectively evaluated. ET was performed according to Ohls 2007 and Turkish Neonatology Society Blood Products Transfusion Guidelines.

Results: 72 infants included in this study. Mean BW was 1325 g (680-2290 g), GA was 30 weeks (25-32), median postnatal age was 36.7±26.9 days (8-129), number of ET during hospitalization was 2±1.2 (1-6). There were no significant changes in mean heart rates (p=0.183) and median respiratory rates before and after ET (p=0.123). Weight gain (16 g/day-11 g/day) was statistically similar before and after ET (p=0.861). A significant decrease in apnea, non-invasive ventilation (NIV) and caffeine therapy requirements after ET was determined (p<0.001, p=0.016 and p=0.016). Serum lactate (2.9-1.5) levels were decreased by ET (p=0.017).

Conclusion: Premature infants should closely follow-up for anemia and related symptoms during NICU stay. ET may help to decrease frequency of apnea of prematurity, requirements of caffeine therapy and NIV. ET improves tissue oxygenation in VLBW infants with anemia. Decision of ET should be made according to severity of symptoms, and should be performed according to international, national or local transfusion guidelines.

Key Words: Anemia, Erythrocyte transfusion, Premature

ÖZ

Amaç: Bu çalışmada prematüre bebeklerde eritrosit transfüzyonunun (ET) klinik etkisinin araştırılması amaçlandı.

Gereç ve Yöntemler: 2012-2018 yılları arasında yenidoğan yoğun bakım ünitesinde (YYBÜ) takip edilen ve gestasyonel haftası (GH)< 32 hafta ve/veya doğum ağırlığı (DA) < 1500 g olan çok düşük doğum ağırlıklı (ÇDDA) bebekler retrospektif olarak değerlendirildi. ET, Ohls 2007 ve Türk Neonatoloji Derneği Kan Ürünleri Transfüzyon Rehberi'ne göre yapıldı.

Bulgular: 72 hasta çalışmaya dahil edildi. Ortalama DA 1325 g (680-2290 g), GH 30 hafta (25-32), ortanca postnatal yaş 36.7±26.9 gün (8-129), hastanede yatış sırasındaki ET sayısı 2±1.2 (1-6)'dı. ET öncesi ve sonrası ortalama kalp hızlarında (p=0.183) ve medyan solunum hızlarında (p=0.123) anlamlı bir değişiklik yoktu. Kilo alımı (16 g/gün-11 g/gün), ET'den önce ve sonra istatistiksel olarak benzerdi (p=0.861). ET sonrası apne, non-invaziv ventilasyon (NIV) ve kafein tedavisi gereksinimlerinde anlamlı azalma saptandı (p<0.001, p=0.016 ve p=0.016). Serum laktat (2.9-1.5) seviyeleri ET ile azaldı (p=0.017).

Sonuç: Prematüre bebekler, YYBÜ'de kaldıkları süre boyunca anemi ve ilgili semptomlar açısından yakın takip edilmelidir. ET prematüre apne sıklığını, kafein tedavisi ve NIV gereksinimlerini azaltmaya yardımcı olabilir. ET anemili ÇDDA



0000-0001-9387-0029 : YAZICI A
0000-0003-3807-4809 : SİYAH BİLGİN B
0000-0002-5538-8888 : ÖZCAN AS
0000-0002-7863-1924 : ÜNAL S

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 Clinical Research Ethics Committee of Ankara Pediatrics Hematology Oncology Training and Research Hospital (2019-016/18.02.2019).

Contribution of the Authors / Yazarların katkısı: **YAZICI A:** 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. **SİYAH BİLGİN B:** Taking responsibility in the writing of the whole or important parts of the study. **ÖZCAN AS:** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. **ÜNAL S:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Yazıcı A, Siyah Bilgin B, Özcan AH and Ünal S. The Efficacy of Erythrocyte Transfusion in Very Low Birth Weight Infants with Premature Anemia. Turkish J Pediatr Dis 2023;17:187-193.

Correspondence Address / Yazışma Adresi:

Aybüke YAZICI
Department of Neonatology, Ankara City Hospital Ankara, Turkey
E-posta: aybukeyzc07@gmail.com

Received / Geliş tarihi : 14.11.2022
Accepted / Kabul tarihi : 21.12.2022
Online published : 17.01.2022
Elektronik yayın tarihi
DOI:10.12956/tchd.1204367

bebelerde doku oksijenasyonunu düzeltir. ET kararı semptomların şiddetine göre verilmeli ve uluslararası, ulusal veya yerel transfüzyon rehberlerine göre yapılmalıdır.

Anahtar Sözcükler: Anemi, Eritrosit Transfüzyonu, Prematüre

INTRODUCTION

Increased tissue oxygenation following onset of postnatal breathing causes closure of ductus arteriosus, suppression of erythropoietin (EPO) production and reduction of erythropoiesis (1-3). In premature infants, anemia develops earlier than term babies and causes more clinical symptoms. Blood loss due to phlebotomy, low erythrocyte life expectancy and decreased iron contribute to the development of anemia in premature infants. Volume of blood for laboratory analysis increases according to severity of infant's disease and low gestational age (4-7).

Approximately, 50-95% of low birth weight (<1500 g) and 95% of extremely low birth weight (<1000 g) infants receive erythrocyte transfusion (ET) at least once during their stay in neonatal intensive care unit (NICU) after birth (8,9). ET administered to 90% of extremely low birth weight and 58% of premature infants with gestational age <32 weeks (10-13). Transfusion increases amount of circulating hemoglobin, improves tissue oxygenation, maintains same oxygen level by decreasing cardiac output (10, 14). It is also associated with increased morbidity and mortality in infants with bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC) and intra-ventricular hemorrhage (IVH) (15-18).

In this study, evaluating benefits of ET on clinical findings and it's relation to BPD, ROP, NEC and IVH in very low birth weight (VLBW) infants with gestational age (GA) equal or below 32 weeks and/or birth weight (BW) equal or below 1500 g were aimed. Improvement of symptoms secondary to anemia particularly heart rate (HR), apnea, respiratory rate (RR) and daily weight gain were analysed before and after ET. Indications of ET and factors affecting number of transfusion were also reviewed.

MATERIALS and METHODS

All of VLBW infants with GA \leq 32 weeks and/or BW \leq 1500 g and hospitalized in our unit between 2012-2018 were retrospectively evaluated (Health Sciences University, Ankara Children's Hematology Oncology Research Hospital). As there is no maternity unit in our hospital, all of patients were transported from other NICUs. Congenital anomalies (esophageal atresia 11, hydrocephalus 4, sacrococcygeal teratoma 2, anal atresia 8, gastroschisis 3, gonadal dysgenesis 4), congenital genetic (trisomy 21 5, trisomy 18 2, Pierre robin syndrome 2, trisomy 13 1, arthrogyrosis multiplex congenita 2, Smith-lemli-opitz syndrome 1), cardiac (congenital aortic stenosis 1, atrioventricular malformation 1, tetralogy of fallot 2) and metabolic disease (congenital lactic acidosis 2) were excluded. Infant's BW, GA, Apgar score, SNAP-PE II score, postnatal age, umbilical vein catheterization (UVK), number of ET, indication for

ET, length of hospitalization, requirement of respiratory support [invasive mechanical ventilation, non-invasive ventilation (NIV)], RDS, ROP, BPD, NEC, patent ductus arteriosus (PDA), IVH, sepsis, problems encountered during transfusion, mother's concomitant disease and hemoglobin (Hb) level were recorded. Infant's concurrent body weight, apnea, caffeine therapy, arterial blood gases, Hb - hematocrit (htc) levels, HR and RR before and after ET during 72 hours were determined.

Indications for ET classified as low Hb level (only anemia), recurrent apnea of prematurity, continuous tachycardia, low oxygen saturation, respiratory failure and suspected sepsis. An apneic episode was defined as a pause in breathing for more than 20 seconds. Severe apnea episodes required bag-mask ventilation, placement on continuous positive airway pressure, or reintubation during management of the episode (19). Tachycardia was defined as HR > 180 beat/minute at least 24 hours. Low oxygen saturation was defined as the infant's increasing oxygen requirement or oxygen saturation lower than target (<88%). Respiratory failure was defined as infant's pressure requirement to maintain target saturations. If infant was hypotonic, hypoactive and had low tissue perfusion at any time, we suspected sepsis. Then, blood culture, hemogram, peripheral smear, acute phase reactants were analysed and empirical antibiotics were administered. Diagnosis of NEC was based on systemic, laboratory and radiographic findings. It's severity was assessed by modified Bell's staging (20). Diagnosis of IVH was made by ultrasound and graded according to Papile's classification (21). ROP screening was performed by ophthalmologist and classified according to International Classification of Retinopathy of Prematurity (22). Diagnostic criteria of BPD were based on those described in National Institutes of Health Workshop (23). Diagnosis of PDA was made by echocardiography within first 24-72 hours with presence of significant PDA (left atrium / aortic root \geq 1.5 and/or ductus diameter \geq 1.5 mm) and presence of clinical findings (24). Ibuprofen and/or paracetamol were applied for PDA closure.

Erythrocyte transfusion was performed according to Ohls 2007 and Turkish Neonatology Society Blood Products Transfusion Guidelines (25,26). Transfusion decision was made by attending neonatologist according to infant's postnatal age, clinical findings and htc level. All infants were provided daily energy intake higher than 100 kcal/kg and at least 70% by enteral nutrition. ABO and Rh appropriate, leukocyte reduced and irradiated erythrocyte suspension was administered at a dose of 15-20 cc/kg in between 2-4 hours. Patients were divided into single or multiple transfused groups, to determine factors effecting number of ET. The patients transfused only once were defined as group 1, and multiple transfused patients were defined as group 2.

The study was approved by the Clinical Research Ethics Committee of Ankara Pediatrics Hematology Oncology Training and Research Hospital (2019-016/18.02.2019).

Statistical Analysis

Statistical analysis was performed by SPSS (Statistical Package for the Social Sciences) computer pocket program (21.0). Distribution of the numerical variables was investigated with Levene and Kolmogorov-Smirnov tests. Descriptive statistics were shown as mean \pm standard deviation or median (minimum-maximum) for continuous numerical variables, as number of cases and % for categorical variables. If parametrical test statistic assumptions were not provided between groups, significance of the difference for continuous numerical variables was examined by Kruskal Wallis test. Spearman's sequence numbers were investigated by correlation test, whether there was a statistically significant correlation between continuous numerical variables. Categorical variables were analysed by means of Exact Test of probability with Chi-Square or Fisher's Continuity Correction.

Significance of change in Hb and hct levels after transfusion was evaluated by dependent t-test. Improvement in apnea, decrease in requirements of NIV and caffeine therapy after transfusion were investigated by McNemar test. A statistically significant change in mean HR and RR, between periods of 72 hours before and after ET, was evaluated by Variance Analysis in Repetitive Measurements using Wilks' Lambda test. Data were analysed by IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). Results for $p < 0.050$ were considered statistically significant.

RESULTS

During study period, there were 135 VLBW infants. Twelve infants died within 21 days of age (sepsis 3, NEC 3, respiratory failure

4, IVH 1 and renal failure 1). Infants with congenital anomalies and inborn error of metabolism were excluded, 72 infants were included in the study. Among them, 33.6% was female and 66.4% was male. Ratio of patients born by spontaneous vaginal delivery was 18.1%. Ratios of mothers with single and multiple pregnancies were 69.4%, 30.6% respectively. Mean BW was 1325 g (680-2290 g), GA was 30 weeks (25-32), median postnatal age was 36.7 ± 26.9 days (8-129), number of ET during hospitalization was 2 ± 1.2 (1-6). Antenatal steroid therapy had not been administered to 79.2% of mothers, besides 1 and 2 doses had been administered to 12.5% and 8.3% of mothers respectively. There was no statistically difference between number of ET and mother's gestational diabetes mellitus, preeclampsia, cervical insufficiency, thyroid disease, anemia, oligohydroamnios, urinary tract infection, premature rupture of membranes, placental detachment and in-vitro fertilization pregnancy ($p > 0.050$), except hypertension during pregnancy ($p = 0.026$), (Table I).

Results of laboratory analysis (Hb, htc, lactate, HCO_3), weight changes, apnea of prematurity, HR and RR were examined before and after ET. There was statistically significant increase in hemoglobin ($8.47 \pm 1.31/12.22 \pm 2.17$) and hematocrit levels ($25.09 \pm 3.85/35.99 \pm 6.78$) after ET ($p < 0.001$, $p < 0.001$). Weight gain (16 g/day - 11 g/day) was statistically similar before and after ET ($p = 0.861$). There was statistically significant decrease in lactate (2.9-1.5) and statistically significant increase in HCO_3 levels (20.2-22.3) after ET ($p = 0.041$, $p = 0.017$). There was statistically significant decrease in apnea, NIV and caffeine therapy requirements after ET ($p < 0.001$, $p = 0.016$ and $p = 0.016$) (Table II).

Patient's mean HR and RR were recorded during 0-72 hours before and after ET. There was no significant changes in mean HRs ($p = 0.183$) and median RRs before and after ET ($p = 0.123$) (Table III).

Table I: The relation between the maternal characteristics and the number of transfusions.

Maternal characteristics	Absent		Present		p [‡]
	n	Number of ET* Mean \pm SD [†]	n	Number of ET* Mean \pm SD [†]	
Gestational diabetes mellitus	69	2.1 \pm 2	3	2 \pm 0	0.466
Hypertension	63	1.9 \pm 2	9	218 \pm 1.39	0.026
Preeclampsia	65	2.1 \pm 2.1	7	2 \pm 0.8	0.448
Cervical insufficiency	70	2.1 \pm 2	2	1.5 \pm 0.7	0.704
PROM [§]	61	2.2 \pm 2.1	11	1.5 \pm 0.5	0.188
Thyroid disease	67	2 \pm 1.9	5	2.8 \pm 1.8	0.297
History of maternal anemia	70	2.1 \pm 2	2	2.5 \pm 0.7	0.268
Oligohydramnios	69	2.1 \pm 2	3	1.7 \pm 1.2	0.689
Urinary infection	67	2.1 \pm 2	5	1.6 \pm 0.9	0.561
Plasental abruption	70	2.1 \pm 2	2	2 \pm 0	0.570
Invitro fertilization	65	2.1 \pm 2	7	2.1 \pm 1.3	0.559

*ET: Erythrocyte transfusion, *SD: Standard deviation, ‡Spearman's rank-order correlation test, §PROM: Premature rupture of membrans.

Table II: The clinical and laboratory findings of the patients before and after erythrocyte transfusion.

Finding	Before transfusion	After transfusion	Difference	p
Hemoglobin	8.47±1.31	12.22±2.17	3.75±1.93	<0.001*
Hematocrit	25.09±3.85	35.99±6.78	10.9±6.35	<0.001
Weight gain	16 (-75 – 80)	11 (-90–130)	0 (-110 – 200)	0.861*
Lactate	2.9 (1.0-5.6)	1.5 (0.7-7.3)	-0.85 (-4.9 – 2)	0.041*
HCO ₃	20.2 (14.8-26.1)	22.3 (15.8-25.2)	1 (-0.9 – 6.4)	0.017*
Apnea of prematurity	12 (17.1) [‡]	1 (1.4) [‡]	11 (15.7) [‡]	<0.001 [†]
NIV [§]	9 (12.7) [‡]	2 (2.8) [‡]	7 (9.9) [‡]	0.016 [†]
Caffeine therapy	23 (32.4) [‡]	16 (22.5) [‡]	7 (9.9) [‡]	0.016 [†]

*Wilcoxon Signed test, †McNemar test, ‡ (%), §NIV: Non-invasive ventilation

Table III: The heart and respiratory rates before and after erythrocyte transfusion.

Time	Heart rate	P	Respiratory rate	P
Before transfusion		0.183 [†]		0.123 [†]
48-72. hours	144±10.6		41 (40-57)	
24-48. hours	147.2±11.2		45 (40-59)	
0-24. hours	148.8±13		47 (40-64)	
After transfusion				
0-24. hours	147.7±11.4		46 (40-70)	
24-48. hours	145.3±11.2		44 (40-72)	
48-72. hours	141.6±10.6		43 (40-72)	

†Mean±standard deviation, ‡Median (minimum-maximum), †Variance Analysis, Wilks's Lambda test, *Friedman test

Table IV: The relation between patient's clinical characteristics and number of erythrocyte transfusion.

Clinical characteristics	Correlation Coefficient	p*
Birth weight	-0.401	<0.001
Gestational age	-0.368	<0.001
Apgar score at 1 st minute	-0.428	<0.001
Apgar score at 5 th minute	-0.328	0.011
Duration of hospitalization	0.568	<0.001
Bronchopulmonary dysplasia	0.336	0.004
Necrotizing enterocolitis stage 2-3	0.273	0.020
Intra-ventricular hemorrhage grade 2-4	0.032	0.789
Retinopathy of prematurity stage 2-5	0.255	0.031
SNAP-PE II score	0.222	0.063
Additional oxygen duration	0.380	<0.001
Respiratory support	0.369	0.032
Hemoglobin at birth	-0.123	0.390
Hematocrit at birth	-0.125	0.383

*Spearman's sequence numbers correlation test

Most common cause of ET was only anemia without accompanying symptoms (45.8%). These patient's Hb and/or htc levels were below limits suggested by Ohls 2007 and Turkish Neonatology Society Blood Products Transfusion Guidelines. Other indications for ET were recurrent apnea of prematurity (16.7%), suspected sepsis (16.7%), low oxygen saturation (13.9%), continuous tachycardia (4.2%) and respiratory failure

Table V: The number of erythrocyte transfusion and patient's clinical features.

Clinical feature	n	Absent		Present		p [†]
		Mean±SD*	n	Mean±SD*	n	
Apnea of prematurity	36	1.5±0.6	36	2.7±2.6	<0.001	
Bronchopulmonary dysplasia	59	1.7±0.9	13	3.6±3.9	0.007	
Necrotizing enterocolitis 2-3	48	1.7±0.8	24	2.8±3.1	0.031	
Intra-ventricular hemorrhage 2-4	57	2.1±2.1	15	1.9±1.1	0.817	
Retinopathy of prematurity 2-5	62	1.7±0.8	10	4.2±4.5	0.032	
Suspected sepsis	18	1.3±0.6	54	2.3±2.2	0.004	
Patent ductus arteriosus	37	1.5±0.8	35	2.6±2.6	0.003	
Umbilical vein catheter	40	1.6±0.8	32	2.7±2.7	0.003	

n: Number of patient, *SD: Standard deviation, †Mann Whitney U test

(2.8%), respectively. Mean duration of respiratory support after ET was 6 days (1-40 days). Decrease of BW, GA, and Apgar scores increased number of ET significantly (p <0.050). Besides, number of ET was significantly increased by advanced stages of BPD, NEC and ROP, prolonged hospital stay, oxygen and mechanical ventilation (MV) supports (p <0.050). However, there was no significant correlation between Hb and htc levels at birth, SNAP-PE II score, IVH degree and number of ET (p <0.050) (Table IV).

There was no significant association between number of ET and sex, delivery route, single/multiple pregnancy (p >0.050). Number of ET and nutritional content (breast milk and fortification, formula or mixed feeding) was also not related (p >0.050, Kruskal Wallis test). The presence of apnea, BPD, NEC, ROP, suspected sepsis, PDA and UVK was significantly increased with number of ET (p <0.050). There was no significant difference between number of ET and spontaneous or drug induced closure of ductus arteriosus (Table V).

Although incidence of BPD, NEC, IVH and ROP was higher in multiple transfused infants; relation was statistically insignificant between the groups (p >0.050) (Table VI).

Table VI: The relation between significant prematurity related disorders and the number of erythrocyte transfusion.

Disease	Single transfusion (n=31)	Multiple transfusion (n=41)	P
Bronchopulmonary dysplasia,*	2 (6.5)	11 (26.8)	0.055 [†]
Necrotising enterocolitis 2-3,*	8 (25.8)	16 (39)	0.355 [†]
Intra-ventricular hemorrhage 2-4,*	6 (19.4)	9 (22)	>0.999 [†]
Retinopathy of prematurity 2-5,*	3 (9.7)	7 (17.1)	0.499 [‡]

*: n(%), [†]Chi-square Exact test of Probability, [‡]Fisher's Continuity Correction

DISCUSSION

Premature infants born ≤ 32 weeks or birth weight ≤ 1500 g and administered erythrocyte transfusion with diagnosis of premature anemia during hospital stay in our neonatal intensive care unit were analysed to determine clinical efficacy of ET transfusion. Frequency of apnea of prematurity, requirements of caffeine therapy and respiratory support were decreased following ET. Besides, serum lactate levels were decreased and HCO_3^- levels were increased after ET. Heart and respiratory rates during 72 hours before and after ET were not changed. Although, optimal nutritional support was provided, weight gain of infants were not different before and after transfusion. There were more infants with advanced stages of NEC, BPD, IVH and ROP in multiple transfusion group, but this was statistically insignificant.

Physiologic anemia develops much earlier in premature infants due to physiological and iatrogenic factors. Erythropoietin (EPO) levels in premature infants are low and their responses to EPO are insufficient. Besides, short life of erythrocytes, rapid growth of infant, frequent blood sampling, accompanying diseases such as sepsis and malnutrition are factors that increase the risk of premature anemia (1,5,27). HbF level is high and 2,3 diphosphoglycerate level is low in premature infants. As HbF has a high affinity to oxygen, tissue hypoxia can be more pronounced. For all these reasons, most of premature infants have been transfused before 3 months of old (28). We thought that VLBW infants should be monitored in the NICU. It is important to reduce the number of phlebotomies, because the most common cause of ET in VLBW infants is frequent blood samplings. Blood sampling should be collected in microcollection tube, blood gas analysis in capillary tube.

Anemia of prematurity can cause tachycardia, inadequate weight gain, increase oxygen need and apnea or bradycardia (13,27,29). In premature infants, anemia becomes symptomatic when imbalance develops between its distribution and consumption. For that reason, symptoms appear at different Hb levels in each premature infant (30). Higher Hb values may be required in infants with cardio-pulmonary or severe diseases. Kasat et al. (31) noticed that tachycardia was the most sensitive predictor of anemia and ET improved apnea, bradycardia, desaturation, tachycardia and oxygen requirements. In this study, indication for ET was only anemia, determined by routine

blood sampling for 45.8% of the patients. Other causes of transfusion were apnea of prematurity (16.7%), suspected sepsis (16.7%), low oxygen saturation (13.9%), tachycardia (4.2%) and respiratory failure (2.8%). Priya also reported that the most common indication of ET was anemia (32). Although maternal factors were not found to be effective on ET in Priya's study, maternal hypertension was found to be effective on ET in our study.

Lowest hemoglobin value in which tissue oxygenation can normally be maintained is defined as critical or threshold of hemoglobin value. Transfusion decision is frequently made according to this value and accompanying clinical findings. Therefore, lower limits of Hb for transfusion should be individualized according to the patient's symptoms, requirements of respiratory and circulatory support. Since there is no clear marker of tissue oxygenation, it is important to know clinical symptoms (3,33). Premature infants should be closely monitored for symptoms related to anemia. ET should be performed in case of clinical necessity and in accordance with transfusion guidelines. Due to increased lactate level and reduction of lactate following ET in infants with premature anemia; we proposed that lactate is a good marker for tissue perfusion in infants with premature anemia.

We determined that ET decreased frequency of apnea of prematurity, NIV and caffeine requirements in VLBW infants. This might be explained by improved tissue oxygenation in central nervous system. There are studies with and without improvement of apnea of prematurity by ET (6,14). We found that HR and RR were not different throughout 72 hours before and after ET. Although nutritional support was adequate, there was no difference in weight gain of VLBW infants followed by ET. There were conflicting results related to weight gain following ET in premature infants. Studies reported both increment and no increment in weight gain following ET (34,35). Nelle et al. (35) described a significant HR drop (from 161 to 149 beats per min) in 33 premature infants followed by ET. Lachance et al. (36) also reported HR drop (from 155 ± 10 to 146 ± 7 beats per min) in 12 premature infants after ET. Similar to our results, Dani et al. (37) (n=14) and Alkalay et al. (38) (n=32) found no difference in HR of premature infants followed by ET. We proposed ET should be individualised and considered according to severity of clinical symptoms in VLBW infants with premature anemia.

Erythrocyte transfusion increases amount of circulating Hb, improves tissue oxygenation, decreases cardiac output, improves blood pressure of infants on MV and improves oxygenation (2,14,30). Studies stated the less BW and GA, the higher need of ET (28). We showed as BW, GA and Apgar scores were decreased, number of ET was increased. We found a positive correlation between ET number and length of hospitalization, supplemental oxygen and respiratory support. Mimica identified increased number of ET with duration of MV (39). Santos determined an association between in number of ET and SNAP-PE II score, moderate-severe IVH, NEC and BPD (40). We determined that apnea, BPD, NEC, ROP, suspected sepsis, PDA and UVC increased number of ET. We thought that increased hospital stay might be related to severity of infant's diseases, lower BW, increased blood sampling and energy requirement due to rapid growth. Both degree of prematurity and iatrogenic causes might be more evident in extreme premature infants. It should be emphasized that unnecessary blood sampling should be avoided.

Besides benefits, there are risks and concerns that erythrocyte transfusion causing development of BPD, ROP, NEC, IVH in premature infants with high morbidity and mortality (2,11,12). The risk-benefit profile for red cell transfusions to treat anaemia is uncertain. It has been suggested that there is frequent iron overload with ET, increasing oxidative stress, developing free radicals and damaging premature lung, intestine and retina (16,28). On the other hand, ET and BPD, ROP, NEC were reported to be irrelevant (6). In some studies, infant's ROP and cranial USG findings in the liberal and restricted groups had not been different (41). Similarly, we found that BPD, NEC, IVH and ROP were not different in the single and multiple ET groups. The implementation of neonatal blood transfusion guidelines should reduce number of transfusion in VLBW infants.

CONCLUSION

Premature infants should closely follow-up for anemia and related symptoms during hospital stay. Erythrocyte transfusion may help decrease frequency apnea of prematurity, requirements of caffeine therapy and respiratory support. ET improve tissue oxygenation in VLBW infants with anemia. However, we found that ET has no effect on weight gain, HR and RR. Infant's disease severity, GA and BW should increase number of ET. Nevertheless BPD, NEC, IVH and ROP were not related to ET. As the potential risks, decision of ET should be individualised. Infant's clinical findings, diseases, treatments, oxygen/pressure support, Hb and/or htc levels, BW, GA and postnatal age should be carefully considered. Decision of ET should be made according to severity of symptoms, and should be performed according to international, national or local transfusion guidelines.

REFERENCES

- Dumitrescu MP, Tanaka DT, Spears TG, Daniel CJ, Kumar KR, Athavale K, et al. Patterns of phlebotomy blood loss and transfusions in extremely low birth weight infants. *J Perinatol* 2019;39:1670-5.
- Dik PHB, Galletti MF, Carrascal MP, Gregorio AD, Pratz LB, Saldano AG, et al. Impact of the volume of blood collected by phlebotomy on transfusion requirements in preterm infants with birth weight of less than 1500 g. A quasi-experimental study. *Arch Argent Pediatr* 2020;118:109-16.
- Bell EF. Red cell transfusion thresholds for preterm infants: finally some answers. *Arch Dis Child Fetal Neonatal Ed* 2022;107:126-30.
- Balasubramanian H, Malpani P, Sindhur M, Kabra NS, Ahmed J, Srinivasan L. Effect of umbilical cord blood sampling versus admission blood sampling on requirement of blood transfusion in extremely preterm infants: a randomized controlled trial. *J Pediatr* 2019;211:39-45
- Meyer MP, O'Connor KL, Meyer JH. Thresholds for blood transfusion in extremely preterm infants: a review of the latest evidence from two large clinical trials. *Front Pediatr* 2022;20;10:957585.
- Kirpalani H, Bell EF, Hintz SR, Tan S, Schmidt B, Chaudhary AS, et al. Higher or lower hemoglobin transfusion thresholds for preterm infants. *N Engl J Med* 2020;383:2639-51.
- Lopriore E. Updates in red blood cell and platelet transfusions in preterm neonates. *Am J Perinatol* 2019;36:37-40.
- Benavides A, Bell EF, Georgieff MK, Josephson CD, Stowell SR, Feldman HA, et al. Sex-specific cytokine responses and neurocognitive outcome after blood transfusions in preterm infant. *Pediatr Res* 2022;91:947-54.
- Aher SM, Ohlsson A. Early versus late erythropoietin for preventing red blood cell transfusion in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2020;2:CD004865.
- Ozcan B, Aydemir O, Isik UD, Bas AY, Demirel N. Severe anemia is associated with intestinal injury in preterm neonates. *Am J Perinatol* 2020;37:603-6.
- Lum TG, Sugar J, Yim R, Fertel S, Morales A, Poeltler D, et al. Two-year neurodevelopmental outcomes of preterm infants who received red blood cell transfusion. *Blood Transfus* 2022;20:180-7.
- Balasubramanian H, Atyalgade M, Garg B, Srinivasan L, Kabra NS, Khapekar S. Effects of blood sampling stewardship and erythropoietin administration in extremely low birth weight infants-a quality improvement non-controlled before-and-after retrospective study. *Eur J Pediatr* 2021;180:1617-26
- Goldstein GP, Rao A, Ling AY, Ding VY, Chang IJ, Chock VY. Influence of enteral feeding and anemia on tissue oxygen extraction after red blood cell transfusion in preterm infants. *Transfusion* 2020;60:466-72.
- Poppe JA, Essen T, Weteringen W, Willemsen SP, Reiss IKM, Simons SHP, et al. Cardiorespiratory monitoring of red blood cell transfusions in preterm infants. *Eur J Pediatr* 2022;181:489-500.
- Fontana C, Raffaelli G, Pesenti N, Boggini T, Cortesi V, Manzoni F, et al. Red blood cell transfusions in preterm newborns and neurodevelopmental outcomes at 2 and 5 years of age. *Blood Transfus* 2022;20:40-9.
- Kalteren WS, Verhagen EA, Mintzer JP, Bos AF, Kooi EMW. Anemia and red blood cell transfusions, cerebral oxygenation, brain injury and development, and neurodevelopmental outcome in preterm infants: a systematic review. *Front Pediatr* 2021;26;9:644462.

17. Maheshwari A, Patel RM, Christensen RD. Anemia, red blood cell transfusions, and necrotizing enterocolitis. *Semin Pediatr Surg* 2018;27:47-51.
18. Song J, Dong H, Xu F, Wang Y, Li W, Jue Z, et al. The association of severe anemia, red blood cell transfusion and necrotizing enterocolitis in neonates. *PLoS One* 2021;16:e0254810.
19. Lorch SA, Srinivasan L, Escobar GJ. Epidemiology of apnea and bradycardia resolution in premature infants. *Pediatrics*. 2011;128:e366-73.
20. Kliegman RM, Walsh MC. Neonatal necrotizing enterocolitis: pathogenesis, classification, and spectrum of illness. *Curr Probl Pediatr*. 1987;17:213-88.
21. Papile LA, Munsick-Bruno G, Schaefer A. Relationship of cerebral intraventricular hemorrhage and childhood neurologic handicaps. *J Pediatr*. 1983;103:273-7.
22. International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity of revisited. *Arch Ophthalmol* 2005;123:991-9.
23. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. *Am J Respir Care Med*. 2001;163: 1723-9.
24. Erdeve O, Yurttutan S, Altuğ N, Ozdemir R, Gokmen T, Dilmen U, et al. Oral versus intravenous ibuprofen for patent ductus arteriosus closure: a randomised controlled trial in extremely low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 2012;97:F279-83.
25. Ohls RK. Transfusions in the preterm infant. *NeoReviews* 2007;8:e377-88.
26. Cetinkaya M, Atasoy B, Perk Y. Turkish neonatal society guideline on the transfusion principles in newborns. *Turk Pediatr Ars* 2018;53:101-8.
27. Ohlsson A, Aher SM. Early erythropoiesis-stimulating agents in preterm or low birth weight infants. *Cochrane Database Syst Rev* 2020;2:CD004863.
28. Saito-Benz MS, Flanagan P, Berry MJ. Management of anaemia in pre-term infants. *Br J Haematol* 2020;188:354-66.
29. El-Lahony DM, Saleh NY, Habib MS, Shehata MA, El-Hawy MA. The role of recombinant Human erythropoietin in neonatal anemia. *Hematol Oncol Stem Cell Ther* 2020;13:147-51.
30. Cibulskis CC, Maheshwari A, Rao A, Mathur MA. Anemia of prematurity: how low is too low? *J Perinatol* 2021;41:1244-57.
31. Kasat K, Hendricks KD, Mally PV. Neonatal red blood cell transfusions: searching for better guidelines. *Blood Transfus* 2011;9:86-94.
32. Priya RAS, Krishnamoorthy R, Panicker VK, Ninan B. Transfusion support in premature neonates <1500 g and/or <32 weeks in a tertiary care center: A descriptive study. *Asian J Transfus Sci* 2018;12:34-41.
33. Lopriore E. Updates in red blood cell and platelet transfusions in preterm neonates. *Am J Perinatol* 2019;36:37-40.
34. Meyer J, Sive A, Jacobs P. Empiric red cell transfusion in asymptomatic premature infants. *Acta Paediatr* 1993;82:30-4.
35. Nelle M, Hocker C, Zilow EP, Linderkamp O. Effects of red cell transfusion on cardiac output and blood flow velocities in cerebral and gastrointestinal arteries in premature infants. *Arch Dis Child Fetal Neonatal Ed* 1994;71:45-8.
36. Lachance C, Chessex P, Fouron JC, Widness JA, Bard H. Myocardial, erythropoietic and metabolic adaptations to anemia of prematurity. *J Pediatr* 1994;125:278-82.
37. Dani C, Pezzati M, Martelli E, Prussi C, Bertini G, Rubaltelli FF. Effect of blood transfusions on cerebral haemodynamics in preterm infants. *Acta Paediatr* 2002;91:938-41.
38. Alkalay AL, Galvis S, Ferry DA, Simmons CF, Krueger RC. Hemodynamic changes in anemic premature infants: are we allowing the hematocrits to fall too low? *Pediatrics* 2003;112:838-45.
39. Mimica AF, Santos NMA, Cunha DH, Guinsburg R, Bordin JO, Chiba A, et al. A very strict guideline reduces the number of erythrocyte transfusions in premature infants. *Vox Sang* 2008;95:106-11.
40. Santos NMA, Guinsburg R, Almeida MFB, Procianny RS, Marba STM, Ferri WAG, et al. Factors associated with red blood cell transfusions in very low-birth-weight premature infants in Brazilian neonatal units. *BMC Pediatrics* 2015;15:113. doi: 10.1186/s12887-015-0432-6.
41. Kirpalani H, Whyte RK. What is new about transfusions for preterm infants? an update. *Neonatology* 2019;115:406-10.

Determinants of Low Disease Activity and Remission in Pediatric Systemic Lupus Erythematosus Patients

Pedriatrik Sistemik Lupus Eritematozus Hastalarında Düşük Hastalık Aktivitesi ve Remisyonun Belirleyicileri

Melike Mehveş KAPLAN, Vildan GÜNGÖRER, Elif ÇELİKEL, Zahide EKİCİ TEKİN, Tuba KURT, Nilüfer TEKGÖZ, Müge SEZER, Cüneyt KARAGÖL, Serkan COŞKUN, Nimet ÖNER, Merve Cansu POLAT, Fatma Şemsa ÇAYCI, Banu ÇELİKEL ACAR

¹Department of Pediatric Rheumatology, University of Health Sciences, Ankara Bilkent City Hospital, Ankara, Turkey

²Department of Pediatric Nephrology, University of Health Sciences, Ankara Bilkent City Hospital, Ankara, Turkey



ABSTRACT

Objective: In our study, it was aimed to investigate the effects of disease symptoms at presentation in pediatric systemic lupus erythematosus (SLE) patients on low disease activity and remission success after the 2nd year of the disease.

Material and Methods: Demographic, clinical, and laboratory data of pediatric SLE patients being followed up at our center were obtained from their electronic medical records and patient files. Disease activity at 2 years after diagnosis was measured based on SLE Disease Activity Index-2000 (SLEDAI-2K) scores.

Results: In this study, 29 patients diagnosed with pediatric SLE and followed up regularly for at least 2 years were included. At 2 years following diagnosis, according to their SLE activity measurements, 14 (48.2%) patients had high disease activity status (HDAS), whereas 15 (51.7%) had low disease activity status (LDAS)-remission. There was no statistically significant difference between the initial presenting symptoms of the two groups. At 5 years following diagnosis, among 15 patients, 6 (40%) had LDAS-remission, and 9 (60%) had HDAS. The 5th-year SLEDAI-2K scores of the patients with HDAS at 2 years were significantly higher than the 5th-year scores of those with LDAS-remission at 2 years ($p=0.028$). It was also found that the HDAS of 8 patients who had active disease at 2 years (80%) continued at 5 years.

Conclusion: The results of our study showed that pediatric SLE presenting symptoms did not have a significant determining effect on low disease activity and remission at 2 years. On the other hand, low disease activity and remission observed at 2 years may be indicative of LDAS and remission at 5 years.

Key Words: Systemic lupus erythematosus, SLEDAI-2K, Prognosis

ÖZ

Amaç: Çalışmamızda pedriatrik sistemik lupus eritematozus (SLE) hastalarında, hastalık prezentasyon bulgularının, hastalığın 2. yılındaki düşük hastalık aktivitesi ve remisyonun ulaşılmadığı etkilerinin incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Merkezimizde takipli olan pedriatrik SLE hastalarının elektronik tıbbi kayıtları ve hasta dosyalarından demografik, klinik ve laboratuvar verileri kaydedildi. Hastalığın 2. yılındaki aktivite ölçümü SLE Hastalığı Aktivite İndeksi-2000 (SLEDAI-2K) skoru baz alınarak hesaplandı. Prezentasyon bulguları ile düşük hastalık aktivitesi ve remisyon arasında ilişki olup olmadığı istatistiksel yöntemlerle incelendi.



0000-0002-8012-2774 : KAPLAN MM
0000-0002-9838-2603 : GÜNGÖRER V
0000-0003-0129-4410 : ÇELİKEL E
0000-0002-5446-667X : EKİCİ TEKİN Z
0000-0003-3711-8347 : KURT T
0000-0002-2235-4489 : TEKGÖZ N
0000-0002-9254-9935 : SEZER M
0000-0002-2987-1980 : KARAGÖL C
0000-0003-2568-9329 : COŞKUN S
0000-0003-0403-151X : ÖNER N
0000-0003-3279-8435 : POLAT MC
0000-0001-6779-275X : ÇAYCI FŞ
0000-0002-1808-3655 : ÇELİKEL ACAR B

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 Ankara City Hospital Clinical Research Ethics Committee (Ethics ID-No: E2-22-1813).

Contribution of the Authors / Yazarların katkısı: KAPLAN MM: All authors made substantial contributions to the conception or design of the work, have approved the final manuscript, and takes full responsibility for the manuscript. GÜNGÖRER V: Reviewed and revised the manuscript. ÇELİKEL E: Reviewed and revised the manuscript. EKİCİ TEKİN Z: Reviewed and revised the manuscript. KURT T: Contributed to the writing of the manuscript. TEKGÖZ N: Contributed to the writing of the manuscript. SEZER M: Contributed to the writing of the manuscript. KARAGÖL C: Contributed to the writing of the manuscript. COŞKUN S: Contributed to the writing of the manuscript. ÖNER N: Contributed to the writing of the manuscript. POLAT MC: Were responsible for data collection and analysis. ÇAYCI FŞ: Contributed to the writing of the manuscript. ÇELİKEL ACAR B: All authors made substantial contributions to the conception or design of the work, have approved the final manuscript, and takes full responsibility for the manuscript, Reviewed and revised the manuscript.

How to cite / Atıf yazım şekli : Kaplan MM, Güngörer V, Çelikel E, Ekici Tekin Z, Kurt T, Tekgöz N, et al. Determinants of Low Disease Activity And Remission in Pediatric Systemic Lupus Erythematosus Patients. Turkish J Pediatr Dis 2023;17:194-200.

Correspondence Address / Yazışma Adresi:

Melike Mehveş KAPLAN
Department of Pediatric Rheumatology,
University of Health Sciences, Ankara Bilkent City Hospital, Ankara, Turkey
E-posta: melikemehves@gmail.com

Received / Geliş tarihi : 15.11.2022

Accepted / Kabul tarihi : 21.12.2022

Online published : 11.01.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1205213

Bulgular: Bu çalışmaya merkezimizde pediatrik SLE tanısı almış ve en az 2 yıl düzenli takibe gelmiş 29 hastayı dahil ettik. Tanıdan sonraki 2. yılda hastalarda SLE aktivite ölçümüne göre 14 hastada (%48.2) HDAS, 15 hastada (%51.7) LDAS-remisyon elde edilmişti. İki grup arasında başlangıçtaki prezentasyon bulguları açısından anlamlı istatistiksel farklılık saptanmadı. 5. yılda 15 hastadan 6'sında (%40) LDAS-remisyon, 9'unda (%60) HDAS mevcuttu. 2. yılda HDAS'a sahip hastaların 5. yıl SLEDAI-2K skorları, 2. yılda LDAS-remisyona sahip hastaların 5. yıl SLEDAI-2K skorlarına göre anlamlı olarak yüksekti ($p= 0.028$). Ayrıca 2. yılda aktif olan 8 hastanın (%80) 5. yılda HDAS'ın devam ettiği gözlemlendi.

Sonuç: Çalışmamızda pediatrik SLE prezentasyon bulgularının hastalığın 2. yılındaki düşük hastalık aktivitesi ve remisyon üzerine belirleyici etkilerinin olmadığını gösterildi. Ayrıca 2. yılda elde edilen düşük hastalık aktivitesi ve remisyon 5. yıldaki düşük hastalık aktivitesi ve remisyonun belirleyicisi olabilir.

Anahtar Sözcükler: Sistemik lupus eritematozus, SLEDAI-2K, Prognoz

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystemic, and autoimmune disease that can affect many organs and systems (1). The progression and prognosis of SLE cannot be predicted. Pediatric SLE is typically more severe than adult SLE, and its 5-year mortality rate reaches 95.3% if it is untreated (2). Disease activity scores have been developed to help in the assessment of disease activity for various organs and systems. Disease activity management is one of the main determinants of prognosis. Thus, it is important to utilize activity scales that will direct the planning of the treatment (3).

The most frequently used scales for SLE are the SLE Disease Activity Index (SLEDAI), SLEDAI-2000 (SLEDAI-2K), and the British Isles Lupus Assessment Group (BILAG) Activity Index (4). SLEDAI-2K, which is the updated version of SLEDAI, which was developed first in 1985, that was introduced in 2002 is a global measure of disease activity for SLE. Low disease activity status (LDAS) and remission that are calculated with current clinical data using SLEDAI-2K have potential applications at clinics monitoring SLE patients (5).

SLEDAI-2K consists of 24 items including nine organ systems. The period assessed to identify disease activity is the previous 10 days. Scores vary between 0 and 105, and higher scores indicate higher disease activity levels (5). SLEDAI-2K can identify patients who are suitable for treatment changes or clinical studies.

In this study, it was aimed to present the demographic, clinical, and laboratory data of pediatric SLE patients who were followed up at our center in a 27-year period, as well as their prognosis. Moreover, the effects of the presenting symptoms of the disease on low disease activity and remission success at 2 years were investigated.

MATERIALS and METHODS

Design and patient selection

This study was a retrospective review of the electronic and chart medical records of 29 SLE patients who were followed regularly at a tertiary referral hospital between January 1995

and August 2022. Inclusion criteria were defined as meeting the revised American College of Rheumatology (ACR) 1982 criteria for SLE and having symptom onset before the age of 18. Patients who had missing data or were followed up for less than 2 years were excluded.

Clinical-laboratory findings and definitions

All patients were systematically evaluated: demographic characteristics, age of disease onset, disease duration, follow-up duration, symptoms, clinical characteristics, laboratory findings, treatments, and treatment outcomes were recorded.

Complete blood counts and differential counts, erythrocyte sedimentation rates (ESR), serum complement levels (C3 and C4), antinuclear antibodies (ANA), anticardiolipin (aCL) IgG/M, antibeta2glycoprotein IgG/M test results, double-stranded DNA (dsDNA) antibodies, and urine test anomalies were recorded. Complete urinalysis anomalies were determined as hematuria (>5 erythrocyte/ per high power field), proteinuria (spot urine protein/creatinine >0.2 in patients aged >2 years; spot urine protein/creatinine >0.5 in patients aged <2 years; nephrotic-level proteinuria defined as spot urine protein/creatinine >2), and pyuria (>5 leukocytes/ per high power field). ANA and anti-dsDNA values were determined using the indirect immunofluorescence method or the enzyme-linked immunosorbent assay (ELISA) method. Serum C3 and C4 values were measured by immunodiffusion or turbidimetric immunoassay.

Treatment and disease management

Induction and maintenance treatment data were collected. Previous and current treatments involving drugs such as prednisone, intravenous pulse methylprednisolone, hydroxychloroquine sulfate, methotrexate, azathioprine (AZA), cyclosporine, mycophenolate (MMF), rituximab, and cyclophosphamide (CYP) were recorded. Angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARBs) were used for hypertension and/or proteinuria as needed. When indicated, anticoagulants were used in patients with secondary antiphospholipid syndrome.

Disease activity

For the measurement of disease activity, SLEDAI-2K scores were obtained from electronic medical records and patient files

for the time at the presentation of the disease and at 2 and 5 years after diagnosis.

SLEDAI-2K score was evaluated by considering the patients' admission and their condition in the 10 days before admission. The patients received 8 points for each parameter in the presence of episodes, psychosis, organic brain lesions, vision disorders, cranial nerve disorders, lupus headaches, cerebrovascular events, or vasculitis, they received 4 points for each parameter in the presence of arthritis, myositis, urinary casts, hematuria, proteinuria, or pyuria, they received 2 points for each parameter in the presence of rashes, alopecia, mucosal ulcers, pleurisy, pericarditis, low complement levels, or elevated anti-dsDNA levels, and they received 1 point for each parameter in the presence of a fever, thrombocytopenia, or leukopenia (5,6).

In the measurement of SLE activity, remission was defined as an SLEDAI-2K score of 0, a prednisolone dose of 5 mg/day or lower, and using immunosuppressives at maintenance doses, LDAS was defined as an SLEDAI-2K score under 4, a prednisolone dose lower than 7.5 mg/day, and using immunosuppressives at maintenance doses, and non-optimal control-active disease (HDAS) was defined as an SLEDAI-2K score higher than 4, a prednisolone dose higher than 7.5 mg/day, and using immunosuppressives at induction doses (7).

The study was approved by the Ankara City Hospital Clinical Research Ethics Committee (Ethics ID-No: E2-22-1813). All procedures were carried out in compliance with ethical rules and the principles of the Declaration of Helsinki.

Statistical Analysis: The statistical analyses were carried out using the SPSS software version 25. The normality of the distributions of the variables was determined using visual methods (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). Descriptive statistics are presented as mean and standard deviation values for the normally distributed variables, medians and ranges for the non-normally distributed ordinal variables, and frequencies for the categorical variables. Intergroup comparisons were made using Student's t-test for the normally distributed variables, the Mann-Whitney U test for the non-normally distributed and ordinal variables, and chi-squared or Fisher's tests for the categorical variables. Parameters with a p-value smaller than 0.025 in the univariate analyses were considered for inclusion in the model. When high correlation values were observed among these variables, they were removed from the model due to low clinical significance or high p-values. First, a univariate logistic regression analysis was conducted on the remaining variables. After the removal of the variables that were not statistically significant from the model, finally, a multivariate analysis was completed. Model fit was analyzed with the Hosmer-Lemeshow test. $p < 0.050$ was accepted as statistically significant.

RESULTS

Among the 29 patients included in the study, 25 (86.2%) were female. The median age of diagnosis was 13 (3.7-17.5) years. 14 patients (48.2%) had constitutional findings. The most common organ and system involvement was renal involvement in 14 patients (48.2%). There was mucocutaneous involvement in 13 patients (44.8%), musculoskeletal involvement in 12 patients (41.3%), hematological involvement in 10 patients (34.4%), neurological involvement in 7 patients (24.1%), cardiovascular involvement in 1 patient (3.4%) and immunological involvement in 28 patients (96.5%). The clinical symptoms and system involvements of the patients at presentation are given in Table I.

Table I: Clinical findings of patients with systemic lupus erythematosus at the time of diagnosis

Gender *	
Female*	25 (86.2)
Male*	4 (13.7)
Age at diagnosis, years [†]	13 (9.5-14.5)
Time to diagnosis, months [†]	1 (0.5-2)
Constitutional findings*	14 (48.3)
Mucocutaneous involvement*	13 (44.8)
Musculoskeletal involvement*	12 (41.4)
Renal involvement*	14 (48.3)
Neurological involvement*	7 (24.1)
Hematological involvement*	10 (34.5)
Cardiovascular involvement*	1 (3.4)
Immunological involvement*	28 (96.6)
Lung involvement*	9 (31)
GIS involvement*	4 (13.8)
Eye involvement*	1 (3.4)

*n (%), [†]median (Q1Q3) (min-max)

Table II: Laboratory findings at the time of diagnosis in patients with systemic lupus erythematosus

WBC [†] (*10 ⁶ /L)	6148 (2400-25500)
Neutrophil [†] (*10 ⁶ /L)	3158 (1000-15800)
Lymphocyte [†] (*10 ⁶ /L)	1652 (300-6900)
PLT [†] (*10 ⁶ /L)	250034 (6000-517000)
Hb [†] (g/L)	11.56 (7.6-15.4)
ESH [†] (mm/hr)	21.55 (2-121)
CRP [†] (mg/L)	14.5 (0.1-33)
C3 [†] (g/L)	0.54 (0.18-0.91)
C4 [†] (g/L)	0.079 (0.01-0.98)
ANA positivity*	26 (89.6)
Anti-ds DNA positivity*	22 (75.8)

*n (%), [†]median (Q1Q3) (min-max), **WBC:** White blood cell, **Hb:** Hemoglobin, **PLT:** Platelet, **ESR:** Erythrocyte sedimentation rate, **CRP:** C- Reactive protein, **C:** Complement, **ANA:** Antinuclear antibody, **Anti-dsDNA:** Anti double-stranded deoxyribonucleic acid

Table III: Relationship of presentation findings with HDAS and LDAS-remission at 2 years in patients with systemic lupus erythematosus

	2 nd year HDAS (n=14)	2 nd year LDAS-Remission (n=15)	p
Gender,*			
Female	11 (78.6)	14 (93.3)	0.330
Male	3 (21.4)	1 (6.7)	
Age at diagnosis, years [†]	13.8 (11-14.6) (8.5-17.5)	12.4 (9.5-15) (3.7-17)	0.450
Time to diagnosis, months [†]	1.5 (0.7-2.3) (0-8)	1 (0-2) (0-33)	0.780
Constitutional findings*	7 (63.6)	7 (87.5)	0.340
Mucocutaneous involvement*	5 (35.7)	8 (53.3)	0.340
Musculoskeletal involvement*	4 (28.6)	8 (53.3)	0.180
Renal involvement*	9 (64.3)	5 (33.3)	0.096
Neurological involvement*	4 (28.6)	3 (20)	0.680
Hematological involvement*	5 (35.7)	5 (33.3)	1.000
Cardiovascular involvement*	1 (7.1)	0 (0)	0.480
Immunological involvement*	13 (92.9)	15 (100)	0.480
Lung involvement*	5 (35.7)	4 (26.7)	0.700
GIS involvement*	2 (14.3)	2 (13.3)	1.000
Eye involvement*	1 (7.1)	0 (0)	0.480
Complement 3 [†]	0.47 (0.33-0.91) (0.18-1)	0.61 (0.39-0.9)	0.250
Complement 4 [†]	0.09 (0.05-0.11) (0.03-0.98)	0.07 (0.05-0.15) (0.01-0.3)	0.780
ANA positivity*	12 (85.7)	14 (93.3)	0.600
Anti ds DNA positivity*	10 (71.4)	12 (80)	0.680
Pulse methylprednisolone	8	10	0.710
0.5-2 mg/kg/d methylprednisolone	5	5	0.890
Cyclophosphamide	6 (42.9)	4 (26.7)	0.450
Mycophenolate Mofetil	2 (14.3)	2 (13.3)	1.000
Azathioprine	2 (14.3)	0 (0)	0.220

*n (%), [†]median (Q1Q3) (min-max), **HDAS:** High disease activity score, **LDAS:** Low disease activity score

Among the patients with hematological involvement, 6 (16.7%) patients had thrombocytopenia, 7 (19.4%) had leukopenia, 6 (16.7%) had hemolytic anemia, and 7 (19.4%) had lymphopenia.

Seven patients (24.1%) had neurological involvement. 4 (11.1%) patients had epileptic seizures, 3 (8.3%) had cognitive deficits, 1 (11.1%) had mononeuritis multiplex, 1 (11.1%) had neuropathy, and 1 (11.1%) had corea. Psychiatric symptoms such as depression, anxiety disorder, and hallucinations were observed in 6 (16.7%) patients. No patients developed organic brain injury, cerebrovascular diseases, cranial nerve disorders, confusion, or pseudotumor cerebri.

Twelve (33.3%) patients had serositis. Among these 12 patients, 10 (27.7%) patients had pleurisy, and 2 (5.5%) had pericarditis. 5 (13.9%) patients had gastrointestinal system involvement (elevated liver enzymes, hepatosplenomegaly, ileocecal wall thickening, acid, and pancreatitis). One (11.1%) patient had ocular involvement (retinal hemorrhage).

Half of the patients had renal involvement. 7 (19.4%) patients had non-nephrotic proteinuria, and 4 (11.1%) had nephrotic proteinuria. Proteinuria was accompanied by hematuria in

4 (11.1%) patients, pyuria in 2 (5.6%) patients, and both hematuria and pyuria in 8 (22.2%) patients. Kidney biopsies were performed on 22 patients. 7 (19.4%) patients were class 4, 1 (2.8%) was class 1, 7 (19.4%) were class 2, 2 (5.6%) were class 3, and 2 (5.6%) were class 5. 2 (5.6%) patients had biopsy findings compatible with C3 glomerulopathy (Table I). The kidney biopsy findings of 1 (2.8%) patient were normal.

No statistically significant relationship was found between the presence of HDAS at 2 years and findings at presentation including clinical, organ involvement, and laboratory findings.

The laboratory findings of the patients at the time of their presentation are shown in Table II. Positive results were found in 33 (91.7%) patients for ANA, 26 (72.2%) patients for anti-dsDNA, and 6 (16.7%) patients for anti-Sm antibody. 10 (27.8%) patients had anticardiolipin IgG/IgM antibodies, 6 (16.7%) had lupus anticoagulants, and 2 (5.6%) had B2 glycoprotein IgG/M antibodies. The direct Coombs tests of 16 (44.4%) patients and the RF tests of 3 (8.3%) patients were positive.

All patients received hydroxychloroquine and glucocorticoids at the time of diagnosis. 18 (62.1%) patients received pulse

methylprednisolone, and 11 (37.9%) received 0.5-2 mg/kg/day glucocorticoids. Glucocorticoid treatment was reduced week by week based on the clinical status of the patients, their major organ involvement status, and disease severity. As induction treatment, the patients were given CYP [n=10, (34.4%)], MMF [n=4, (13.7%)], and AZA [n=2, (6.8%)] in the first 2 years based on their organ involvement and disease severity. At 2 years after diagnosis, all (n=29, 100%) SLE patients were using glucocorticoids. Among these patients, 12 (41.4%) patients were using low-dose glucocorticoids at <7.5 mg/day, 9 (31%) were using them at 7.5-15 mg/day, and 8 (27.6%) were using doses higher than 15 mg/day.

The median presentation SLEDAI-2K score of the participants was 15 (7-22.5). Their median SLEDAI-2K score at 2 years was 4 (0-11). According to the SLE activity measurements, 14 (48.2%) patients had HDAS, while 15 (51.7%) had LDAS-remission. We had 15 patients with regular follow-ups at 5 years after their diagnosis. Their mean SLEDAI-2K score at 5 years was 6 (2-8). At 5 years, among these 15 patients, 6 (40%) patients had LDAS-remission, and 9 (60%) had HDAS. At 5 years, LDAS-remission could be achieved in 2 of the 10 patients who had HDAS at 2 years. Moreover, at 5 years, LDAS-remission was maintained among 4 of the 5 patients who had LDAS-remission at 2 years and continued their follow-ups for 5 years. There was no statistically significant difference between the SLE activity measurements of the two groups. However, the 5th-year SLEDAI-2K scores of the patients with HDAS at 2 years were significantly higher than the 5th-year scores of those with LDAS-remission at 2 years ($p=0.028$). Furthermore, the HDAS status of 8 patients who had active disease at 2 years (80%) continued at 5 years. Graphic 1 shows the relationship between disease activity and SLEDAI-2K scores.

DISCUSSION

Pediatric SLE is a chronic and potentially fatal autoimmune disease that shows high variability in terms of disease presentation and progression (8). In this study, it was aimed to investigate whether symptoms at diagnosis can predict symptoms in the second year in pediatric SLE. It was shown that pediatric SLE presenting symptoms did not have a significant effect on LDAS-remission success or HDAS. On the other hand, the patients who achieved LDAS-remission at 2 years following their diagnosis had significantly lower SLEDAI-2K scores at 5 years.

In pediatric SLE cases, the goal of the clinician is to achieve LDAS-remission. Variables associated with the probability of achieving LDAS or remission in SLE, which as very high morbidity and mortality rates when untreated, guide the clinician in reaching this goal. LDAS at the time of diagnosis, lower damage index values, or the absence of lupus nephritis are indicative of lower disease severity. Older age is also

predictive of LDAS (9). It was shown that patients who were younger at the onset of the disease had a higher likelihood of having active disease compared to those with an older age of onset (10). As our sample consisted of pediatric SLE patients, it may be expected that their achievement of LDAS-remission could be more difficult in comparison to patients at older ages. However nowadays, appropriate treatment approaches that can be aggressive when necessary make the goal of LDAS-remission possible.

In general, compared to adult-onset SLE patients, pediatric SLE patients are more likely to have more severe disease at the beginning with higher rates of organ involvement and a more aggressive clinical course (8). In the first year of diagnosis, 35-90% of pediatric cases may have constitutional symptoms, 20-80% may have nephritis, 20-74% may have musculoskeletal system symptoms, 60-80% may have any form of skin involvement, 15-30% may have neuropsychiatric diseases, 5-30% may have cardiovascular diseases, and 18-40% may have pulmonary diseases (11). While renal involvement was detected in 48.2% of the patients in our study, 24.1% of the patients had neurological involvement, 34.4% had hematological involvement, and 3.4% had cardiovascular involvement. Major organ involvement such as kidney and central nervous system, which are the determinants of morbidity and mortality at the onset of the disease, are high in pediatric cases. In our study, it was shown that major organ/system involvements at presentation did not have a significant effect on disease activity at 2 years. We suggest that our finding of no significant relationship between systemic involvements at presentation and LDAS-remission and HDAS outcomes was caused by the rapid and appropriate treatment of organ/system involvements by the clinician at the time of diagnosis.

Low disease activity and remission are newly emerging concepts that provide a simple method of predicting a favorable prognosis in pediatric SLE patients. High disease activity was shown to be associated with increased organ injury risk and other negative outcomes (7). Therefore, disease activity measurement is an indispensable part of current recommendations for disease management in SLE cases (12). Although there are a few recommended disease severity indices, their definitions are usually complicated (13). One of the severity indices that have been used recently involves the parameters of corticosteroid or immunosuppressant treatment requirements, as well as specific organ involvement (14). In the calculation of SLEDAI scores, the parameters are identified if symptoms are present at presentation or in the previous 10 days (6). Patients receive 8 points for each parameter in the presence of episodes, psychosis, organic brain lesions, vision disorders, cranial nerve disorders, lupus headaches, cerebrovascular events, or vasculitis, they receive 4 points for each parameter in the presence of arthritis, myositis, urinary casts, hematuria, proteinuria, or pyuria, they receive 2 points for each parameter in the presence of rashes, alopecia, mucosal

ulcers, pleurisy, pericarditis, low complement levels, or elevated anti-dsDNA levels, and they receive 1 point for each parameter in the presence of a fever, thrombocytopenia, or leukopenia. SLEDAI-2K scores vary from 0 to 105, and higher scores indicate higher disease activity levels (5,6). Among the patients included in our study, the median SLEDAI-2K score at 2 years was 4 (0-11). According to the SLE activity measurements, 14 (48.2%) patients had HDAS, while 15 (51.7%) had LDAS-remission. We had 15 patients with regular follow-ups at 5 years after their diagnosis. Their mean SLEDAI-2K score at 5 years was 6 (2-8). At 5 years, among these 15 patients, 6 (40%) patients had LDAS-remission, 9 (60%) had HDAS and LDAS-remission could be achieved in 2 of the 10 patients who had HDAS at 2 years. The 5th-year SLEDAI-2K scores of the patients with HDAS at 2 years were significantly higher than the 5th-year scores of those with LDAS-remission at 2 years. Furthermore, the HDAS status of 8 patients who had active disease at 2 years (80%) continued at 5 years. This revealed that long-term prognoses could be predictable from earlier periods of the disease, such as 2 years following diagnosis. As shown in our study, the early management of the disease allows for a good prognosis in the long term for this disease, which is difficult to manage.

The Lupus Low Disease Activity State (LLDAS) measure was developed recently by Franklyn et al. (15) LLDAS was defined as an SLEDAI-2K score of ≤ 4 , no activity or active involvement in major organs (kidneys, central nervous system, cardiopulmonary organs, vasculitis, fever, hemolytic anemia, or gastrointestinal system), the absence of new lupus disease activity compared to a previous assessment, a global assessment value of ≤ 1 determined by a physician, the use of prednisone (or equivalent) at a dose of ≤ 7.5 mg/day, and the use of immunosuppressive drugs and approved biological agents at standard maintenance doses that are tolerated well. The researchers reported a significantly lower degree of damage and significantly lower SLE damage index values among patients who showed LLDAS in at least two consecutive years compared to those who never showed LLDAS. They stated that 84% of patients with LLDAS on average met remission criteria (16). Understanding predictive factors for LLDAS-50 will allow better clinical management of SLE patients. In a recent study, it was shown that only 37.6% of 1169 SLE patients achieved LLDAS-50. In the multivariate model of the same study, African American ethnicity, hypocomplementemia, serositis, kidney involvement, arthritis, anti-RNP, anti-dsDNA, vasculitis, malar rash, discoid rash, thrombocytopenia, and immunosuppressive use were found as negative predictors of LLDAS-50. Older age at the time of diagnosis, longer disease durations, higher education levels, and higher hydroxychloroquine intake rates were positive predictors of LLDAS-50 (17,18,19). Likewise, it has been shown that LLDAS is an achievable goal in clinical practice, but the achievement of LLDAS is more difficult among patients with discoid rashes, high anti-dsDNA levels, and hypocomplementemia (19). SLEDAI scores higher than 10 have

been associated with longer HDAS episodes and an increased risk of damage. Having HDAS episodes for longer than 2 years in total and experiencing 4 or more HDAS episodes may lead to an increased risk of damage (20).

The limitations of our study are that it was conducted in a single center and its retrospective design. However, its strength is that it presents the 27-year experience of a tertiary referral hospital and reflects long-term outcomes.

In conclusion, the results of our study showed that pediatric SLE presenting symptoms did not have a significant determining effect on low disease activity and remission at 2 years. We also showed that the 5th-year SLEDAI-2K scores of the patients with HDAS at 2 years were significantly higher than the 5th-year scores of those with LDAS-remission at 2 years. The majority of patients with active disease at 2 years maintained HDAS at 5 years. This suggested that the long-term prognosis of pediatric SLE patients may be associated with successful disease management in the first 2 years of the disease. Multicenter studies including larger numbers of pediatric SLE patients are needed to reveal the determinants of LDAS-remission.

REFERENCES

1. Klein-Gitelman MS, Beresford MW. Systemic Lupus Erythematosus, Mixed Connective Tissue Disease, and Undifferentiated Connective Tissue Disease. In: Petty RE, Lindsley CB, Laxer RM, Wedderburn L, eds. Textbook of pediatric rheumatology. 8th ed. Philadelphia : Elsevier, 2020: 295-330.
2. Malattia C, Martini A. Paediatric-onset systemic lupus erythematosus. *Best Pract Res Clin Rheumatol* 2013;27:351-62.
3. Hoi A, Nim HT, Koelmeyer R, Sun Y, Kao A, Gunther O, et al. Algorithm for calculating high disease activity in SLE. *Rheumatology Oxford* 2021;60 :4291-7.
4. Lattanzi B, Consolaro A, Solari N, Ruperto N, Martini A, Ravelli A. Measures of disease activity and damage in pediatric systemic lupus erythematosus. *Arthritis Care Res* 2011;63: 112-7.
5. Jesus D, Rodrigues M, Matos A, Henriques C, Pereira da Silva JA, Inês LS. Performance of SLEDAI-2K to detect a clinically meaningful change in SLE disease activity: a 36-month prospective cohort study of 334 patients. *Lupus* 2019;28:607-12.
6. Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002;29:288-91.
7. Ugarte-Gil MF, Gamboa-Cárdenas RV, Reátegui-Sokolova C, Medina-Chinchón M, Zevallos F, Elera-Fitzcarrald C, et al. Better Health-Related Quality of Life in Systemic Lupus Erythematosus Predicted by Low Disease Activity State/Remission. *Arthritis Care Res* 2020;72:1159-62.
8. Charras A, Smith E, Hedrich CM. Systemic Lupus Erythematosus in Children and Young People. *Curr Rheumatol Rep* 2021;23:20.
9. Ugarte-Gil MF, Wojdyla D, Pons-Estel GJ, Quintana R, Gómez-Puerta JA, Catoggio LJ, et al. Predictive factors of flares in systemic lupus erythematosus patients: data from a multiethnic Latin American cohort. *Lupus* 2018;27:536-44.
10. Aljohani R, Gladman DD, Su J, Urowitz MB. Disease evolution in late-onset and early-onset systemic lupus erythematosus. *Lupus* 2017;26:1190-96.

11. Levy DM, Kamphuis S. Systemic lupus erythematosus in children and adolescents. *Pediatr Clin North Am* 2012;59:345-64.
12. Bertsias GK, Tektonidou M, Amoura Z, Aringer M, Bajema I, Berden JH et al. EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. *Ann Rheum Dis* 2008; 67:1771-82.
13. Dima A, Caraiola S, Delcea C, Ionescu RA, Jurcut C, Badea C. Self-reported disease severity in women with systemic lupus erythematosus. *Rheumatol Int* 2019;39:533-39.
14. Doria A, Amoura Z, Cervera R, Khamastha MA, Schneider M, Richter J, et al. Annual direct medical cost of active systemic lupus erythematosus in five European countries. *Ann Rheum Dis* 2014;73:154-60.
15. Franklyn K, Lau CS, Navarra SV, Louthrenoo W, Lateef A, Hamijoyo L, et al. Asia-Pacific Lupus Collaboration. Definition and initial validation of a Lupus Low Disease Activity State (LLDAS). *Ann Rheum Dis* 2017;76:1615-21.
16. Zen M, Iaccarino L, Gatto M, Saccon F, Larosa M, Ghirardello A, et al. Lupus low disease activity state is associated with a decrease in damage progression in Caucasian patients with SLE, but overlaps with remission. *Ann Rheum Dis* 2018;77:104-10.
17. Babaoglu H, Li J, Goldman D, Magder LS, Petri M. Predictors of predominant Lupus Low Disease Activity State (LLDAS-50). *Lupus* 2019; 28:1648-55.
18. Golder V, Kandane-Rathnayake R, Hoi AY, Huq M, Louthrenoo W, An Y, et al. Asia-Pacific Lupus Collaboration. Frequency and predictors of the lupus low disease activity state in a multi-national and multi-ethnic cohort. *Arthritis Res Ther* 2016;18:260-9.
19. Hao Y, Oon S, Ji L, Gao D, Fan Y, Geng Y, et al. Determinants and protective associations of the lupus low disease activity state in a prospective Chinese cohort. *Clin Rheumatol* 2022;41:357-66.
20. Koelmeyer R, Nim HT, Nikpour M, Sun YB, Kao A, Guenther O, et al. High disease activity status suggests more severe disease and damage accrual in systemic lupus erythematosus. *Lupus Sci Med* 2020;4:372-80.

Why Do Mothers Use or Not Use Walkers for Their Babies?

Anneler Bebekleri İçin Niçin Yürüteç Kullanıyorlar veya Kullanmıyorlar?

Tülin ÇATAKLI¹, Hüsnüye YÜCEL²

¹Department of Child Health and Diseases, Lokman Hekim University, Ankara, Turkey

²Department of Child Health and Diseases, University of Health Sciences, Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital, Ankara, Turkey



ABSTRACT

Objective: Baby Walkers (BWs) are used by many parents in the pre-walking period for various reasons. The aim of this study is to investigate the thoughts and usage practices of mothers about the baby walkers, walker-induced accidents and to determine the role of walkers in crawling and independent walking.

Material and Methods: The research was conducted between February and April 2022 with 354 mothers who had infants aged 6-24 months-old and also agreed to participate. The mothers have been interviewed and so-obtained data documented on a pre-designed questionnaire. The data gathered from the baby walker users was compared with that of non-users. Data were collected using a semi-structured questionnaire by face-to-face interview method.

Results: 58.1% of all mothers were using baby walkers for their children. Baby Walker usage was first started at 7.3±0.98 months of age. There was no significant difference between baby walkers user and non-user groups in terms of crawling and independent walking ages ($p>0.050$). Among the baby walker user group, 47.5% stated that "it allowed them to do housework;" while 34.4% of the non-users stated that "it could harm their babies' genitals". Working mothers used baby walkers more than housewife mothers ($p<0.006$). 9.2% of infants have been exposed to baby walkers associated injuries.

Conclusion: Although there are concerns that walkers may cause gait disturbances and walker-related accidents; it was observed that mothers used walkers for different reasons. It is important that health professionals raise awareness about the walkers in routine child health follow-ups.

Key Words: Baby walker, Infants, Injury, Walking

ÖZ

Amaç: Yürüteçler pek çok ebeveyn tarafından çeşitli nedenlerle yürüme öncesi dönemde kullanılmaktadır. Bu çalışmanın amacı, annelerin yürüteç hakkındaki düşüncelerini ve kullanım pratiklerini öğrenmek, yürüteç kaynaklı kazaları, emekleme ve bağımsız yürümede yürüteçlerin rolünü belirlemektir.

Gereç ve Yöntemler: Araştırma Şubat-Nisan 2022 tarihleri arasında 6-24 aylık bebeği olan ve katılmayı kabul eden 354 anne ile yapılmıştır. Annelerle görüşmeler yapılmış ve bu şekilde elde edilen veriler önceden tasarlanmış olan bir anket formuna kaydedilmiştir. Bebek yürüteci kullananlardan toplanan veriler, kullanmayanların verileriyle karşılaştırılmıştır. Veriler, yüz yüze görüşme yöntemiyle yapılandırılmış bir anket kullanılarak toplanmıştır.



0000-0001-6670-1078 : ÇATAKLI T
0000-0002-7477-0302 : YÜCEL H

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: Clinical Research Ethics Committee of University of Health Sciences - Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Ankara, Turkey, registered with number E-22/02-270 Protocol No. 2020-KAEK-141/277 dated 02/02/2022

Contribution of the Authors / Yazarların katkısı: **ÇATAKLI H:** 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. **YÜCEL H:** 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.

How to cite / Atıf yazım şekli : Çatakli T and Yücel H. Why Do Mothers Use Or Not Use Walkers For Their Babies?. Turkish J Pediatr Dis 2023;17:201-206.

Correspondence Address / Yazışma Adresi:

Hüsnüye YÜCEL

Department of Child Health and Diseases, University of Health Sciences,
Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital, Ankara, Turkey
E-posta: husniyeyucel@gmail.com

Received / Geliş tarihi : 11.05.2022

Accepted / Kabul tarihi : 07.09.2022

Online published : 28.09.2022

Elektronik yayın tarihi

DOI: 10.12956/tchd.1115588

Bulgular: Annelerin %58.1'i çocukları için yürüteç kullandığını belirtmiştir. Yürüteç kullanımının ilk olarak 7.3±0.98 aylıkken başladığı tespit edilmiştir. Yürüteç kullanan ve kullanmayan gruplar arasında emekleme ve bağımsız yürüme yaşları açısından anlamlı fark saptanmamıştır ($p>0.050$). Yürüteç kullanan annelerin %47.5'i "ev işi yapmalarına olanak verdiğini"; kullanmayanların %34.4'ü "bebeklerinin cinsel organlarına zarar verebileceğini" belirtmiştir. Çalışan anneler ev hanımı annelere göre daha fazla yürüteç kullanmıştır ($p<0.006$). Bebeklerin %9.2'si yürüteçlerle ilişkili yaralanmalara maruz kalmıştır.

Sonuç: Yürüteçlerin yürüme bozukluklarına ve yürüteçle ilgili kazalara neden olabileceği endişeleri olmasına rağmen; annelerin farklı gerekçelerle yürüteç kullandığı görülmüştür. Rutin çocuk sağlığı izlemlerinde sağlık profesyonellerinin yürüteç hakkında farkındalık sağlamaları önemlidir.

Anahtar Sözcükler: Yürüteç, Bebekler, Yaralanma, Yürüme

INTRODUCTION

Baby walkers (BWs) are intended for use by young children of generally 5 to 15 months age before they develop the ability to walk independently. Several studies have shown that the usage rate of baby walkers ranges from 50% to 95% (1-5). Parents' attitudes to use BW vary based on their cultural beliefs and lifestyles. Many parents see BWs as ideal for encouraging children to begin walking while keeping them entertained, quiet, and safe (1, 6). The serious concerns of the mothers may be noted as the effects of assisted walking on the child's development, and the probable safety issues. The studies on the effects of the use of BWs on infants' motor functions have yielded varying results. Some studies have reported that use of BWs interfered with the expected motor development process such as crawling, standing and walking independently, and may cause developmental delay by preventing the visual experience that is important in this process, some others proposed that these devices had no effect on neuromotor development (1, 5-10). Another concern with BWs use has been the rate of accidents / injuries, which has been shown to occur in 12% to 50% of users (11-13). The ease of movement that walkers provide for young children facilitates the access to hazardous factors such as heaters, hot drinks and poisons, which increase the risk of accidents. After the setup of the standards for the safety of walkers in the USA, there has been a decrease in infant walker-related injuries. However, they still continue to be a cause of serious and preventable injuries (12).

The frequency of BWs use in Turkey has been reported as between 54.0% to 75.4% and the frequency of accidents among BW users was reported as between 7.8 % to 28.9 % (2, 9, 14). There is currently no legislation in our country regarding the use and/or safety of BWs.

It has been reported that the motor and cognitive developmental progress of children is affected by the use of baby walkers (5, 8). Since the amount of studies on the use of baby walkers is limited in our country, we aimed to study the information containing the thoughts of a group of 6-24 months old children's mothers about the baby walkers, and their usage practice to obtain a picture of our population on this issue.

METHOD

After receiving the institutional ethics committee's approval (with the decision from the Clinical Research Ethics Committee of University of Health Sciences - Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Ankara, Turkey, registered with number E-22/02-270 Protocol No. 2020-KAEK-141/277 dated 02/02/2022), the study was conducted over 345 mothers having children of ages between 6-24 months. The participants were those who have initially applied for vaccinations, routine checkups, or for childhood ailments at the pediatric outpatient clinics of one public and one private hospital in Ankara of Turkey, in 3 months duration from February to April, 2022. Infants known to have any congenital abnormality, chronic illnesses, or complications causing loss of locomotor skills and prematurity were excluded from the study. Fathers or other caregivers were not included in the study since the applicants for healthcare were mostly mothers. The data of the study were obtained by two pediatricians in accordance with the questions prepared in accordance with the literature (1, 9, 15). The questionnaire form used is attached as Supplement 1. Mothers were informed about the aim of and the expectations from the study, and verbal consent on their willing to participate in the study was obtained. The questionnaire form was filled out using a face-to-face interview technique, which was taking about 10-12 minutes. Queries included the sociodemographic characteristics of the family, the number of their children, their parental attitudes towards the use of baby walkers, their reasons for using a walker and also the parents' awareness of walker-associated hazards. Reports of injuries in infants who used walkers, particularly serious injuries (those requiring emergency care, or hospitalization or resulting in mortality) were documented. The infants' crawling and walking ages were noted. The data belonging to those who use or do not use a baby walker were separated and compared.

Statistical analyses were done using SPSS 16 (Chicago, IL, USA). Categorical and quantitative variables were presented as percentages or as mean and standard deviation, respectively. Chi-square or Fisher's exact test were done to examine categorical data for two groups. An independent t-test was used for comparison of means for quantitative variables. ' $p < 0.050$ ' was considered statistically significant.

RESULT

The ages of the mothers were between 19-43 years, with a mean of 32 years. 38.0% of the mothers were high school graduates, while 39.5% had graduated from a university. 58.4% of the mothers had a job.

The mean age of children was 16 months (min: 6, max: 24) and 41.5% of them were female. 48.9% (n=173) were the first baby, and 50.3% were born in a private hospital. The frequency of BW use was 58.1%. The mean age of onset of BW use was 7.3 ± 0.98 months. The majority of the infants were introduced to BW use at 7 and 8 months (70.0 %). The usage of walkers by boys when compared to girls was slightly higher but the difference was not significant ($p=0.920$). The mean age mothers of BW using children was 32.2 ± 4.5 , and that of the non-users' was 31.5 ± 4.6 . No statistically significant association was determined between the age of the mothers and the use of BW ($p=0.170$). No statistically significant correlation was found between the types of family, the education levels of the mothers, and number of children in the family (respectively; $p=0.722$, $p=0.992$, $p=0.161$). When the mothers' working status and BW usage attitudes are evaluated; 64.5% of the working mothers were using BW while this ratio was 34.5% in non-working mothers.

There was a statistically significant difference between the working statuses of the mothers and their BW usage attitudes ($p<0.006$). The sociodemographic characteristics of the entire data are shown in Table I.

Table I: Comparison of socio-demographic properties of the mothers between users and non-users of BW.

	BW user (n=206) n (%)	BW non-user (n=148) n (%)	p
Gender of the children			0.92
Female	86 (41.7)	61 (41.2)	
Male	120 (58.2)	87 (58.7)	
Family type			0.722
Nuclear	193 (93.6)	140 (94.5)	
Extended	13 (6.3)	8 (5.4)	
Mother's working status			0.006
Working	133 (64.5)	74 (50.0)	
Not working	73 (34.5)	74 (50.0)	
Maternal education			0.992
Primary	43 (20.8)	31 (20.9)	
High school	115 (55.8)	82 (55.4)	
University	48 (23.3)	35 (23.6)	
Number of children in family			0.161
One	94 (45.6)	79 (53.3)	
More than one	112 (54.3)	69 (46.6)	
No	64 (31.0)	73 (49.3)	

BW: Baby walker

Table II: The reasons of mothers for using and not using a baby walker for their children.

	n (%)
Users	
To be able to do housework	98 (47.5)
To keep the baby occupied and entertained	54 (26.2)
Parental wish	37 (18.0)
To make the baby's legs stronger	9 (4.3)
Promotes early walking	8 (3.8)
Total	206 (100)
Non-users	
Give harm to their sons' genital organs	51 (34.4)
It may impair the baby's walking	35 (23.6)
Pediatrician did not suggest	26 (17.5)
The baby bored	11 (7.4)
Because the baby walked early	10 (6.7)
Associated with injuries	9 (6.0)
No reason	6 (4.0)
Total	148 (100)

The mothers' rationales for BW use were as follows: use of BW made housework more possible to do (47.5%); the baby was kept busy and entertained (26.2%); elders' recommendation (18.0%); and belief on contribution to strengthening of legs (4.3%). Mothers stating no usage of a BW provided several reasons for their decision: the BW could harm the genital organs of their sons (34.4%); no recommendation received from a pediatrician (17.5%); and that it may impair the baby's walking (23.6%). The responses to the BW usage questionnaire are shown in Table II.

The mean daily time duration of BW usage was 70 minutes (Min: 45 Max: 90). In addition, the mean duration of BW usage before discontinuing was 1.9 months. No significant difference was observed in the mean age of beginning crawling and independent walking between the two groups (respectively; $p=0.667$, $p=0.614$). 9.2% of 206 children using BW had an accident / injury history. 13 of these accidents were related with the use of walker, and 6 were due to the problems related with the walker's mechanism. There was no statistically significant difference between the amounts of BW-related accidents and the education levels of the mothers ($p=0.790$). The factors involving the presence of helpers at home ($p=0.740$) and the genders of the infants ($p=0.514$) also did not have any statistically significant differences. The mothers have benefited from various sources when establishing their preferences for the use of BW, such as: 36.5% grandmother, 24.6% own experience, 16.7% close friends, 17.5% pediatricians, 7.4% media, and 2.3% literature knowledge. 75% of the 207 BW user mothers have owned them by purchase and two thirds of those purchasers have not performed any investigation beforehand about the features of the BWs like brand, made, safety etc.

DISCUSSION

The baby walker is commonly used all around the world. In our study, baby walkers were used in the majority (about 58.1%) of infants. Similarly Mete et al. (9) reported that the frequency of BW use was 57.5%. About half of the mothers using BW thought that they could spare time for both housework and themselves, while a quarter thought that the baby was happier when using BW. The mothers' reasons for using BW are similar to the results of previous studies on this subject (2,7,10,16,17).

It has been reported that the education level of the mother was effective in determining the attitude about BW use, and young mothers with lesser education used BW more frequently (1,18). On the other hand, studies reporting that education level does not affect BW use have also been reported (9, 15, 19). In our study, no relationship was determined between the level of education and the attitude about BW use. The use of BW continues as a traditional behavior, and problem-oriented education rather than formal education may be more effective in changing traditional attitudes (20).

Although it has been reported that families with one child use BWs more than families with more than one child, our study has revealed no relationship between the number of children in the family and the attitude towards BW use. Similarly Mete et al.(9) reported that no relationship between the number of children in the family and the attitude towards BW use was found (1).

The working statuses of mothers in the family affect the attitude about BW use. In our study, working mothers were shown to use BW more than the housewives mothers. It was thought that the possible reason for this was the effort of working mothers to be with their baby during the rest of the work and be able to control him. Similarly, Yaghini et al. (19) reported that BW usage was higher in working mothers. On the other hand, Mete et. al. (18) reported just the opposite that housewives use BWs more than working mothers. In our study, mothers were not asked about the sector they worked in. This is the limitation of the study; because the word "working" is a broad concept and not every mother's working conditions are the same.

In our study, approximately one-third of mothers not using BWs have stated as a reason that it could harm the genital organs of their boys. Dogan et al. (2) reported that families used baby walkers less frequently for boys due to similar worries. Despite such concerns, boys were found to use baby walkers more than girls do. The traditional belief that boys are valued more and should be protected more considering the continuity of the lineage is still popular, especially in the oriental societies (21). Although there is no data in the literature on mothers' reluctance to use BWs for their boys, this approach may be favored since it protects them from other negative effects of BWs.

In this study some of the mothers thought that using BW would help the infant to have stronger leg muscles (4.3%) and Promotes early walking (3.8%). This opinion has also been

Table III: The comparison of the time to gain the gross motor skills of the children between BW users and non-users.

Age of onset of gross motor skills (months)	BW user		BW non-user		p
	Mean±SD	n	Mean±SD	n	
Crawling	9.1±1.2	198	9.0±1.4	140	0.667
Walking independently	12.3±1.4	184	12.4±1.3	139	0.614

reported among the reasons for using BW in some studies (1,9). Studies about the effects of BW use on child development report conflicting results, some studies have reported that use of BWs interfered with the expected motor development process such as crawling, standing and walking independently, some others proposed that these devices had no effect on neuromotor development (1,5-10). In our study, there was no statistically significant difference between the crawling and independent walking ages in the BW user and non-BW user groups (Table III).

In our study, some (23.6%) of the mothers not using BWs had concerns that "it might disrupt the baby's gait" and "may cause toe walking". The mothers stated that the source of such thoughts was their own experiences, grandparents or friends. In two separate studies conducted by Mete et al.(18) in 2017 and 2019, they reported that the prevalence of toe walking was higher in children using BW than those who did not (9). On the other hand, Martín-Casas et al.(22) reported that BW usage would not cause toe-walking in children in their study where neurodevelopmental characteristics of preschool children were investigated. The most commonly observed type is idiopathic toe walking. It may also occur through anatomic or neuromuscular disorders (23). The past BW usage information to be collected from the families complaining about toe-walking may provide valuable data to the pediatricians and family physicians.

A significant proportion of serious walker-related injuries are head and neck injuries of the child occurred by rolling down the stairs while in the BW (11). A decrease in BW-related injuries has been reported after the United States introduced a design regulation to prevent BW passages through stair fence gates (12). In our study, 9.2% of BW-user mothers reported BW-related accidents. Only one infant was hospitalized for a forearm fracture. Other accidents included bruising and soft-tissue injuries that did not require medical treatment. These have occurred by falling over the carpet, crushing the door or the wall, and having the BW broken down. Frequency of injuries related to BWs in our study was found lower compared to previous reports (1,2,9,13,15). In our study, the fact that almost all of the families lived in single-storey apartments and that the caregivers were mostly close relatives such as grandmothers may have diminished serious BW-related accidents significantly. Since the data of our study were obtained from mothers in the pediatric outpatient clinic, the frequency of BW-related accidents may

have revealed lower. Also, majority of the mothers both using and not using BW were aware of BW-related accidents and the need to close monitoring their babies to prevent these accidents, which may also explain the low frequency.

Mothers' decisions and practices on BW usage are influenced by their daily life routines and the recommendations of their parents and pediatricians (10). In this study, 36.5% of the mothers decided to use or not to use BW upon the advices of their grandmothers. 17.5% of mothers did not use BW due to the warnings by their pediatricians that the use of baby walker may adversely affect the motor development of infants. Similarly, Mete et al.(9) reported that 20% of the mothers received advice from their pediatricians not to use BW. It has been noted in a study in the literature that pediatricians are aware of the risks and disadvantages and therefore do not recommend the use of BWs. However, no satisfactory alternatives could be offered to the parents to replace BWs (24).

About two-thirds of the mothers did not research the features (such as the brand, the material used, the safety mechanism that can prevent it from falling, etc.) before purchasing BW. They just chose a model that fit their budget. They had not received any warnings about possible safety hazards and related precautions from the store they bought it from.

The limitations of our study; the data have been collected as verbal statements of the mothers. The children's gait and development were not followed up and the developmental tests were not applied regularly. Since it is a hospital-based study, the data were not representative for the whole population.

CONCLUSION

In this study, we observed that mothers' decisions to use BWs were not homogeneous. Therefore it is important to provide information to the mothers or other caregivers based on the literature and evidence in routine child health follow-ups.

REFERENCES

- Shiva F, Ghotbi F, Yavari S. The use of baby walkers in Iranian infants. *Singapore Med J* 2010;51:645-9.
- Dogan DG, Bilici M, Yilmaz AE, Catal F, Keles N. Baby walkers: a perspective from Turkey. *Acta paediatr* 2009;98:1656-60.
- Thein M, Lee J, Tay V, Ling S. Infant walker use, injuries, and motor development. *Inj Prev* 1997;3:63-6.
- Alessa M, Humoud M, Al Qabandi W. Parental attitudes toward the use of baby walkers. *Int J Health Sci* 2015;3:109-13.
- Garrett M, McElroy A, Staines A. Locomotor milestones and babywalkers: cross sectional study. *BMJ* 2002;324:1494.
- Siegel AC, Burton RV. Effects of baby walkers on motor and mental development in human infants. *J Dev Behav Pediatr* 1999;20:355-61.
- Herzog JI, Schmahl C. Adverse childhood experiences and the consequences on neurobiological, psychosocial, and somatic conditions across the lifespan. *Front Psychiatry* 2018;9:420.
- Talebian A, Honarpishe A, Taghavi A, Fakharian E, Parsa M, Mousavi GA. Do infants using baby walkers suffer developmental delays in acquisition of motor skills? *Iran J Child Neurology* 2008;2;15-8.
- Melike M, Devocioğlu E, Boran P, Yetim A, Pazar A, Gökçay G. Baby Walker Use and Its Consequences in a Group of Turkish Children. *J Child* 2017; 17:158-62.
- Chagas PS, Mancini MC, Tirado MG, Megale L, Sampaio RF. Beliefs about the use of baby walkers. *Rev Bras Fisioter* 2011;15:303-9.
- American Academy of Pediatrics. Injuries associated with infant walkers. *Pediatrics* 2001;108:790-2.
- Sims A, Chounthirath T, Yang J, Hodges NL, Smith GA. Infant Walker-Related Injuries in the United States. *Pediatrics* 2018;142:e20174332.
- Barss P, Grivna M, Al-Hanaee A, Al-Dhahab A, Al-Kaabi F, Al-Muhairi S. Baby walker injury, disability, and death in a high-income middle eastern country, as reported by siblings. *Inj Epidemiol* 2016;3:17.
- Özdemir AA, Kurt FY, Köse S, Oğul T. Annelerin çocuklarında yürüteç kullanma durumları ve yürütece bağlı kazaların incelenmesi: Doğu ve batı örneği. *Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi* 2018;21:189-95.
- Al-Nouri L, Al-Isami Sa. Baby walker injuries. *Ann Trop paediatr* 2006;26:67-71.
- Kendrick D, Marsh P. Babywalkers: prevalence of use and relationship with other safety practices. *Inj Prev* 1998;4:295-8.
- Bar-on ME, Boyle RM, Endriss EK. Parental decisions to use infant walkers. *Inj Prev* 1998;4:299-300.
- Mete M, Keskindemirci G, Gokçay G. Baby walker use and child development. *Int J Pediatr Res* 2019;5:051.
- Yaghini O, Goodarzi M, Khoei S, Shirani M. Effect of Baby Walker Use on Developmental Status based on Ages and Stages Questionnaire Score (ASQ). *Iran J Child Neurol* 2020;14:105-11.
- Shahsavari H, Zare Z, Parsa-Yekta Z, Griffiths P, Vaismoradi M. Learning situations in nursing education: A concept analysis. *Res a Theory Nurs Pract* 2018;32:23-45.
- Abeykoon A. Sex preference in south Asia: Sri Lanka an outlier. *Asia Pac Popul J* 1995;10:5-16.
- Martín-Casas P, Ballesteró-Pérez R, Meneses-Monroy A, Beneit-Montesinos J, Atín-Arratibel M, Portellano-Pérez J. Neurodevelopment in preschool idiopathic toe-walkers. *Neurología* 2017;32:446-54.
- Ruzbarsky JJ, Scher D, Dodwell E. Toe walking: causes, epidemiology, assessment, and treatment. *Curr Opin Pediatr* 2016;28:40-6.
- Rhodes K, Kendrick D, Collier J. Baby walkers: paediatricians' knowledge, attitudes, and health promotion. *Arch Dis Child* 2003;88:1084-5.

Supplement 1: Baby Walker Questionnaire (Survey answered by only mother)

Maternal age

Maternal education

Primary

High school

University

Family type

Nuclear

Extended

Mother's working status

Working

Not working

Home caregiver; Yes-No

Gender of the children; Female - Male

Mean age of child (months)

Number of children in family

One

More than one

Crawling age?

Independent walking age?

Does the baby use a Baby Walker?

Why use Baby Walker?

To be able to do housework

To keep the baby occupied and entertained

Parental wish

To make the baby's legs stronger

Promotes early walking

Why not use Baby Walker?

Give harm to their sons' genital organs

It may impair the baby's walking

Pediatrician did not suggest

The baby bored

Because the baby walked early

Associated with injuries

No reason

Age at starting to use Baby Walker?

Daily use of walker (minutes)?

Getting knowledge about Baby walker?

Health care professional

Other(grandmother, self-experience)

Origin of Baby Walker (Purchased/transferred/borrowed?)

Decision-making on the type of BW (Brand/safety/material/budget?)

Baby walker related accident?

Type of accident?

Clinical and Sociodemographic Characteristics of Patients Hospitalized in a Child and Adolescent Psychiatry Inpatient Unit

Bir Çocuk ve Ergen Yataklı Psikiyatri Servisinde Tedavi Gören Hastaların Klinik ve Sosyodemografik Özellikleri

Merve ONAT, Elif AKÇAY, Ayşegül DEMİR, Ümran Gül AYVALIK BAYDUR, Zeynep GÖKER, Gülser ŞENSES DİNÇ, Esra ÇÖP

Department of Child and Adolescent Psychiatry, Bilkent City Hospital, Ankara, Turkey



ABSTRACT

Objective: In this study, it was aimed to examine the clinical and sociodemographic characteristics of patients hospitalized in Ankara City Hospital Child and Adolescent Psychiatry Inpatient Unit during the pandemic period.

Material and Methods: Medical records of children and adolescents who were hospitalized in Ankara City Hospital Child and Adolescent Psychiatry Inpatient Unit between March 2021 and March 2022 were retrospectively analyzed. Patients were evaluated in terms of sociodemographic characteristics, clinical diagnosis and treatment, duration of hospitalization, and Clinical Global Impression Scale (CGI) scores at admission and discharge.

Results: In our study, the mean age of 132 cases (86 girls, 46 boys) was found 15.1±1.8 years. The main diagnoses of the subjects were 30.3% (n=40) major depressive disorder, 25% (n=33) psychotic disorder, 14.4% (n=19) eating disorders, and the remaining 30.3% (n=40) were other disorders. Comorbidity was found in 63.6% (n=84) of the cases. The presence of eating disorders, comorbidity and antidepressant use were found significantly higher in females. There was a significant differences in major depressive disorder (MDD), bipolar disorder (BD), psychotic disorder, eating disorder, conduct disorder, and post-traumatic stress disorder (PTSD) between admission and discharge CGI-Severity (CGI-S) scores. In addition, there was a significant difference between admission and discharge CGI side effects scores only for BD.

Conclusion: In our study, major depressive disorder, psychotic disorder, and eating disorder were the most common diagnoses of cases hospitalized in inpatient unit. There was a comorbidity accompanying two out of every three cases. There are few child and adolescent psychiatry services in our country, and studies on this subject are scarce. It is thought that our study will contribute to the literature on child and adolescent psychiatry inpatient units.

Key Words: Adolescent, Child psychiatry, Hospitalization, Inpatients, Psychopathology, Treatment

15

0000-0002-1970-672X : ONAT M
0000-0002-4673-6254 : AKÇAY E
0000-0002-7828-1194 : DEMİR A
0000-0002-3553-8287 : AYVALIK BAYDUR UG
0000-0002-6489-3800 : GÖKER Z
0000-0001-5556-3175 : ŞENSES DİNÇ G
0000-0001-8451-0099 : ÇÖP E

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 ethics committees of Ankara City Hospital dated 27.04.2022 and numbered E2-22-1692.

Contribution of the Authors / Yazarların katkısı: **ONAT M:** 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. **AKÇAY E:** 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. **DEMİR A:** 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. **AYVALIK BAYDUR UG:** 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. **GÖKER Z:** 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, Reviewing the article before submission scientifically besides spelling and grammar. **ŞENSES DİNÇ 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, Reviewing the article before submission scientifically besides spelling and grammar. **ÇÖP E:** 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, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Onat M, Akçay E, Demir A, Ayvalık Baydur UG, Göker Z, Şenses Dinç G, et al. Clinical and Sociodemographic Characteristics of Patients Hospitalized in A Child and Adolescent Psychiatry Inpatient Unit. Turkish J Pediatr Dis 2023;17:207-213.

Correspondence Address / Yazışma Adresi:

Merve ONAT
Department of Child and Adolescent Psychiatry,
Bilkent City Hospital, Ankara, Turkey
E-posta: merve_01_10@hotmail.com

Received / Geliş tarihi : 29.11.2022

Accepted / Kabul tarihi : 29.12.2022

Online published : 26.01.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1211443

ÖZ

Amaç: Bu çalışmada pandemi sürecinde Ankara Şehir Hastanesi Çocuk ve Ergen Psikiyatri Servisinde yatarak tedavi gören hastaların klinik ve sosyodemografik özelliklerinin incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Mart 2021-Mart 2022 tarihleri arasında Ankara Şehir Hastanesi Çocuk ve Ergen Psikiyatri Servisinde yatarak tedavi gören hastaların yatış dosyaları geriye dönük olarak incelenmiştir. Hastalar sosyodemografik veriler, yatış sırasında aldıkları tanı ve tedaviler, yatış süresi, yatış ve taburculuk sırasındaki Klinik Global İzlenim Ölçeği (KGIÖ) puanları açısından değerlendirilmiştir.

Bulgular: Çalışmamızda toplam 132 olgunun (86 kız, 46 erkek) yaş ortalaması 15.1±1.8 yıl olarak bulunmuştur. Olguların %30.3'ü (n=40) major depresif bozukluk (MDB), %25'i (n=33) psikotik bozukluk, %14.4'ü yeme bozuklukları (n=19) ve %30.3'ü (n=40) diğer bozukluklar idi. Olguların %63.6'sında (n=84) klinik bozukluk tanısına eşlik eden komorbid başka bir bozukluğun varlığı saptanmıştır. Kız cinsiyetinde yeme bozukluğu, komorbidite varlığı ve antidepresan kullanımı anlamlı yüksek bulunmuştur. Hastaların almış olduğu tanılara göre yatış-çıkış Klinik Global İzlenim Ölçeği hastalık şiddeti (KGIÖ-HŞ) skorları karşılaştırıldığında, MDB, bipolar bozukluk (BPB), psikotik bozukluk, yeme bozukluğu, davranım bozukluğu ve travma sonrası stres bozukluğu (TSSB)'nun anlamlı düzeyde farklılık gösteren bozukluklar olduğu saptanmıştır. Yatış-çıkış KGIÖ yan etki skorları arasında ise yalnızca BPB için anlamlı düzeyde farklılık saptanmıştır.

Sonuç: Çalışmamızda serviste yatarak tedavi gören hastaların en sık major depresif bozukluk, psikotik bozukluk ve yeme bozukluğu tanıları olduğu ve her 3 olgudan ikisine eşlik eden bir komorbidite varlığı saptanmıştır. Ülkemizde çocuk ve ergen psikiyatri servisleri az sayıda olup bu konuda yapılan çalışmalara az rastlanmakta, çalışmamızın çocuk ruh sağlığı yataklı servisleri hakkındaki alan yazına katkı sağlayacağı düşünülmektedir.

Anahtar Sözcükler: Ergen, Çocuk psikiyatri, Hastane yatışı, Yatan hasta, Psikopatoloji, Tedavi

INTRODUCTION

It is known that most of psychiatric disorders emerge during childhood and adolescence (1). Inpatient psychiatry units are of great importance in treatment of children and adolescents who need intensive professional support and cannot be treated in outpatient clinic (2). Despite the development of medical treatment options in recent years, it has been determined that there is a gradual increase in children and adolescents who need inpatient treatment. Nevertheless, the number of child and adolescent psychiatry units worldwide is not sufficient, and many children cannot benefit from inpatient treatment opportunities (3).

Children and adolescents should receive treatment in the least restrictive environment possible, therefore hospitalization should be considered in the presence of severe psychiatric disorders where the child poses a danger to himself or others and has significant impairment in functionality. The main reasons for hospitalization of patients with psychiatric disorders are to intervene in crisis, ensure the safety of the patient, make a comprehensive assessment and long-term treatment planning (3). Besides, compulsory hospitalization may be required in treatment-resistant psychiatric diseases such as psychotic disorders and in cases with poor response to treatment (4). Additionally, in patients with suicidality, self-harm behavior, uncontrollable aggressive behaviors, and diagnostic uncertainty, inpatient treatment may be considered necessary (5).

Childhood and adolescence are critical periods in which biological and social changes are seen, in order to reduce the long-term negative effects of psychiatric diseases (6). Thus, child and adolescent psychiatry inpatient units are of great importance in treatment. It is known that the number of inpatient child and adolescent psychiatry units in our country is few. Therefore, the literature about the patients treated in the

child and adolescent psychiatry unit and the level of benefit they receive from the treatment is insufficient. It is thought that this study will contribute to the literature about the effects of child and adolescent psychiatry units on treatment and the factors associated. In our study, it is aimed to retrospectively examine the sociodemographic characteristics, psychiatric diagnoses, treatments, duration of hospitalization, disease severity during hospitalization and response to treatment at discharge of inpatients in Ankara City Hospital Child and Adolescent Psychiatry Inpatient Unit.

MATERIALS and METHODS

In our study, medical records of patients under the age of 18 who were hospitalized in Ankara City Hospital Child and Adolescent Psychiatry Inpatient Unit between March 2021 and March 2022 were retrospectively analyzed. Patients whose hospitalization duration was shorter than one day due to treatment refusal or hospitalization data were missing were not included in the study. Using the patient follow-up form prepared by the researchers, the patients' age, gender, family characteristics, socioeconomic status, clinical diagnosis, and treatments received during hospitalization, duration of disease and age at onset, duration of hospitalization, Clinical Global Impression Scale (CGI) disease severity, improvement, and side effect scores at admission and discharge were recorded. The diagnoses of patients during their hospitalization were made through clinical interviews according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) of the American Psychiatric Association. This study was approved by the ethics committees of Ankara City Hospital dated 27.04.2022 and numbered E2-22-1692.

CGI (Clinical Global Impression Scale): CGI is a clinician-rated scale which is developed by Guy et al. in 1976. It is a scale

that evaluates the severity of the disease, the improvement in symptoms and the level of side effects of the treatment. It grades the severity of the disease (GGI-S) and the degree of improvement (CGI-I) between 0 and 7, and the severity of side effects between 1 and 4 (7).

Statistical analysis

Statistical analysis in the study was performed using SPSS 24.0 (The Statistical Package for Social Sciences) program. The distributions of continuous variables were evaluated with the "Kolmogorov-Smirnov" test. Normally distributed variables were expressed as arithmetic mean and standard deviation (SD), and non-normally distributed variables were expressed as median and interquartile range (IQR). Categorical variables were expressed as frequency (n) and percentage (%). Student t test, Mann Whitney U test, Pearson- χ^2 test, and paired t test were used for comparisons. $p < 0.050$ was accepted as the significance level.

RESULTS

It was found that there were 150 patients who were hospitalized in our Child and Adolescent Psychiatry Inpatient Unit in a one-year period. Ten of them were discharged on the same day of admission because of treatment refusal. Eight of them were excluded from the study due to missing data. Among 132 patients who met the inclusion criteria, 86 (65.2%) were girls and 46 (34.8%) were boys. The mean age of the patients was 15.1 ± 1.8 years, the median was 15.6 (7-16) years. The mean age of girls was 15.3 ± 1.6 , median was 15.8 (7-18) years, and the mean age of boys was 14.8 ± 2.1 , median was 15.0 (8-18) years.

The most common diagnoses during hospitalization were major depressive disorder (MDD) (n=40, 30.3%), psychotic disorders (n=33, 25%), and eating disorders (n=19, 14.4%). Other common diagnoses are bipolar disorder (BD) (n=10, 7.6%), conduct disorder (n=9, 6.8%), post-traumatic stress disorder (PTSD) (n=7, 5.3%), anxiety disorder (n=3, 2.3%), obsessive compulsive disorder (OCD) (n=3, 2.3%), intellectual disability (ID) (n=3, 2.3%), and dissociative disorder (n=3, 2.3%) was determined. In addition, one patient (0.8%) was diagnosed with autism spectrum disorder (ASD) and another patient (0.8%) was diagnosed with conversion disorder. As well as at least one comorbid psychiatric disorder was found in 84 (63.6%) patients. Having an eating disorder diagnosis in girls was found to be statistically significantly higher (22.1% vs. 0%, $p=0.004$). Again, comorbid psychiatric disorders were found to be significantly higher in girls (69.8% vs. 52.2%, $p=0.045$).

There were no significant differences between boys and girls with respect to disease duration, age at onset, duration of hospitalization ($p > 0.050$ for all variables, Table I). Means of

duration of hospitalization was 22.2 ± 11.3 for MDD, 46.9 ± 35.0 for psychotic disorder, 42.1 ± 24.6 for eating disorder, 37.2 ± 26.3 for BD, 25.6 ± 8.0 for conduct disorder, 26.4 ± 11.4 for PTSD, 26.7 ± 28.9 for anxiety disorder, 43.7 ± 24.5 for OCD, 24.3 ± 6.0 for ID, 16.3 ± 9.1 for dissociative disorder. Likewise, mean values of admission and discharge CGI scores of both genders were found to be similar ($p > 0.050$, Table I). While it was the first hospitalization of 82.5% (n = 109) of the cases, it was the second or more hospitalization of 17.5% (n=23). The frequency of hospitalization was found to be similar between both genders ($p=0.910$). While single psychotropic medication was used in only 11.4% (n=15) of the cases, dual combination was used in 52.3% (n=69) and triple or more psychotropic combination was used in 36.4% (n=48) of them. The number of medication combinations was found to be similar between both genders ($p > 0.050$, Table II). However, antidepressant use was found to be significantly higher in girls (73.3% vs. 37%, $p < 0.001$).

There was a significant difference between admission-discharge CGI-S scores with respect to MDD ($p < 0.001$), psychotic disorder ($p < 0.001$), eating disorder ($p < 0.001$), BD ($p=0.040$), conduct disorder ($p < 0.001$) and PTSD ($p=0.001$). In addition, admission-discharge CGI-I scores were differ for MDD ($p < 0.001$), psychotic disorder ($p < 0.001$), eating disorder ($p < 0.001$), BD ($p < 0.001$), conduct disorder ($p < 0.001$), PTSD ($p < 0.001$), and anxiety disorder ($p=0.038$). There was a significant difference between admission and discharge CGI side effect scores only for BD ($p=0.009$) (Table III).

DISCUSSION

In this study, sociodemographic characteristics, duration of hospitalization, diagnosis and treatment, and admission and discharge CGI scores of the patients treated in the Child and Adolescent Psychiatry Inpatient Unit were retrospectively examined. In our study, the number of girl inpatients was found to be approximately twice the number of boys. Although girls are seen at a higher rate among child and adolescent inpatients according to studies conducted in recent years, gender ratio were found to be close to each other in some of them (8, 9). It was thought that the high prevalence of diagnoses such as major depressive disorder and eating disorder in our inpatient unit, which are frequently seen in girls, could explain the girl predominance (10, 11).

In our study, it was found that almost a third of the patients were hospitalized for major depressive disorder and a fourth of them were hospitalized for psychotic disorder. The findings of our study are consistent with the results of previous studies (12, 13). In accordance with similar studies conducted in our country, major depressive disorder was found to be the most common diagnosis in child and adolescent psychiatry inpatient units (13, 14). However, in a recent study, bipolar disorder was found to

Table I: Comparison of demographic and clinical characteristics of 132 children and adolescents hospitalized in inpatient unit by gender

	Total n = 132	Female n = 86	Male n = 46	Statistics t, z / X ²	p
Demographic					
Age (year)*	15.6 (2.4)	15.7 (1.9)	15.0 (3.5)	-1.276	0.202
Mother's age (year)†	43.4 (6.1)	43.6 (6.2)	43.2 (6.0)	0.326	0.745
Father's age (year)†	48.0 (7.6)	48.6 (8.2)	47.1 (6.2)	0.999	0.320
Mother's educational status (year)*	6.5 (9)	5 (8)	8 (10)	-0.020	0.984
Father's educational status (year)*	8 (10)	8 (10)	8 (10)	-0.381	0.704
Number of siblings,§				0.235	0.889
Single	21 (16.2)	13 (15.5)	8 (17.4)		
Two	40 (30.8)	27 (32.1)	13 (28.3)		
Three or more	69 (53.1)	44 (52.4)	25 (54.3)		
Order of siblings,§				3.219	0.200
First	60 (46.2)	39 (46.4)	21 (45.7)		
Second	38 (29.2)	28 (33.3)	10 (21.7)		
Third or more	32 (24.6)	17 (20.2)	15 (32.6)		
Clinical characteristics					
Diagnose,§				11.247	0.004
MDD	40 (30.3)	33 (38.4)	7 (15.2)		
Psychotic disorder	33 (25.0)	14 (16.3)	19 (41.3)		
Eating disorder	19 (14.4)	19 (22.1)	0		
BD	10 (7.6)	6 (7.0)	4 (8.7)		
Conduct disorder	9 (6.8)	4 (4.7)	5 (10.9)		
PTSD	7 (5.3)	6 (7.0)	1 (2.2)		
Anxiety disorder	3 (2.3)	1 (1.2)	2 (4.3)		
OCD	3 (2.3)	0	3 (6.5)		
ID	3 (2.3)	1 (1.2)	2 (4.3)		
Dissociative disorder	3 (2.3)	2 (2.3)	1 (2.2)		
Conversion disorder	1 (0.8)	0	1 (2.2)		
ASD	1 (0.8)	0	1 (2.2)		
Comorbidity,§	84 (63.6)	60 (69.8)	24 (52.2)	4.009	0.045
Smoking,§	24 (18.2)	14 (16.3)	10 (21.7)	0.601	0.438
Alcohol use,§	12 (9.1)	8 (9.3)	4 (8.7)	0.013	0.908
Duration of disorder (month)*	18 (28.75)	18 (28)	24 (30)	-0.034	0.973
Age at onset (year)*	13 (3)	13 (3)	12 (4.25)	-1.737	0.082
Duration of hospitalization (day)*	26 (18)	27 (18.5)	24 (18)	-1.075	0.282
Order of hospitalization,§				0.391†	0.910
First	109 (82.5)	70 (81.4)	39 (84.8)		
Second	20 (15.2)	14 (16.3)	6 (13.0)		
Third or more	3 (2.3)	2 (2.3)	1 (2.2)		
Admission CGI (score)†					
Severity	4.8 (0.9)	4.8 (0.8)	4.6 (1.0)	0.329	0.743
Improvement	4.3 (0.7)	4.3 (0.7)	4.1 (0.7)	1.478	0.142
Side effects	1.3 (0.5)	1.2 (0.5)	1.4 (0.5)	-1.717	0.088
Discharge CGI (score)†					
Severity	3.7 (0.9)	3.8 (0.7)	3.6 (1.2)	0.986	0.326
Improvement	2.7 (0.5)	2.8 (0.5)	2.7 (0.7)	0.970	0.334
Side effects	1.3 (0.5)	1.3 (0.5)	1.4 (0.6)	-1.143	0.255

*: Median (IQR), †: Arithmetic mean (Standard deviation), ‡: Fisher's exact test, §: n (%), **MDD**: Major depressive disorder, **BD**: Bipolar disorder, **PTSD**: Post-traumatic stress disorder, **OCD**: Obsessive-compulsive disorder, **ID**: Intellectual Disability, **ASD**: Autism spectrum disorder, **CGI**: Clinical Global Impression Scale

Table II: Comparison of medical treatments utilized in inpatient unit by gender

	Total n = 132	Female n = 86	Male n = 46	Statistics Pearson χ^2	p
Combination,*					
Single	15 (11.4)	6 (7.0)	9 (19.6)	5.231	0.073
Dual	69 (52.3)	49 (57.0)	20 (43.5)		
Triple or more	48 (36.4)	31 (36.0)	17 (37.0)		
Psychotropic,*					
Antipsychotics	128 (97.0)	82 (95.3)	46 (100.0)	2.206 [†]	0.137
Antidepressants	80 (60.6)	63 (73.3)	17 (37.0)	16.540	0.000
Benzodiazepine	33 (25.0)	21 (24.4)	12 (26.1)	0.044 [†]	0.836
Mood stabilizers	19 (14.4)	11 (12.8)	8 (17.4)	0.515 [†]	0.603
Psychostimulants	14 (10.6)	9 (10.5)	5 (10.9)	0.005 [†]	1.000

†:n(%), *: Fisher's exact test

be more common among mood disorders (9). According to a study performed in the USA, it was found that attention deficit hyperactivity disorder, specific learning disorder and conduct disorder were the most common diagnosis group after major depressive disorder, bipolar disorder and anxiety disorders (15). In another study conducted in Japan, it was shown that the most common diagnoses in patients hospitalized in the child and adolescent psychiatry inpatient unit were obsessive-compulsive disorder and eating disorder, respectively (16). It is thought that the variability between the diagnosis rates may be related to the fact that studies conducted in different samples and among different age groups.

In this study, it was found that the third common diagnose was eating disorder, and 15% of hospitalized patients were diagnosed with eating disorder. In other studies conducted in our country, this rate was found between 3-5% (9, 12, 17). Although there are conflicting findings in the literature, it is thought that there is an increase in the frequency of eating disorders according to some studies (18). It is suggested that management of eating disorders, which are very challenging in outpatient clinic, may require a multidisciplinary approach. It is thought that the low number of child and adolescent psychiatry inpatient units in our country and the fact that patients with a compelling disease such as eating disorder need to be hospitalized may explain the higher incidence of eating disorders in our study. In our inpatient unit, referred patients with eating disorders diagnosed from all over the country are approached by a team of child psychiatrists, pediatricians, psychologists, nurses and dietitians, results in treatment of patients with eating disorders is achieved successfully.

According to the findings of our study, it was observed that approximately 2/3 of the patients treated in the service has at least one comorbidity. In the study conducted by Serim Demirgören et al. (17), the comorbidity rate was found to be 36% in inpatient child and adolescents. High comorbidity rates are expected since patients with severe and treatment resistant psychiatric disorders are mostly treated in child and adolescent psychiatry inpatient units. However, it is thought that comorbidity rates may vary depending on the difference in the diagnosis rates of inpatients in different studies. In addition, the

rate of comorbidity in girls was found significantly higher in our study compared to males. The diagnoses of MDD and eating disorder were more common in girls in our inpatient unit. In the literature, it has been shown that high rates of comorbidity in adolescents with MDD or eating disorders (19, 20). It is thought that this may explain the higher comorbidity rate in girls in our study.

Another findings of our study is that the most frequently utilized medications were antipsychotics and antidepressants, respectively. Consistent with our findings, it was observed that the most frequently used medication was antipsychotics, and latter antidepressants in similar studies conducted in our country (9, 12). In addition, it was found that the utilization of multiple combination of medications was higher than single psychotropic use in our study. In the study of Coşkun et al. (12), single medication treatment was used in 27% of the patients, while 65% of them treated with combination of psychotropic. Moreover, it was found that polypharmacy is required 78% of child and adolescent inpatients in another research (13). It was thought that the high rates of antipsychotic drug use and polypharmacy may be associated with the admission of treatment-resistant and agitated patients into the psychiatry inpatient units. In our study, antidepressant use was found significantly higher in girls. This may be explained by that the patients hospitalized with the diagnosis of MDD in our service are mostly girls.

In our study, duration of hospitalization was found 26 days. According to studies conducted in our country duration of hospitalization in children and adolescent inpatient psychiatric units vary from 14 days to 22 days (9, 12, 14). In studies carried out in different countries, it is observed that there is a difference between the duration of hospitalization (8, 15, 16). It is suggested that the variability between the duration of hospitalization in different studies may be related to the sample group, the diagnosis rates, and the differences in the health policies of the countries.

Finally, it was determined in our study that there was a significant decrease in severity of the disease and improvement in symptoms in accordance with CGI scale for the diagnoses of

Tablo III: Distribution of admission and discharge CGI values according to disorders

Diagnose	n (%)	Admission CGI M (SD)	Discharge CGI M (SD)	Statistics Paired t	p
MDD	40 (30.3)	4.5 (0.8)	3.5 (0.6)	6.504	<0.001
CGI-S		4.4 (0.7)	2.9 (0.5)	11.699	<0.001
CGI-SE		1.1 (0.3)	1.1 (0.3)	0.681	0.500
Psychotic disorder	33 (25.0)	5.2 (0.9)	4.1 (1.0)	5.116	<0.001
CGI-S		4.4 (0.7)	2.8 (0.6)	11.081	<0.001
CGI-SE		1.5 (0.7)	1.7 (0.6)	-1.320	0.196
Eating disorder	19 (14.4)	5.1 (0.6)	3.7 (0.7)	12.929	<0.001
CGI-S		4.2 (0.7)	2.7 (0.4)	13.077	<0.001
CGI-SE		1.2 (0.4)	1.2 (0.4)	0.000	1.000
BD	10 (7.6)	4.8 (0.9)	3.8 (1.2)	2.400	0.040
CGI-S		4.1 (0.7)	2.7 (0.5)	5.513	<0.001
CGI-SE		1.4 (0.4)	2.1 (0.7)	-3.284	0.009
Conduct disorder	9 (6.8)	4.4 (0.5)	2.8 (0.7)	6.074	<0.001
CGI-S		3.9 (0.9)	2.0 (0.0)	6.107	<0.001
CGI-SE		1.3 (0.4)	1.3 (0.4)	0.000	1.000
PTSD	7 (5.3)	4.9 (0.4)	4.0 (0.0)	6.000	0.001
CGI-S		4.0 (0.0)	2.8 (0.3)	12.021	<0.001
CGI-SE		1.0 (0.0)	1.0 (0.0)	NA	NA
Anxiety disorder	3 (2.3)	4.7 (0.6)	4.2 (1.0)	1.732	0.225
CGI-S		4.3 (0.6)	2.7 (0.6)	5.000	0.038
CGI-SE		1.0 (0.0)	1.0 (0.0)	NA	NA
OCD	3 (2.3)	4.3 (0.6)	3.5 (0.5)	1.890	0.199
CGI-S		3.7 (0.6)	3.0 (0.0)	2.000	0.184
CGI-SE		1.0 (0.0)	1.0 (0.0)	NA	NA
ID	3 (2.3)	5.7 (1.2)	4.5 (0.9)	1.941	0.192
CGI-S		4.0 (0.0)	2.0 (0.0)	0.000	1.000
CGI-SE		1.3 (0.6)	1.3 (0.6)	NA	NA
Dissociative disorder	3 (2.3)	4.0 (0.0)	3.5 (0.7)	1.000	0.500
CGI-S		4.0 (0.0)	3.0 (0.0)	NA	NA
CGI-SE		1.5 (0.7)	1.5 (0.7)	NA	NA

NA: not-applicable, **M(SD):** mean (standart deviation), **CGI:** Clinical Global Impression Scale, **CGI-S:** Clinical Global Impression Scale-Severity, **CGI-I:** Clinical Global Impression Scale-Improvement, **CGI-SE:** Clinical Global Impression Scale-Side effects, **MDD:** Major depressive disorder, **BD:** Bipolar disorder, **PTSD:** Post-traumatic stress disorder, **OCD:** Obsessive-compulsive disorder, **ID:** Intellectual Disability

MDD, psychotic disorder, eating disorder, BD, conduct disorder and PTSD. However, no significant change was found in CGI scores with respect to diagnosis of ASD, ID, and OCD. This suggests that inpatient units' benefits may be more limited in patients with neurodevelopmental disorders such as ASD and ID, and in disease groups such as OCD with a high rate of resistance, compared to other disorders. In the study conducted by Demirgören et al. (19), the functionality levels were evaluated with the Child Global Assessment Scale (CGAS). In this study, it was found that CGAS scores increased from 37 points to 61 in inpatients. Although the functionality levels of patients are evaluated with different scales in various studies, it is observed

that there is an increase in the functionality of children and adolescents hospitalized in psychiatric inpatient units.

LIMITATIONS

The most important limitation of our study is retrospective examining of medical records. Another limitation is lack of factors such as follow-up after discharge, using scales other than CGI, investigating changes in medication and diagnosis between admission and discharge, and psychotherapy practices applied during hospitalization. However, examining the data of a larger

number of patients compared to other studies constitutes the strength of our study.

IMPLICATIONS

Despite the increasing need for child and adolescent psychiatry units in our country, the number of them is few. For this reason, some of the children and adolescents are hospitalized in adult inpatient units or they cannot be hospitalized and get the treatment they need. Children and adolescents diagnosed with eating disorders, who especially need to hospitalization, are handled, and successfully treated with a multidisciplinary approach in our service. Studies on this subject are rare in our country, and it is thought that our study will contribute to the literature on child and adolescent inpatient psychiatry units.

REFERENCES

- Solmi M, Radua J, Olivola M, Croce E, Soardo L, Salazar de Pablo G, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry* 2022;27:281-95.
- Hayes C, Simmons M, Simons C, Hopwood M. Evaluating effectiveness in adolescent mental health inpatient units: A systematic review. *Int J Ment Health Nurs* 2018;27:498-513.
- Reynolds EK, Gorelik S, Kook M, Kellermeyer K. Acute psychiatric care for pediatric patients. *Int Rev Psychiatry* 2020;32:272-83.
- Lay B, Kawohl W, Rössler W. Predictors of Compulsory Re-admission to Psychiatric Inpatient Care. *Front Psychiatry* 2019;10:120, doi: 10.3389/fpsy.2019.00120.
- McEnany FB, Ojugbele O, Doherty JR, McLaren JL, Leyenaar JK. Pediatric Mental Health Boarding. *Pediatrics* 2020;146:e20201174.
- Hickie IB, Scott EM, Cross SP, Iorfino F, Davenport TA, Guastella AJ, et al. Right care, first time: a highly personalised and measurement-based care model to manage youth mental health. *Med J Aust* 2019;211:3-46.
- Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edmont)* 2007;4:28-37.
- Imran N, Bodla ZH, Asif A, Shoukat R, Azeem MW. Pakistan's First Child & Adolescent Psychiatry Inpatient Unit: Characteristics of admitted patients and response to treatment over a 7-year period. *Pak J Med Sci* 2021;37:305-11.
- Karadağ M, Türk N, Gökçen C, Topal Z. Bir Üniversite Hastanesi Çocuk ve Ergen Psikiyatrisi Kliniğinde Yatan Hastaların Sosyodemografik ve Tanısal Özellikleri. *Türk J Child Adolesc Ment Health* 2021;28:7-11.
- Malhi GS, Mann JJ. Depression. *Lancet* 2018;392:2299-312.
- Ranalli DN, Studen-Pavlovich D. Eating Disorders in the Adolescent Patient. *Dent Clin North Am* 2021;65:689-703.
- Coşkun M, Bozkurt H, Ayaydın H, Karakoç S, Süleyman F, Üçok A. Bir üniversite hastanesi psikiyatri servisinde yatarak tedavi edilen ergen hastaların klinik ve sosyodemografik özellikleri. *Çocuk ve Gençlik Ruh Sağlığı Dergisi* 2012;19:17-24.
- Taş FV, Güvenir T, Miral S. Bir Çocuk ve Ergen Psikiyatrisi Kliniğinde Yatarak Tedavi Gören Hastalarda İlaç Kullanımı. *Çocuk ve Gençlik Ruh Sağlığı Dergisi* 2007;14:139-50.
- Usta MB, Ürer E, Aral A, Say GN, Karabekiroğlu K. Çocuk Psikiyatrisi Hastalarında Yatış Süresine Etki Eden Faktörler. *Klinik Psikiyatri Dergisi* 2017;20:263-7.
- Meagher SM, Rajan A, Wyshak G, Goldstein J. Changing trends in inpatient care for psychiatrically hospitalized youth: 1991–2008. *Psychiatr Q* 2013;84:159-68.
- Setoya Y, Saito K, Kasahara M, Watanabe K, Kodaira M, Usami M. Evaluating outcomes of the child and adolescent psychiatric unit: A prospective study. *Int J Ment Health Syst* 2011;5:1-8.
- Serim Demiregoren B, Ozbek A, Gencer O. Factors affecting improvement of children and adolescents who were treated in the child and adolescent psychiatry inpatient unit. *J Int Med Res* 2017;45:1318-23.
- Litmanen J, Fröjd S, Marttunen M, Isomaa R, Kaltiala-Heino R. Are eating disorders and their symptoms increasing in prevalence among adolescent population? *Nord J Psychiatry* 2017;71:61-6.
- Li F, Cui Y, Li Y, Guo L, Ke X, Liu J, et al. Prevalence of mental disorders in school children and adolescents in China: diagnostic data from detailed clinical assessments of 17,524 individuals. *J Child Psychol Psychiatry* 2022;63:34-46.
- Neale J, Hudson LD. Anorexia nervosa in adolescents. *Br J Hosp Med (Lond)* 2020;81:1-8.

Evaluation of Leflunomide Treatment in Patients with Juvenile Idiopathic Arthritis: A Single Center Experience

Jüvenil İdiopatik Artritli Hastalarda Leflunomid Tedavisinin Değerlendirilmesi: Tek Merkez Deneyimi

Elif ARSLANOĞLU AYDIN¹, Semanur ÖZDEL¹, İlknur BAĞRUL¹, Nesibe Gökçe KOCAMAZ¹, Esra BAĞLAN¹, Şerife TUNCEZ¹, Mehmet BÜLBÜL²

¹Department of Pediatric Rheumatology, Ankara Etlik City Hospital, Ankara, Turkey

²Department of Pediatric Nephrology and Rheumatology, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, Turkey



ABSTRACT

Objective: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood. Disease-modifying antirheumatic drugs (DMARD) such as methotrexate (MTX), leflunomide (LFN) are first-line treatment in JIA. MTX is the most commonly prescribed drug. Studies predominantly demonstrate the efficacy and safety of it, but the data on LFN are limited. This study aimed to present our experience with LFN treatment in JIA patients.

Material and Methods: This retrospective study included JIA patients who were followed-up regularly and had received LFN. Data on patient demographics, clinical and laboratory characteristics were obtained from medical charts.

Results: The study included 18 patients (15 female and 3 male) with a median (interquartile range) age at onset of disease 7.3 (3.1-12.0) years. Among them, 8 had oligoarticular JIA, seven had polyarticular JIA, two had systemic JIA and one had enthesitis-related arthritis (ERA). All patients received MTX as initial therapy (except one patient diagnosed with ERA was treated with sulfasalazine). MTX was discontinued and LFN treatment was started in all patients who initially received MTX due to gastrointestinal system (GIS) intolerance. Six of 7 patients with low disease activity, who had GIS intolerance while taking MTX before, were given LFN treatment because the disease activity was low. These patients achieved a complete remission with LFN. Four patients followed in remission with MTX had disease activation. These patients, who had previously experienced MTX intolerance, were given LFN treatment. Remission was achieved with LFN in 3 of 4 patients. Biological therapy was started in 6 patients with moderate or high disease activity who could not achieve remission with only MTX. These patients who did not have an adequate response were switched to LFN. Inactive disease was obtained in only 1 patient with the combination of LFN and biological agent. The patient with ERA was switched to LFN treatment due to inadequate response to sulfasalazine treatment. This patient achieved a complete remission with LFN.

Conclusion: LFN therapy may be beneficial in patients with low disease activity and/ or remission with other DMARDs and relapse after drug discontinuation.

Key Words: Disease-modifying antirheumatic drug, Juvenile idiopathic arthritis, Leflunomide

0000-0002-1287-4683 : ARSLANOĞLU AYDIN E
0000-0001-5602-4595 : ÖZDEL S
0000-0002-5585-0198 : BAĞRUL I
0000-0003-2149-3396 : KOCAMAZ NG
0000-0001-5637-8553 : BAĞLAN E
0000-0001-8606-1995 : TUNCEZ S
0000-0001-9007-9653 : BÜLBÜL M

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 carried out by Ankara Dr. It was approved by the Clinical Research Ethics Committee of Sami Ulus Obstetrics, Gynecology and Gynecology Training and Research Hospital (E-22/02-290).

Contribution of the Authors / Yazarların katkısı: **ARSLANOĞLU AYDIN E:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, 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. **ÖZDEL S:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in logical interpretation and conclusion of the results, Organizing, supervising the course of progress and taking the responsibility of the research/study. **BAĞRUL I:** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. **KOCAMAZ NG:** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. **BAĞLAN E:** Organizing, supervising the course of progress and taking the responsibility of the research/study, Reviewing the article before submission scientifically besides spelling and grammar. **TUNCEZ S:** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. **BÜLBÜL M:** Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Arslanoğlu Aydın E, Özdel S, Bağrul I, Kocamaz NG, Bağlan E, Tuncez S, et al. Evaluation of Leflunomide Treatment in Patients with Juvenile Idiopathic Arthritis: A Single Center Experience. Turkish J Pediatr Dis 2023;17: 214-218.

Correspondence Address / Yazışma Adresi:

Elif ARSLANOĞLU AYDIN
Department of Pediatric Rheumatology,
Ankara Etlik City Hospital, Ankara, Turkey
E-posta: arslanoglu0107@gmail.com

Received / Geliş tarihi : 30.12.2022

Accepted / Kabul tarihi : 02.01.2023

Online published : 01.03.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1212198

ÖZ

Amaç: Juvenil idiyopatik artrit (JİA), çocukluk çağıının en sık görülen kronik romatizmal hastalığıdır. Metotreksat (MTX), leflunomid (LFN) gibi hastalık modifiye edici antiromatizmal ilaçlar (DMARD) JİA'da birinci basamak tedavilerdir. MTX en sık reçete edilen ilaçtır ve çalışmalar ağırlıklı olarak MTX etkinliğini ve güvenliğini ele almaktadır. Ancak LFN ile ilgili veriler sınırlıdır. Bu çalışmada, JİA hastalarında LFN tedavisi ile ilgili kliniğimizin deneyimlerini sunmayı amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışmaya hastanemiz çocuk romatoloji polikliniğinde düzenli olarak takip edilen ve LFN tedavisi verilmiş JİA hastaları dahil edildi. Hasta demografik bilgileri, klinik ve laboratuvar özellikleri ile ilgili veriler tıbbi dosyalardan elde edildi.

Bulgular: Çalışmaya ortanca (çeyrekler arası aralık) hastalık başlangıç yaşı 7.3 (3.1-12.0) yıl olan 18 hasta (15 kadın ve 3 erkek) dahil edildi. 8 hastada oligoartiküler JİA, 7 hastada poliartiküler JİA, 2 hastada sistemik JİA ve 1 hastada entezitle ilişkili artrit (ERA) vardı. Tüm hastalara başlangıç tedavisi olarak MTX verildi (ERA tanısı konan bir hasta sulfasalazin ile tedavi edildi hariç). Gastrointestinal sistem (GİS) intoleransı nedeniyle başlangıçta MTX alan tüm hastalarda MTX kesildi ve LFN tedavisi başlandı. Daha önce MTX alırken GİS intoleransı gelişen hastalık aktivitesi düşük olan yedi hastadan altısına LFN tedavisi verildi. Bu hastalarda LFN ile tam remisyona sağlandı. MTX ile remisyonda izlenen dört hastada hastalık aktivasyonu görüldü. Daha önce MTX intoleransı olan bu hastalara LFN tedavisi verildi. Dört hastanın üçünde LFN ile remisyona sağlandı. MTX ile remisyona sağlanamayan orta ve yüksek hastalık aktivitesine sahip altı hastaya biyolojik tedavi başlandı. Yeterli yanıt alınamayan bu hastalarda MTX kesilerek LFN tedavisi başlandı. LFN ve biyolojik ajan kombinasyonu ile sadece bir hastada inaktif hastalık elde edildi. ERA tanılı bir hastada sulfasalazin tedavisine yetersiz yanıt alması üzerine LFN tedavisine geçildi ve LFN ile tam remisyona elde edildi.

Sonuç: LFN tedavisi, diğer DMARD'larla düşük hastalık aktivitesi ve/veya remisyona olan ve ilaç kesildikten sonra nüks olan hastalarda faydalı olabilir.

Anahtar Sözcükler: Hastalık modifiye edici antiromatizmal ilaç, Juvenil idiyopatik artrit, Leflunomid

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood (1). It is characterized by the arthritis of unknown etiology with onset before the age of 16 years and a minimum of 6 weeks duration (1). It is divided into 7 subtypes according to the International League of Associations for Rheumatology (ILAR) classification: oligoarticular (persistent or extended), polyarthritis rheumatoid factor (RF)-positive, polyarthritis RF-negative, systemic (sJIA), juvenile psoriatic arthritis, enthesitis-related arthritis, and undifferentiated JIA (2). JIA causes progressive joint destruction in untreated patients (1). The primary goals of JIA treatment are to achieve clinically inactive disease and prevent deformities. Non-steroidal anti-inflammatory drugs (NSAIDs), systemic and intra-articular glucocorticoids, disease-modifying antirheumatic drugs (DMARDs), and biological agents are treatments for JIA (3). The American College of Rheumatology recommends DMARDs (methotrexate (MTX), leflunomide (LFN), and sulfasalazine) as first-line treatments for JIA (3). As MTX is the most commonly prescribed drug, studies predominantly demonstrate the efficacy and safety of it. Although LFN is widely used in adults, it is not preferred in pediatric patients (4). In this report, we presented our experience with LFN treatment in JIA as a single center.

MATERIALS and METHODS

Patients followed in the pediatric rheumatology clinic of our hospital between January 2017 and January 2022 were included in the study. The inclusion criteria for the study were as follows: having JIA according to the ILAR criteria (2), receiving

LFN treatment for at least six months, and being under the age of 21 years. According to the disease activity assessment, patients were divided into complete remission, low, moderate, and high activity groups (5).

In our clinical practice, the first-line treatment of JIA is either MTX (with a dosage of 15 mg/m²/week) or sulfasalazine (with a dosage of 50 mg/kg/day [maximum 2.000 mg/day]). If remission is not achieved in the 3rd month of MTX or sulfasalazine therapy, biological agent is combined with DMARDs. Patients who cannot tolerate MTX are switched to LFN. LFN treatment was given to patients under 20 kg with the dose of 10 mg on alternate days. Patients with a body weight of 20-40 kg were treated with a dose of 10 mg/day. Patients above 40 kg were treated with LFN at a dose of 20 mg/day.

Demographic data (age, sex), clinical findings, affected joints, JIA subtypes, laboratory parameters ((white blood cell [WBC] count, erythrocyte sedimentation rate [ESR], c-reactive protein [CRP], anti-nuclear antibody [ANA] positivity, rheumatoid factor [RF] positivity, human leukocyte antigen [HLA]-B27 positivity), treatments were recorded.

Disease activity was evaluated by the juvenile arthritis disease activity score 71 (JADAS 71) for patients with JIA (5) and by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scoring system for patient with ERA (6). The JADAS-71 score is based on the following four parameters: 1) patient/parent's global disease assessment on a 0–10 visual analog scale (VAS), 2) physician's global disease assessment on a 0–10 visual analog scale (VAS), 3) active joint numbers (includes 71 joints), 4) ESR (5). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) disease activity questionnaire contains six items: fatigue, spinal pain, joint pain/swelling, localized tenderness, morning stiffness severity, and morning stiffness

duration. Each item is scored from on a 0–10 VAS during the previous week (6).

Gastrointestinal system (GIS) complaints (such as nausea, vomiting) or elevated transaminase levels (more than 1.5 times the upper limit of normal) were considered MTX intolerance.

The study was consistent with the principles of the Declaration of Helsinki and approved by the Clinical Research Ethics Committee of Ankara Dr. Sami Ulus Gynecology, Obstetrics and Gynecology Training and Research Hospital (E-22/02-290). Informed consent was obtained from all patients and their parents for publication.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences ver. 21.0 (SPSS Inc., Chicago, Illinois, USA). All numerical measurements were presented with median and interquartile ranges. Qualitative data was presented with numbers and percentages.

RESULTS

General characteristics of the patients

The study included 18 patients (15 female and 3 male). Among them, 8 had oligoarticular JIA, seven had polyarticular JIA, two had systemic JIA (due to persistent chronic arthritis), and one had ERA. Only one patient had JIA-associated uveitis. The demographical, clinical, and laboratory findings of the patients are shown in Table I.

Patients' median (IQR) follow-up period during LFN treatment was 12 (6-40) months. While 17 of the patients were given MTX

and NSAID as initial therapy (in addition, 15 patients received bridging steroid therapy), only one patient with the diagnosis of ERA received sulfasalazine (Figure 1). Methotrexate was discontinued because of gastrointestinal (GIS) intolerance (nausea, vomiting, elevated liver function tests) and LFN treatment was started in all 17 patients. Median (IQR) duration of MTX treatment was 12 (3-18) months. At the time of initiation of LFN treatment, four patients had a relapse after complete remission, 7 had low disease activity, and 6 had moderate-to-high disease activity. The median JADAS-71 score at the time of LFN initiation was 16.0 (7.5-25.0).

Responses to treatments of JIA patients with low disease activity

Six of 7 patients with low disease activity, who had GIS intolerance with MTX, achieved a complete remission at three months with LFN. Median (IQR) follow-up period of these patients was 8 (6-18) months. Since remission was not achieved in only one patient, biological agent treatment was started. Four patients who achieved complete remission with MTX and were followed up without treatment. These patients followed without medication relapsed after 24 (12-36) months. These patients, who had previously suffered from GIS intolerance while taking MTX, were given LFN therapy as they had low disease activity. Complete remission was achieved with LFN in 3 patients.

Responses to treatments of JIA patients with moderate to high disease activity

Complete remission could not be achieved with MTX and biologic agents (2 adalimumab, 1 tocilizumab, 2 etanercept, 1 canakinumab) in 6 patients with moderate to high disease activity and GIS intolerance during the median (IQR) follow-up of 10 (3-36) months. MTX was discontinued and LFN therapy was started instead. Complete remission was achieved at three months with LFN treatment in only one of these six patients. Other biological agent treatments were applied in the other five patients because disease activation could not be controlled. Three of five patients were in remission with tocilizumab treatment, with a median (IQR) of 2 (1-3) years of follow-up. In two patients, complete remission was still not achieved despite multiple biologic agent changes.

Response to leflunomide treatment of the patient with enthesitis-related arthritis

The patient with ERA was switched to LFN treatment at six months due to inadequate response (morning stiffness and enthesitis) to sulfasalazine treatment. Remission was achieved at six months with LFN treatment. This patient, who received LFN treatment for three years, has been followed for two years without medication and is in remission.

Adverse effects

No adverse effects related to LFN were observed in any of the patients.

Table I: The demographical, clinical, and laboratory findings of the patients

Sex, Female,*	15 (83)
Subtypes of juvenile idiopathic arthritis	
Oligoarticular juvenile idiopathic arthritis*	8 (44)
Polyarticular juvenile idiopathic arthritis*	7 (39)
Systemic juvenile idiopathic arthritis (due to persistent chronic arthritis)*	2 (11)
Enthesitis related arthritis*	1 (5.5)
Age of symptom onset†, years	7.3 (3.1-12.0)
Age at diagnosis†, years	8 (3.8-13.3)
Current age†, years	18.5 (14.5-20.0)
Laboratory parameters	8.230 (7.185–11.100)
White blood cell†, /mm ³	8 (4-33)
Eritrocyte sedimentation rate†, mm/hour	
C-reactive protein†, mg/l	3 (3–5)
Anti-nuclear antibody positivity*	4 (22)
Human leukocyte antigen B-27 positivity*	1 (5.5)
Rheumatoid factor positivity*	3 (17)
Anti-cyclic citrulline peptideantibody*	1 (5.5)

*n (%), †Median (IQR)

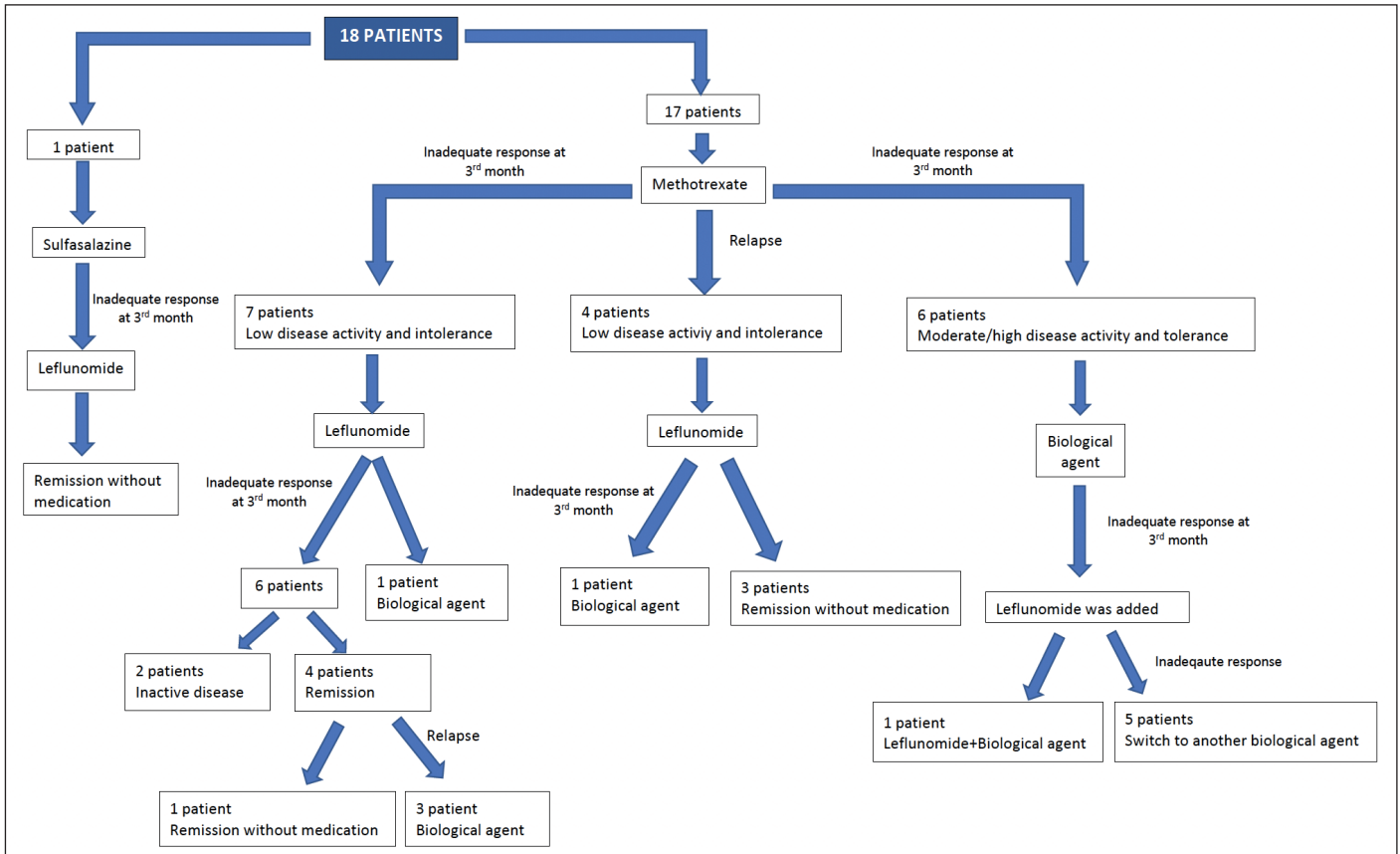


Figure 1: Treatments of patients with juvenile idiopathic arthritis

DISCUSSION

This study revealed that LFN treatment can be safely preferred in JIA patients with mild disease activity. According to our results, complete remission was achieved with LFN in 61% (n=11) of 18 patients. Seven patients did not benefit from LFN treatment. Pediatric rheumatologists prefer LFN treatment less than MTX treatment. There are few studies evaluating the efficacy of LFN treatment in JIA. In an observational study, LFN treatment was given to 32 patients with polyarticular JIA who did not respond to MTX treatment (7). At 3 months, 68% of the patients had an American College Rheumatology (ACR) 30 response, and 85% had an ACR 30 response. Only 2 patients had LFN side effects (7). In a multicenter, multinational, randomized controlled trial, the MTX group had a better ACR 30 response than the LFN group at 16 week (8). Foeldvari and Wierk evaluated 58 patients diagnosed with JIA who received LFN. They showed that 30% of patients achieved remission with LFN. They demonstrated that it may be a safe and effective agent for JIA patients who cannot tolerate or respond to MTX monotherapy (9). LFN, isolated or combined with MTX, has been found to be safe and effective in patients with JIA unresponsive to MTX (10). Aktay Ayaz et al. (11) demonstrated in their study involving 38 patients that LFN is an effective treatment in patients with MTX intolerance and low disease activity. Our results also suggest that LFN therapy can be used in JIA patients with low disease activity in the presence of MTX intolerance.

Studies addressing the safety of LFN are also limited. Abdominal pain, gastritis, dyspepsia, diarrhea, nausea, vomiting, anorexia, alopecia, weight loss, rash, elevated liver transaminases, can be seen as side effects of LFN therapy (7, 8, 12). Aktay Ayaz et al. (11) reported side effects in 2/38 (lymphopenia in 1 patient and elevated liver enzymes in 1 patient) patients in their study. Alcântara et al. (10) reported the intolerance with LFN in 7/43 patients (nausea and abdominal pain in 3 patients, elevated liver enzymes in 4 patients). In an observational study, LFN-related side effects were seen in 2/32 children with polyarticular JIA (gastritis in 1 patient and elevated liver enzymes in 1 patient) (7). In a controlled study comparing the efficacy and safety of MTX and LFN therapy in 94 patients with polyarticular JIA, the rates of side effects were similar in both groups (8). In our study, no side effects related to LFN were recorded in our patients.

The most important limitation of our study is the small number of patients. Another limitation is that the study design is retrospective. The present report may be useful for pediatric rheumatologists, as data on LFN in children with JIA are still limited.

On conclusion, LFN therapy may be beneficial, especially in patients with low disease activity and/ or remission with other DMARDs and relapse after drug discontinuation. More pediatric data are needed on the efficacy and safety of LFN therapy.

REFERENCES

1. Zaripova LN, Midgley A, Christmas SE, Beresford MW, Baildam EM, Oldershaw RA. Juvenile idiopathic arthritis: from aetiopathogenesis to therapeutic approaches. *Pediatr Rheumatol Online J* 2021;19:135.
2. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004;31:390-2.
3. Ringold S, Angeles-Han ST, Beukelman T, Lovell D, Cuello CA, Becker ML, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis Care Res (Hoboken)* 2019;71:717-34.
4. Osiri M, Shea B, Robinson V, Suarez-Almazor M, Strand V, Tugwell P, et al. Leflunomide for the treatment of rheumatoid arthritis: A systematic review and metaanalysis. *J Rheumatol* 2003;30:1182-90.
5. McErlane F, Beresford MW, Baildam EM, Chieng SE, Davidson JE, Foster HE, et al. Validity of a three-variable juvenile arthritis disease activity score in children with new-onset juvenile idiopathic arthritis. *Ann Rheum Dis* 2013;72:1983-8.
6. Akkoc Y, Karatepe AG, Akar S, Kirazli Y, Akkoc N. A Turkish version of the bath ankylosing spondylitis disease activity index: reliability and validity. *Rheumatol Int* 2005;25:280-4.
7. Chickermane PR, Khubchandani RP. Evaluation of the benefits of sequential addition of leflunomide in patients with polyarticular course juvenile idiopathic arthritis failing standard dose methotrexate. *Clin Exp Rheumatol* 2015;33:287-92.
8. Silverman E, Mouy R, Spiegel L, Jung LK, Saurenmann RK, Lahdenne P, et al. Leflunomide in Juvenile Rheumatoid Arthritis (JRA) Investigator Group. Leflunomide or methotrexate for juvenile rheumatoid arthritis. *N Engl J Med* 2005;352:1655-66.
9. Foeldvari I, Wierk A. Effectiveness of leflunomide in patients with juvenile idiopathic arthritis in clinical practice. *J Rheumatol* 2010;37:1763-7.
10. Alcântara AC, Leite CA, Leite AC, Sidrim JJ, Silva FS Jr, Rocha FA. A longterm prospective real-life experience with leflunomide in juvenile idiopathic arthritis. *J Rheumatol* 2014;41:338-44.
11. Aktay Ayaz N, Karadağ ŞG, Çakmak F, Çakan M, Tanatar A, Sönmez HE. Leflunomide treatment in juvenile idiopathic arthritis. *Rheumatol Int* 2019;39:1615-9.
12. Rozman B. Clinical experience with leflunomide in rheumatoid arthritis. Leflunomide Investigators' Group. *J Rheumatol Suppl* 1998;53:27-32.

Assessment of Risk Factors for Obesity in Children Aged 6-17 Years Where Obesity Reaches Peak

Obezitenin Zirve Yaptığı 6-17 Yaş Aralığındaki Çocuklarda Obezite Gelişiminde Rol Oynayan Risk Faktörlerinin Değerlendirilmesi: Tek Merkez Deneyimi

Onur KAŞLI¹, Ayşe Derya BULUŞ², Mesut KOÇAK³, Uğur Ufuk İŞİN⁴

¹Department of Child Health and Diseases, Bilecik Training and Research Hospital, Bilecik, Turkey

²Department of Pediatric Endocrinology, Ankara Atatürk Sanatorium Training and Research Hospital, Ankara, Turkey

³Department of Child Health and Diseases, Ankara Yıldırım Beyazıt University, Ankara, Turkey

⁴Department of Child Health and Diseases, Ankara Atatürk Sanatoryum Training and Research Hospital, Ankara, Turkey

ABSTRACT

Objective: Obesity is an important health problem affecting 25-30% of children and adolescents. This study, it was aimed to determine the age intervals in which obesity reaches to peak incidence and risk factors playing role in the development obesity among children and adolescents aged 6-17 years who presented to pediatrics outpatient clinic of Ankara Keçiören Training and Research Hospital.

Material and Methods: This cross-sectional study included 3.000 children and adolescents aged 6-17 years and their parents who presented with any reason to pediatrics outpatient clinic of Ankara Keçiören Training and Research Hospital between October, 2019 and December, 2019.

Results: Obesity was detected in 21.4% of children while 78.6% were not obese. A significant correlation was detected between birth weight and obesity ($p=0.001$). A significant correlation was found between obesity and time spent for TV, computer and video games per day ($p<0.001$). The obesity was significantly decreased by increasing duration of physical activity. In the study, the obesity incidence was 1.77-folds (1.25-2.50) higher in children with obese mother and 2.01-folds (1.42-2.85) in children with obese father.

Conclusion: The obesity incidence is progressively increasing in childhood as with other age groups. To prevent such increase, measures should be taken as early as possible. An adequate and balanced nutrition and physical activity are of important in prevention and treatment of obesity. Although primary goal is to achieve lifestyle modifications, pharmacotherapy or surgery may be attempted in the presence of severe obesity-related complications.

Key Words: Childhood, Nutrition, Obesity, Physical Activity

ÖZ

Amaç: Obezite, çocuk ve adölesanların %25-30'unu etkileyen önemli bir sağlık problemidir. Bu çalışmada, Keçiören Eğitim ve Araştırma Hastanesi çocuk sağlığı ve hastalıkları polikliniğine başvuran 6-17 yaş aralığındaki çocuklarda hangi yaşlarda obezitenin zirve yaptığı ve obezite gelişiminde rol oynayan risk faktörlerinin (beslenme, aktivite, aile öyküsü) belirlenmesi amaçlanmıştır.



0000-0002-5620-8199 : KAŞLI O
0000-0003-2865-4420 : BULUŞ AD
0000-0002-5620-8199 : KOÇAK M
0000-0003-1684-1624 : İŞİN UU

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 Ethics Committee of Ankara Keçiören Training and Research Hospital (2012-KAEK-15/1968 - 11.09.2019).

Contribution of the Authors / Yazarların katkısı: KAŞLI O: 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 the writing of the whole or important parts of the study. BULUŞ AD: 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, Reviewing the article before submission scientifically besides spelling and grammar. KOÇAK M: 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, Reviewing the article before submission scientifically besides spelling and grammar. İŞİN UU: 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, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Kaşlı O, Buluş AD, Koçak M and İşin UU. Assessment of Risk Factors for Obesity in Children Aged 6-17 Years Where Obesity Reaches Peak. Turkish J Pediatr Dis 2023;17:219-226.

Correspondence Address / Yazışma Adresi:

Ayşe Derya BULUŞ
Department of Pediatric Endocrinology,
Ankara Atatürk Sanatorium Training and Research Hospital, Ankara, Turkey
E-posta: drderyabulus@hotmail.com

Received / Geliş tarihi : 23.06.2022

Accepted / Kabul tarihi : 02.01.2023

Online published : 01.03.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1130690

Gereç ve Yöntemler: Çalışma kesitsel olarak planlanıp, Ekim 2019- Aralık 2019 tarihleri arasında Ankara Keçiören Eğitim ve Araştırma Hastanesi Pediatri Polikliniğine herhangi bir sebeple başvuran 3000 adet 6-17 yaş arası çocuklar ve velileri dahil edilmiştir.

Bulgular: Çocukların %78.6'sında obezite yok iken %21.4'ünde obezite mevcuttu. Doğum ağırlığı ile obezite arasında anlamlı ilişki bulunmuştur ($p=0.001$). Televizyon izleme, bilgisayar ile uğraşma, video oyun oynama için ayrılan günlük sürenin ile obezite arasında anlamlı ilişki saptanmıştır ($p<0.001$). Spor, bisiklet sürme, dışarıda oynama gibi fiziksel aktiviteler ile obezite arasında anlamlı ilişki saptanmıştır ($p=0.045$). Obezite oranı fiziksel aktivite süresinin artması ile anlamlı derecede azalmıştır. Çalışmamızda annesi obez olan çocuklarda obezite 1.77 (1.25-2.50) kat, babası obez olan çocuklarda obezite 2.01 (1.42-2.85) kat daha fazla görülmüştür ($p<0.001$).

Sonuç: Tüm yaş gruplarında olduğu gibi çocukluk çağına da obezite görülme sıklığı giderek artmaktadır. Bu artışın önüne geçebilmek için gerekli önlemlerin en erken safhada alınması gerekmektedir. Çocuklarda obezitenin önlenmesi ve tedavisinin temelinde yeterli ve dengeli beslenme ve fiziksel aktivitenin önemi büyüktür. Öncelikli amaç yaşam tarzı değişikliği olmasına rağmen obeziteye bağlı ciddi komplikasyonların varlığında gereklilik halinde farmakoterapi veya cerrahi tedavi de denenebilmektedir.

Anahtar Sözcükler: Çocukluk Çağı, Beslenme, Obezite, Fiziksel Aktivite

INTRODUCTION

Obesity, affecting 25-30% of children and adolescents, is a complex, multifactorial metabolic disease defined as abnormal or excessive fat accumulation in the body due to high energy intake at a level which may impair health (1, 2). At childhood, the obesity incidence is progressively increasing worldwide. The obesity prevalence at childhood was increased from 4.2% in 1990 to 6.7% in 2010. It is estimated that the obesity prevalence will most likely continue to increase and that 9.1% of children will be obese in 2020 worldwide. The excessive consumption of fats in carbohydrates in the context of dietary patterns and tendency towards spending time for TV and video games rather than physical activity among children emerged by the contemporary life are playing important role in this increase of obesity prevalence. Besides, genetic, psychogenic and sociocultural factors as well as hormonal disorders also play important role in obesity. Moreover, it was shown that the prevalences of overweight and obesity was 2-folds higher in developed countries when compared to emerging countries (3).

Although obesity is seen at childhood, adolescence and adult life at varying rates, similar factors play role in all ages and obesity remains to be an important public health problem. Thus, we aimed to evaluate risk factors involved in the obesity among children and adolescents aged 6-17 years.

MATERIAL and METHODS

The study was approved by Ethics Committee of Ankara Keçiören Training and Research Hospital (2012-KAEK-15/1968 - 11.09.2019). All parents gave written informed consent before participation. The study was conducted between 01 October, 2019 and 31 December, 2019. The study included 3.000 children and adolescents aged 6-17 years who presented to pediatrics outpatient clinic of Ankara Keçiören Training and Research Hospital. All subjects completed a questionnaire including 25 items about age, gender, birth weight, type of infant feeding, age at onset of overweight, maternal age at birth, daily eating habits, additional food intake between meal and before sleeping, favorite foods as snack, food intake at school,

activities in spare times, whether he/she walks to school, education level of parents, occupation of parents, economic status of family, maternal height and weight, paternal height and weight, family history of obesity, family type, caregiver at infancy, current diseases, previous diseases, medication, blood pressure as measured in a physician visit and family history of diabetes, hypertension or heart disease.

Physical Examination and Measurements

In children included, body weight measurement was performed with light clothing and without shoes at morning hours using an digital scale with sensitivity of ± 100 g (Seca). Height measurement was performed using a portable stadiometer while he/she is at standing position without shoes; head, back, hip and heels being at contact to wall and hands by side. The height was recorded as the distance from the point over head to base. The body mass index (BMI) was calculated as body mass (kg) divided by square of height (m^2). The overweight and obesity were defined based on Centre for Disease Control (CDC2000) criteria according to age-specific BMI as follows: $>85^{th}$ percentile, overweight; and $>95^{th}$ percentile, obese (4). The age- and sex-specific height and weight percentiles were calculated using growth charts prepared for Turkish children (5).

Data Assessment and Analysis

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows version 23.0 (IBM SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using plots (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov test and Shapiro-Wilk test). All data were considered as parametric. The descriptive statistics are presented as median and maximum-minimum values (median \pm max-min). The results are presented with 95% confidence interval. A p value <0.050 was considered as statistically significant.

RESULTS

The study included 3.000 subjects. The median age was 11 years (6-17 years). Of the subjects included, 59.4% were girls while 40.6% were boys. The median age at onset of overweight

Table I: Association between parameters at infancy and obesity.

	No Obesity*	Obesity*	Total*	Crude OR (%95CI)	p
Birth weight (n=2805)					
<2500 g	483 (21.9)	63 (10.6)	546 (19.5)	0.43 (0.26-0.71)	0.001
2500-4000 g	1596 (72.3)	477 (79.9)	2073 (73.9)	1.00	
>4000 g	129 (5.8)	57 (9.5)	186 (6.6)	1.47 (0.83-2.60)	
Type of infant feeding (n=2865)					
Exclusively breastfeeding within first 4-6 months	1605 (71.5)	447 (72.0)	2052 (71.6)	1	0.784
Breastfeeding plus formula within first 4-6 months	501 (22.3)	129 (20.8)	630 (22.0)	0.92 (0.63-1.35)	
Exclusively formula within first 4-6 months	138 (6.1)	45 (7.2)	183 (6.4)	1.48 (0.84-2.60)	
Maternal age at birth (n=2988)					
≥26 years	1254 (53.5)	324 (50.5)	1578 (52.8)	1	0.438
≤26 years	1092 (46.5)	318 (49.5)	1410 (47.2)	1.12 (0.83-1.52)	
Caregiver at infancy (n=2997)					
Mother at home	1659 (70.5)	477 (74.3)	2136 (71.3)	1	0.761
Grandmother-grandfather at home	498 (21.1)	105 (16.4)	603 (20.1)	0.73 (0.48-1.09)	
Nursery	144 (6.1)	39 (6.1)	183 (6.1)	0.94 (0.49-1.78)	
Caregiver	54 (2.3)	21 (3.3)	75 (2.5)	1.35 (0.55-3.29)	

*n (%)

Table II: Association between family structure, dietary habits and obesity.

	No Obesity*	Obesity*	Total*	Crude OR (%95CI)	P
Family structure (n=2994)					
Nuclear family	2028 (86.1)	504 (78.9)	2532 (84.6)	1	0.009
Extended family	327 (13.9)	135 (21.1)	462 (15.4)	1.66 (1.12-2.44)	
Having regular breakfast, lunch and dinner everyday (n=3000)					
Yes	1632 (69.2)	483 (75.2)	2115 (70.5)	1	0.087
No or sometimes	726 (30.8)	159 (24.8)	885 (29.5)	0.74 (0.52-1.04)	
Nutrition status at school (n=2943)					
Prepared at home	1605 (69.8)	477 (74.3)	2082 (70.8)	1	0.405
Cafeteria	498 (21.6)	105 (16.3)	603 (20.5)	0.70 (0.47-1.06)	
Dining hall	144 (6.3)	39 (6.1)	183 (6.2)	0.91 (0.48-1.72)	
From outside	54 (2.3)	21 (3.3)	75 (2.5)	1.30 (0.53-3.18)	
Does he/she eat snack or additional food between meals and before sleeping? (n=2997)					
Yes	1101 (46.8)	300 (46.7)	1401 (46.7)	1	0.995
No or sometimes	1254 (53.2)	342 (53.3)	1596 (53.3)	1.00 (0.74-1.35)	
Additional food as snack at school (n=3000)					
Fruit, milk, yoghurt	1515 (64.2)	387 (60.3)	1902 (63.4)	1	0.285
Candy, Chocolate, Cake etc.	843 (35.8)	255 (39.7)	1098 (36.6)	1.79 (1.35-2.38)	

*n (%)

was 8 years (6-16 years). The median maternal age at birth was 26 years (15-45 years).

The correlation between obesity and gender was assessed by including all age groups. Of obese children, 55.1% of obese subjects were girls while 44.9% were boys. Similarly, of non-obese subjects, 60.6% were girls while 39.4% were boys. No significant difference was detected between obese and non-obese children regarding gender ($p=0.152$).

A significant correlation was detected between birth weight and obesity ($p=0.001$). When compared to children with birth weight between 2500 and 4000 g, the likelihood of obesity was lower 0.43-folds (0.26-0.72) lower in children with birth weight <2500 g. When compared to children with birth weight

<2500 g, the likelihood of obesity was 2.29-folds (1.10-3.73) higher in children with birth weight between 2500 and 4000 g whereas 3.38-folds (1.67-6.86) higher in children with birth weight >4000 g. No significant correlation was found between obesity and type of infant feeding at infancy (exclusively breastfeeding, breastfeeding plus formula or only formula within first 4-6 months), maternal age at birth (<26 years or 26 years) and caregiver at infancy (mother, grandmother or grandfather at home or a caregiver or preschool) ($p=0.780$; $p=0.430$; $p=0.760$) (Table I).

When family type was assessed, 78.9% of children with obesity were from nuclear family while 86.1% of children without obesity were from nuclear family. Again, 21.1% of obese children were from extended family while 13.9% of non-obese children were

Table III: Association between daily activities and obesity.

	No Obesity*	Obesity*	Total*	Crude OR (%95CI)	p
Time spent with TV, computer or video games per day (n=3000)					
No	843 (35.7)	138 (21.5)	981 (32.7)	1	<0.001
0-1 hours	384 (16.3)	114 (17.8)	498 (16.6)	1.81(1.12-2.92)	
1-2 hours	573 (24.3)	171 (26.6)	744 (24.8)	1.82 (1.18-2.80)	
2-4 hours	282 (12.0)	84 (13.1)	366 (12.2)	1.81 (1.07-3.07)	
≥4 hours	276 (11.7)	135 (21.0)	411 (13.7)	2.98(1.86-4.79)	
Time spent for painting, homework and reading per day (n=3000)					
No	1524 (64.6)	405 (63.1)	1929 (64.3)	1	0.224
0-1 hours	228 (9.7)	69 (10.7)	297(9.9)	1.13(0.68-1.88)	
1-2 hours	360 (15.3)	93 (14.5)	453 (15.1)	0.97 (0.62-1.50)	
2-4 hours	159 (6.7)	30 (4.7)	189 (6.3)	0.71(0.35-1.43)	
≥4 hours	87 (3.7)	45 (7.0)	132 (4.4)	1.94(1.01-3.73)	
Time spent for sports, cycling and outdoor games (n=3000)					
No	1506 (63.9)	477 (74.3)	1983 (66.1)	1	0.045
0-1 hours	126 (5.3)	33 (5.1)	159 (5.3)	0.82 (0.41-1.64)	
1-2 hours	315 (13.3)	66 (10.3)	381 (12.7)	0.66 (0.40-1.08)	
2-4 hours	216 (9.2)	30 (4.7)	246 (8.2)	0.43 (0.22-0.87)	
≥4 hours	195 (8.3)	36 (5.6)	231 (7.7)	0.58 (0.30-0.95)	
Walking time to school (n=3000)					
Not walking	828 (35.1)	225 (35.0)	1053 (35.1)	1	0.964
0-15 min	1134 (48.1)	306 (47.7)	1440 (48.0)	0.99 (0.70-1.38)	
15-30 min	306 (13.0)	90 (14.0)	396 (13.2)	0.99 (0.70-1.38)	
>30 min	90 (3.8)	21 (3.3)	111 (3.7)	0.85 (0.36-2.03)	

*n (%)

Table IV: Association between obesity and history of chronic and metabolic disease.

	No Obesity*	Obesity*	Total*	Crude OR (%95CI)	p
Blood pressure measured in previous physician visit (n=3000)					
Not measured	783 (33.2)	195 (30.4)	978 (32.6)	0.93 (0.67-1.30)	0.004
Normal	1530 (64.9)	408 (63.5)	1938 (64.6)	1	
High	45 (1.9)	39 (6.1)	84 (2.8)	3.25 (1.51-6.99)	
Cholesterol and lipid level in previous physician visit (n=3000)					
Not measured	1095 (46.5)	204 (31.8)	1299 (43.3)	0.61 (0.44-0.85)	<0.001
Normal	1215 (51.5)	369 (57.5)	1584 (52.8)	1	
High	48 (2.0)	69 (10.7)	117 (3.9)	4.73 (2.42-9.24)	
Family history of diabetes mellitus, hypertension and heart disease (n=2988)					
No	1737 (73.9)	438 (68.9)	2175 (72.8)	1	0.148
Ye	615 (26.1)	198 (31.1)	813 (27.2)	1.20 (0.91-1.77)	
Presence of chronic disease in child (n=3000)					
No	1974 (83.7)	519 (80.8)	2493 (83.1)	1	0.320
Yes	384 (16.3)	123 (19.2)	507 (16.9)	1.21 (0.82-1.79)	

*n (%)

from extended family. The likelihood of obesity was 1.66-folds (1.12-2.44) higher in children from extended family when compared to those from nuclear family. There was a significant correlation between obesity and family structure. Table II presents associations between obesity and family structure, eating habits (regular intake of breakfast, lunch and dinner every day), nutrition status at school, eating snacks between meals and before sleeping, snacks at school and dietary patterns.

When association between physical activity and obesity was assessed, it was found that 21.5% of obese children were engaged to TV, computer and video games for ≥4 hours per day while only 11.5% of non-obese children for ≥4 hours per day. Again, 21.5% of obese children and 35.8% of non-obese children do not spend time with TV, computer and video games. When compared to children not spending time with TV, computer and video games, the likelihood of obesity

was 1.81-folds (1.12-2.92) higher in children spending 0-1 hours per day with TV, computer and video games whereas 1.82-folds (1.18-2.80) higher in children spending 1-2 hours per day, 1.82-folds (1.07-3.7) higher in children spending 2-4 hours per day and 2.98-folds (1.86-4.79) higher in children spending ≥ 4 hours per day. There was a significant correlation between obesity and daily time spent with TV, computer and video game activities. Table III summarizes associations between obesity and daily duration of TV, computer and video game activities; daily time spent with activities such as painting, homework and reading; daily time spent with cycling-playing outdoor games; and walking time to school.

There was obesity in 5.1% of children not spending no time for cycling-playing outdoor game whereas in 10.3% spending 1-2 hours per day, in 4.7% of children spending 2-4 hours per day, and in 5.6% of children spending ≥ 4 hours per day. The obesity rate was found as 35.1% in children not walking to school while it was 48.0% in children walking for 0-15 minutes to school, 13.2% in those walking for 15-30 minutes and 3.7% in those walking for >30 minutes. A significant difference was detected between daily time spent with TV, computer and video game activities and daily time spent for cycling-playing outdoor games ($p=0.001$; $p=0.045$).

When association between obesity and hypertension was assessed, it was found that there was hypertension in 2.8% of children; of these, obesity was detected in 6.1% while no obesity was observed in 1.9% ($p=0.004$). High cholesterol and lipid levels were found in 3.9% of children included; of these, there was obesity in 10.7% while no obesity in 2% ($p=0.001$). There was family history of diabetes mellitus, hypertension or heart disease in 27.2% of children included; of these, obesity was detected in 31.1%. There was a chronic disease in 16.9% of children included; of these, obesity was detected in 19.2% while no obesity was observed in 16.3% ($p=0.148$; $p=0.320$) (Table IV).

In our study, obesity was detected in 21.0% of mothers of children with obesity but not in 79.0%. Again, obesity was detected in 19.9% of fathers of children with obesity but not in 80.1% ($p=0.001$).

When education level of mothers was assessed in children, it was found that education level was university degree or higher among 18.2% of mothers of obese children and 12.6% of mothers of non-obese children. In addition, it was primary or secondary school degree in 47.7% of mothers of obese children and 51.1% of mothers of non-obese children. No significant correlation was detected between obesity in children and education level of mother ($p=0.164$; $p=0.924$). The occupation was housewife in 79.0%, self-employment 13.1% and worker or government official in 7.9% of mothers of obese children. These rates were 5.2%, 52.3% and 42.5% of fathers of obese children ($p=0.092$, $p=0.264$).

DISCUSSION

Obesity is a multifactorial disorder which is commonly seen among children. In order to identify underlying factors which are currently unknown and re-consider measures to be taken and treatment approaches, we aimed to determine the ages in which obesity reaches to peak incidence and risk factors (nutrition, activity, family history) playing role in the development of obesity among children and adolescents aged 6-17 years who presented to pediatrics outpatient clinic of our hospital.

The obesity was detected in 21.4% while no obesity was detected in 78.6% of 3.000 children and adolescents included to the study. In parallel to our study, obesity rate was found as 21.8% in a study including children aged 11-16 years (6). In Turkey Childhood Obesity Surveillance Initiative trial including grade 2 students across Turkey, it was found that 1.5% of children were underweight whereas 14.6% were overweight and 9.9% were obese. According WHO criteria, overweight and obesity are assessed as a whole; based on this consumption, 24.5% of children were found to be obese in the study (7). In emerging countries, obesity incidence was found as 23.9% in boys aged 10-14 years in Saudi Arabia whereas 35% in children aged 12-17 years in Qatar, 28.8% in Northern Brazil and 25.7% in Southern Brazil. It is proposed that the rapid socioeconomic transformation is the cause of high obesity incidence in emerging countries (8, 9). The obesity incidence was found as 22.5% in COSI TUR 2013 survey and was further increased up to 24.5% in COSI TUR 2016 survey (10), indicating that obesity is progressively increasing over years and that strict measures should be taken rapidly in order to prevent obesity.

When gender was assessed in the study population, it was found that 55.1% of obese children were girls and 44.9% were boys while 60.6% of non-obese children were girls and 39.4% were boys. In our study, no significant difference was detected in obesity according to gender. In another study including 82.661 children aged 6-16 years, no significant difference was detected in obesity incidence according to gender in agreement with our study (10.1% and 2.4% of girls were overweight and obese vs. 8.5% and 2.6% of boys were overweight and obese) (11). This may be due to fact that the hormonal fluctuations seen during pregnancy or menopause which are thought to lead higher obesity rates in adult women are lacking in the age groups studied in our study. On contrary, in European Childhood Obesity Surveillance Initiative (COSI) trials conducted in 2008 and 2013, it was reported that obesity was more common among boys than girls at primary school age group (3, 99). The higher obesity incidence in boys was attributed to excessive use of technology and internet; and resultant limitation of physical activity and intake of junk food (12-17).

In our study, a significant correlation was detected between obesity and birth weight. The birth weight was >4.000 g in 9.5% of obese children and in 5.8% of non-obese children

while it was <2.500 g in 10.6% of obese children and in 21.9% of non-obese children. The likelihood of obesity was 3.38 folds (1.67-6.86) higher in children with birth weight >4.000 g. In a study on 1.253 student aged 6-14 years, it was found that the obesity incidence was significantly higher among children with higher birth weight in agreement with our study (18). In a large-scale study on children aged 9-11 years, it was found that the obesity risk was higher in children with birth weight>4.000 g when compared to those with low birth weight (19). In a study by Leonard et al. (20), it was found that the birth weight of a child affects time needed to become adult and body structure in adult life.

The association between breastfeeding and obesity have been investigated in several studies. According to COSI TUR trial, 95.5% of children had been fed by breastfeeding while 3.6% of children had never been fed by breastfeeding. In many studies, it was shown that breastfeeding during first 6 months of life alone is protective against childhood obesity while lack of breastfeeding during first 6 months or early withdrawal of breastfeeding increases on obesity (21-24). In our study, 71.6% of the children were exclusively fed by breastfeeding while 22.0% were fed by breastfeeding plus formula and 6.4% were exclusively fed by formula within first 4-6 months of life. On contrary to literature, it was found that there was no association between obesity and type of infant feeding in our study. In similar studies, no association of breastfeeding or duration of breastfeeding with obesity has been shown (18-25).

The maternal age at birth was ≤ 26 years in 52.8% whereas >26 in 47.2% of the subjects in our study. No significant association was found between obesity and maternal age at birth. In a study by Saadet et al. (21), it was found that the rate of low birth weight infant was higher than normal weight infants among mothers aged >35 years and those aged <18 years; however no significant conclusion could be drawn. In a study by Sedat et al. (22), it was reported that maternal age at birth had influence on birth weight and potential short-term and long-term complications related to birth weight. They also reported that younger and older mothers were more likely to have low birth weight infant.

In our study, 70.5% of children were having regular breakfast, lunch and dinner every day. However, no significant correlation was found between obesity and having regular meals. On contrary, a significant correlation was observed between dietary pattern and obesity in another study. The obesity incidence was found to be higher in children not having regular breakfast, lunch and dinner at home (11). It is thought majority of children and adolescents misses breakfast; thus, a negative correlation was detected between obesity and having breakfast and energy intake from breakfast. It was found that the group missing breakfast had larger waist circumference. As supported by literature, behavioral factors such as consumption of carbonated or sweetened beverages and foods with high fat and energy content and insufficient consumption of fruit and vegetables

have been linked to obesity (23-25). In a review including more than 50 studies worldwide, it was reported that children aged 6-19 years consumed healthy food such as fresh vegetables and fruits insufficiently; rather, they consumed unhealthy foods and sweetened or carbonated beverages excessively (26).

When the association between daily activities and obesity was assessed, it was found that 21.5% of children with obesity were engaged to TV, computer and video games for ≥ 4 hours per day while only 11.5% of children without obesity for ≥ 4 hours per day. Again, 21.5% of children with obesity and 35.8% of children without obesity do not spend time with TV, computer and video games. When compared to children not spending time with TV, computer and video games, the likelihood of obesity was 1.81-folds (1.12-2.92) higher in children spending 0-1 hours per day for TV, computer and video games whereas 1.82-folds (1.18-2.80) higher in children spending 1-2 hours per day, 1.82-folds (1.07-3.7) higher in children spending 2-4 hours per day and 2.98-folds (1.86-4.79) higher in children spending ≥ 4 hours per day. There was a significant correlation between obesity and daily duration of TV, computer and video game activities. In a study by American Academy of Pediatrics, a significant correlation was detected between BMI values and time spent for TV and computer among children; thus, it is recommended that children and adolescents should spend less than 2 hours per day for TV and computer (28). Again, in another study, it was observed that activities such as watching television or playing computer games enhanced likelihood of obesity by limiting physical activities and increasing consumption of foods with high energy content (29). In our study, no significant correlation was detected between obesity and activities such as painting, homework or reading and time spent for such activities. The likelihood of obesity was 0.43-folds lower in children spending 2-4 hours per day for physical activities such as sports, cycling or outdoor games when compared to those spending no time for such activities. It was 0.58-folds lower when time spent for these activities exceeded 4 hours.

In a study including 366 students aged 6-12 years (2005), it was observed that total cholesterol and LDL values were significantly higher in obese children. In our study, obesity incidence was 4.73-folds (2.42-9.24) higher in children with high cholesterol and lipid level as measured in previous visit when compared to those with normal cholesterol and lipid levels. This may be interpreted dyslipidemia due to obesity. In our study, blood pressure was high in 6.1% of obese children and in 1.9% of non-obese children. When compared to children with normal blood pressure, likelihood of obesity was 3.25-folds (1.51-6.99) higher in children with elevated blood pressure. No significant difference was found in obesity according to blood pressure. In a study conducted in a primary school from Sakarya province, obesity increased the risk for hypertension by 2.25 folds when (34). It is thought that mechanisms such as autonomic dysfunction, increased insulin level, vascular impairment in

dysfunction and enhanced renin-angiotensin-aldosterone axis in the pathophysiology of obesity-related hypertension (30, 31).

The presence of obesity in family history implies a genetic component involved in the obesity in children; however, dietary habits and patterns of the family, food preference and insufficient physical activity also play important role in the development of obesity (32).

In our study, no significant association was detected between obesity development and education level or occupation of parents.

In conclusion, there was obesity in 21.4% of children included a significant association was found between birth weight and obesity. On the other hand, no significant association was found between obesity and type of infant feeding, maternal age at birth, caregiver at infancy, dietary patterns at home and school, family history of chronic disease, presence of chronic disease in child or education level and occupation of parents.

Of the families included 84.6% were nuclear families and the obesity incidence was found to be significantly lower in children from nuclear families. A significant correlation was detected with time spent for TV, computer and video games; physical activities such as sports, cycling or outdoor games; increased blood pressure; elevated cholesterol and lipid levels and presence of obesity in parents ($p < 0.001$).

REFERENCES

1. Aarons GA, Sklar M, Mustanski B, Benbow N, Brown CH. Scaling-out evidence-based interventions to new populations or new health care delivery systems. *Implementation Science* 2017;12: 111.
2. Wilhelmsen CK, Skalleberg K, Raanaas RK, Tveite H, Aamodt G. Associations between green area in school neighbourhoods and overweight and obesity among Norwegian adolescents. *Prev Med Rep* 2017;7:99-105.
3. Manandhar S, Suksaroj TT, Rattanapan C. The association between green space and the prevalence of overweight/obesity among primary school children. *Int J Occup Environ Med* 2019;10:1-10.
4. Barlow SE, Butte NF, Hoelscher DM, Salahuddin M, Pont SJ. Strategies to Recruit a Diverse Low-Income Population to Child Weight Management Programs From Primary Care Practices. *Preventing chronic disease* 2017;14:138-38.
5. Atlas of Childhood Obesity. October 2019. World Obesity Federation. http://s3-eu-west-1.amazonaws.com/wofiles/11996_Childhood_Obesity_Atlas_Report. (access: 11.03.2020).
6. COSI-TUR, (2016). Türkiye Çocukluk Çağı (İlkokul 2. Sınıf Öğrencileri) Şişmanlık Araştırması, Sağlık Bakanlığı, Halk Sağlığı Genel Müdürlüğü, Millî Eğitim Bakanlığı, Dünya Sağlık Örgütü Avrupa Bölge Ofisi, Sağlık Bakanlığı Yayın No: 1080, Ankara 2017.
7. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü, <https://hsgm.saglik.gov.tr/tr/obezite/turkiyede-obezitenin-gorulme-sikligi>. (access: 05.03.2020).
8. Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, et al. Origins of lifetime health around the time of conception: causes and consequences. *Lancet* 2018;391:1842-52.
9. Shafei AE, Nabih ES, Shehata KA, Abd Elfatah ESM, Sanad ABA, Marey MY, et al. Prenatal exposure to endocrine disruptors and reprogramming of adipogenesis: an early-life risk factor for childhood obesity. *Child Obes* 2018;14:18-25.
10. Berger NA. Young adult cancer: influence of the obesity pandemic. *Obesity (Silver Spring, Md)* 2018;26:641-50.
11. Taşkın Kılıç G. Ankara'da Seçilmiş Okullarda Öğrencilerin Beslenme Özelliklerinin Beslenme Dostu Okul Olma Durumuna Göre Değerlendirilmesi. Ankara Üniversitesi Sağlık Bilimleri Enstitüsü Halk Sağlığı Hemşireliği Yüksek Lisans Tezi 2018.
12. Özcebe H, Bağcı B, Yardım N, Çelikkaya E, Çelikkaya N, Keskinlikçi B, et al. Türkiye'de çocuklarda fazla kiloluluk ve şişmanlık prevalansları. *TAF Prev Med Bull* 2015;14:145-52.
13. Voerman E, Santos S, Patro Golab B, Amiano P, Ballester F, Barros H, et al. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: an individual participant data meta-analysis. *PLoS Med* 2019;16:1002-744.
14. Savaşan Ç, Sarı O, Aydoğan Ü, Muhammed E. İlkokul çağındaki çocuklarda obezite görülme sıklığı ve risk faktörleri. *Türkiye Aile Hekim Derg* 2015;19:14-21.
15. Smego A, Woo JG, Klein J, Suh C, Bansal D, Bliss S, et al. High body mass index in infancy may predict severe obesity in early childhood. *J Pediatr* 2017;183:87-93.
16. Mohaç G. KKTC Mağusa Bölgesi'nde ilkököl öğrencilerinin bilgisayar oyun bağımlılığı ile obezite arasındaki ilişki. Doğu Akdeniz Üniversitesi, Lisansüstü Eğitim, Öğretim ve Araştırma Enstitüsü, Beslenme ve Diyetetik, Yüksek lisans tezi; 2015.
17. Jang M, Grey M, Sadler L, Jeon S, Nam S, Song H-J, et al. Obesity-risk behaviours and their associations with body mass index (BMI) in Korean American children. *J Clin Nurs* 2018; 3408-17.
18. Ergin A, Meydan Acımıs N, Ozdemir C, Akbay B, Kınacı Cimen Y, Uzuner N, Demireliden U. Obesity prevalence and associated factors in children at 6-14 years of age in a semi-rural area. *Pam Med J* 2019;12:475-84.
19. Au LE, Zhu SM, Nhan LA, Plank KR, Frongillo EA, Laraia BA, et al. Household food insecurity is associated with higher adiposity among US schoolchildren ages 10-15 years: the Healthy Communities study. *J Nutr* 2019;149:1642-50.
20. Leonard SA, Petito LC, Rehkopf DH, Ritchie LD, Abrams B. Weight gain in pregnancy and child weight status from birth to adulthood in the United States. *Pediatr Obes* 2017;12:18-25.
21. Bray GA, Heisel WE, Afshin A, Jensen MD, Dietz WH, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev* 2018;39:79-132.
22. Tambalis KD, Mourtakos S, Panagiotakos DB, Sidossis LS. Association of exclusive breastfeeding with risk of obesity in childhood and early adulthood. *Breastfeed Med* 2018. doi: 10.1089/bfm.2018.0117.
23. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 2019;139:5e6-e528.
24. Heron M. Deaths: leading causes for 2017. *Natl Vital Stat Rep* 2019;68:1-77.
25. Steinberger J, Daniels SR, Hagberg N, Isasi CR, Kelly AS, Lloyd-Jones D, et al. Cardiovascular health promotion in children: challenges and opportunities for 2020 and beyond: a Scientific Statement from the American Heart Association. *Circulation* 2016;134:236-55.

26. Anstey AH, Chen J, Elam-Evans LD, Perrine CG. Racial and geographic differences in breastfeeding—United States, 2011–2015. *MMWR* 2017;66:723–7.
27. WHO (2017). World Health Organization. Obesity and Overweight Fact Sheet, <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> (access: 05.32.2020).
28. Baldrige AS, Huffman MD, Taylor F, Xavier D, Bright B, Van Horn LV, et al. The healthfulness of the US packaged food and beverage supply: a cross-sectional study. *Nutrients* 2019;11:1704.
29. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ* 2017;356.
30. Hope S, Micali N, Deighton J, Law C. Maternal mental health at 5 years and childhood overweight or obesity at 11 years: evidence from the UK Millennium Cohort Study. *Int J Obes (Lond)* 2019; 43: 43–52.
31. Bates CR, Buscemi J, Nicholson LM, Cory M, Jagpal A, Bohnert AM. Links between the organization of the family home environment and child obesity: A systematic review. *Obesity Reviews* 2018;19: 716–27.
32. Warnakulasuriya LS, Fernando MMA, Adikaram AVN, Thawfeek ARM, Anurasiri WL, et al. Metformin in the Management of Childhood Obesity: A Randomized Control Trial. *Childhood obesity* 2018;14: 553–65.

Evaluation of Chronic Cough Etiologies in Children

Çocuklarda Kronik Öksürük Sebeplerinin Değerlendirilmesi

Özge YILMAZ TOPAL

Department of Pediatric Immunology and Allergy, Gaziantep Cengiz Gökçek Gynecology and Pediatrics Hospital, Gaziantep, Türkiye



ABSTRACT

Objective: Cough is one of the leading causes of hospitalization in children worldwide. It should be considered important because it can be a symptom of various serious diseases and affects the quality of life of the child. A differential diagnosis should be performed on all children with a chronic cough. This study aimed to determine the etiologies in patients evaluated for chronic cough.

Material and Methods: The study included patients admitted to the pediatric immunology and allergy outpatient clinic, with the complaint of chronic cough between the ages of 0–18 years. Clinical and demographic characteristics of patients were recorded.

Results: This study included 323 patients between the ages of 0-18 years. The median age of the patients was 7 (interquartile range: 5-9.7) years. One hundred and forty five (45%) of the patients were female. One hundred seventy-nine (55.4%) patients had a family history of atopic diseases such as asthma and/or allergic rhinitis. The presence of aeroallergen sensitivity was demonstrated in 127 patients. One hundred and forty-four (44.6%) patients were diagnosed with asthma, 75 (23.2%) patients with wheezing, 54 (16.7%) patients with post-infectious cough, 43 (13.3%) patients with postnasal drip syndrome, 4 (1.2%) patients with gastroesophageal reflux, 2 (0.6%) patients with foreign body aspiration, and 1 (0.3%) patient with psychogenic cough. Moreover, two patients with asthma, and one patient with wheezing had reflux symptoms in addition to the diagnosis of asthma and wheezing. One patient was found to have a partial IgA deficiency, and 18 patients had hypogammaglobulinemia. Immunoglobulin replacement therapy was initiated for a patient with hypogammaglobulinemia. Of the 219 patients diagnosed with asthma or wheezing, 144 had an atopic disease in the family ($p<0.001$). It was found that one hundred and eighty-five patients (57.3%) had domestic smoke exposure. Furthermore, smoke exposure was observed in 58 (77.3%) of 75 patients under the age of 6 years who were followed up with the diagnosis of wheezing ($p= 0.010$).

Conclusion: In our study, asthma, which is one of the most common causes of chronic cough in the literature, was found to be the most common cause. For a correct approach when making a differential diagnosis in pediatric patients presenting with chronic cough, the patient's history, physical examination, laboratory tests, and risk factors should be evaluated as a whole with systematic evaluation.

Key Words: Chronic Cough, Child, Asthma, Wheezy Infant

ÖZ

Amaç: Öksürük, tüm dünyada çocukluk çağında en sık hastaneye başvuru sebeplerinden biridir. Çeşitli ciddi hastalıkların da belirtisi olabilmesi ve çocuğun hayat kalitesini etkilemesi nedeniyle önemsenmelidir. Tüm kronik öksürüğü olan çocuklar ayırıcı tanı açısından değerlendirilmelidir. Bu çalışmada kronik öksürük sebebiyle değerlendirilen hastalarda etyolojilerin belirlenmesi amaçlanmıştır.



0000-0001-5245-2488: YILMAZ TOPAL Ö

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 approval for the study was obtained from the Gaziantep University Clinical Research Ethics Committee (no:2022/372).

Contribution of the Authors / Yazarların katkısı: Yılmaz Topal Ö: 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.

How to cite / Atıf yazım şekli : Yılmaz Topal Ö. Evaluation of Chronic Cough Etiologies in Children. Turkish J Pediatr Dis 2023;17: 227-232.

Correspondence Address / Yazışma Adresi:

Özge YILMAZ TOPAL

Department of Pediatric Immunology and Allergy,
Gaziantep Cengiz Gökçek Gynecology and Pediatrics Hospital, Gaziantep, Türkiye
E-posta: ozgeyilmaztopal@gmail.com

Received / Geliş tarihi : 09.12.2022

Accepted / Kabul tarihi : 10.01.2023

Online published : 26.01.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1216596

Gereç ve Yöntemler: Çalışmaya çocuk immünoloji ve alerji polikliniğine 0-18 yaş aralığında kronik öksürük şikayeti ile başvuran hastalar dahil edildi. Hastaların klinik ve demografik bilgileri retrospektif olarak dosyalarından kayıt edildi.

Bulgular: Bu çalışmada 0-18 yaş aralığında 323 hasta yer almaktaydı. Hastaların yaş ortancası 7 yıl (çeyreklerarası aralık:5-9.7)'di. Hastaların 145'i (%45) kızdı. Yüz yetmişdokuz (%55.4) hastanın ailesinde atopik hastalık öyküsü vardı. Hastaların 127'sinde aeroalerjen duyarlılığının varlığı gösterildi. Yüz kırkdört (%44.6) hastaya astım, 75 (%23.2) hastaya hişiltılı çocuk, 54 (%16.7) hastaya postenfeksiyöz öksürük, 43 (%13.3) hastaya postnazal akıntı sendromu, 4(%1.2) hastaya reflü, 2 (%0.6) hastaya yabancı cisim aspirasyonu, 1 (%0.3) hastaya psikojenik öksürük tanısı konuldu. Ayrıca iki hastada astım, bir hastada ise hişiltılı çocuk tanısına ek olarak reflü semptomlarının olduğu görüldü. Bir hasta parsiyal IgA eksikliği, 18 hasta da hipogamaglobulinemi sebebiyle takibe alındı. Onsekiz hastanın birine ise immunoglobulin replasman tedavisi başlandı. Astım veya hişiltılı çocuk tanısı alan 219 hastanın 144'ünde aile de atopik bir hastalık olduğu öğrenildi ($p<0.001$). Yüz seksenbeş hastada (%57.3) ev içi sigara maruziyeti olduğu öğrenildi. Ayrıca 6 yaş altında hişiltılı çocuk tanısı ile takibe alınan 75 hastanın 58'inde (%77.3) sigara maruziyeti olduğu görüldü ($p= 0.010$).

Sonuç: Literatürde kronik öksürüğün en sık nedenleri içinde yer alan astım, bizim çalışmamızda da en sık sebep olarak saptanmıştır. Kronik öksürük ile başvuran çocuk hastalarda ayırıcı tanı yaparken, sistematik değerlendirme ile hastanın öykü, fizik muayene ve laboratuvar tetkikleri ile risk faktörleri bütün olarak değerlendirilmelidir.

Anahtar Sözcükler: Kronik Öksürük, Çocuk, Astım, Hişiltılı Çocuk

INTRODUCTION

Chronic cough is defined as a cough that lasts more than 3–4 weeks and is one of the most common childhood symptoms (1, 2). Furthermore, cough is one of the leading causes of hospitalization in children worldwide (3, 4). It is a major source of concern for parents in the pediatric population. (5)

Chronic cough in children differs from chronic cough in adults in terms of etiology and management, as it may be a symptom of an underlying disease (6). Young children are likely to cough more as they are more likely to have infections. In the light of the data based on the subjective observations of the parents, it has been reported that up to 10% of preschool- and early-school-aged children have a chronic cough without wheezing at any time (7). Another study reported that 35% of preschool children reported coughing in any month (8). A multicenter study of children aged 7 to 11 found that 9% of them had a chronic cough (9).

Chronic cough is often nonspecific and may be accompanied by causes that cannot be easily identified during the initial assessment (10). Congenital airway problems, postnasal drip, rhinitis, rhinosinusitis, asthma, eosinophilic bronchiolitis, and gastroesophageal reflux disease (GERD), foreign body aspirations, and protracted bacterial bronchiolitis are the underlying reasons for this problem (11, 12). Asthma was found to be the most common cause in three studies focusing on the etiology of chronic cough in children in Turkey, while postnasal drip syndromes were found to be the most common cause in another study (13-16).

Chronic cough in children is associated with impaired quality of life, school absences, multiple doctor visits, (17) and inappropriate use of antibiotics (18, 19). A differential diagnosis should be performed on all children with a chronic cough.

This study aimed to determine the etiologies in patients evaluated for chronic cough.

MATERIALS and METHODS

The study included patients admitted to the pediatric immunology and allergy outpatient clinic at Gaziantep Cengiz Gökçek Gynecology and Pediatrics Hospital between 01.02.2022-08.08.2022 with the complaint of chronic cough between the ages of 0–18 years. The approval for the study was obtained from the Gaziantep University Clinical Research Ethics Committee (no:2022/372).

Coughs are classified as acute, prolonged acute, or chronic based on their duration. Acute cough includes coughs lasting up to 14 days. Prolonged acute coughing includes coughs lasting between 2 and 4 weeks. Chronic cough is a cough that lasts longer than 4 weeks (20). In this study, chronic cough was defined as cough lasting more than 4 weeks. The patients were evaluated by taking into account the American College of Chest Physicians (ACCP) guidelines on the approach to chronic cough (21). Accordingly, further examinations were planned for the differential diagnosis of patients with specific disease symptoms based on the initial evaluations. After the evaluation of the lung x-rays of the patients, the patients with no specific findings were followed up, and in the case of their complaints not regressing, the necessary treatment was started based on the nature of the cough.

Demographic characteristics of patients such as gender, age at clinical visit, personal and family history of allergic and chronic diseases, cigarette smoke exposure history of the patient, symptoms and physical examination results, and skin prick test results were recorded. Immunoglobulin (Ig) levels were requested in (22) patients with frequent infections and findings defined as "10 alarm findings" for primary immunodeficiency, and these results were also recorded retrospectively. The patients' Ig values were classified as low or normal according to the relevant age-related reference intervals for each Ig value. For these reference intervals, we used reference systems based on age-related normal Ig ranks determined in Turkish children (23).

A skin prick test was performed on patients with suspected allergen sensitivity in their history.

Skin Prick test:

Skin prick tests with dermatophagoides farinae (Allergopharma), Dermatophagoides pteronyssinus (ALK), Alternaria (ALK), Aspergillus (Lofarma), Canis familiaris (ALK), Cat epithelia (Allergopharma), Cockroach (ALK), Grasses/cereals (Allergopharma), 7-grass polen mix solution (Phleum pratense, Dactylis glomerate, Poa Pratensis, Agrostis capillaris, Festuca pratensis, rye, sweet vernal grass) (ALK), Olive tree (Allergopharma), Composite mix (Mugwort, Golden Rod, Sunflower, Cocklebur) (Lofarma), willow tree (Allergopharma), Birch mix (Grey Alder,White Birch (Betulacea Mix)) (Lofarma), Sheep dander (Inmunotek) were performed in patients with positive (histamine) and negative (saline) controls and were interpreted 15 minutes after the application of the allergens to the skin. A positive SPT result was accepted as a wheal diameter of 3 mm or larger.

Statistical Analysis:

Statistical methods: Statistical analyses were performed using SPSS version 22 (IBM Corp, Armonk, NY). Data were reported as number and percentage for nominal variables and as mean and SD, or median and interquartile range (IQR) for continuous variables. The Chi-square test was used for comparisons of nonparametric data.

RESULTS

This study included 323 patients between the ages of 0-18 years. The median age of the patients was 7 (interquartile range: 5-9.7) years. One hundred and forty five (45%) of the patients were female, and 178 (55%) were male.

One hundred and forty-four (44.6%) patients were diagnosed with asthma, 75 (23.2%) patients as wheezy infant, 54

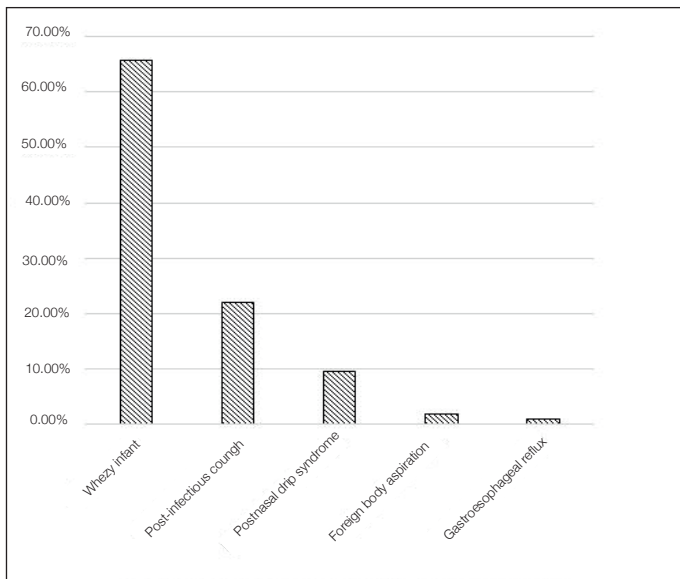


Figure 1: Etiologies of chronic cough of 114 patients < 6 years of age.

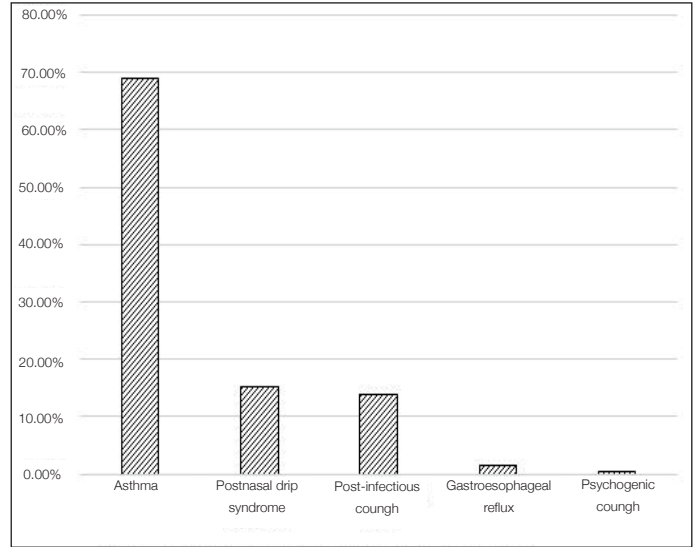


Figure 2: Etiologies of chronic cough of 209 patients ≥ 6 years of age.

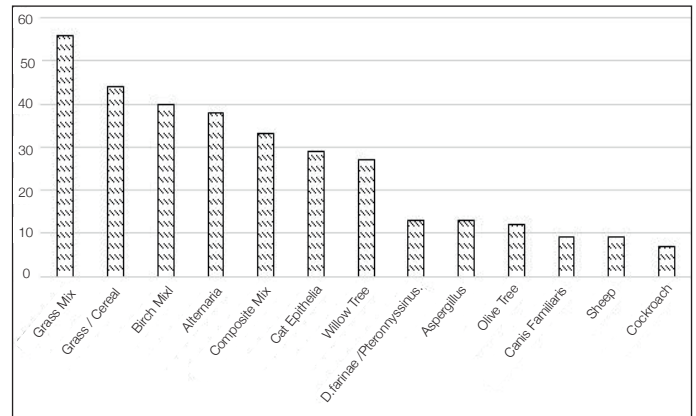


Figure 3: Aeroallergen sensitivities of the patients. (D.farinae / Pteronyssinus: Dermatophagoides farinea / Pteronyssinus.)

(16.7%) patients with post-infectious cough, 43 (13.3%) patients with postnasal drip syndrome, 4 (1.2%) patients with gastroesophageal reflux, 2 (0.6%) patients with foreign body aspiration, and 1 (0.3%) patient with psychogenic cough. Moreover, two patients with asthma, and one patient with wheezing had GERD symptoms in addition to the diagnosis of asthma and wheezy infant. Figures 1 and 2 show the etiology of chronic cough according to whether the patients were under or above the age of 6.

Inhaled corticosteroids (ICS) treatment was started on 216 patients (66.9%). 24 patients were treated with antibiotics, 1 patient with nasal steroid (NS) and leukotriene receptor antagonist (LTRA), 3 patients with antihistamines (AH) and NS, 3 patients with anti-GERD treatment, and 1 patient with LTRA, while 184 patients were started on ICS treatment alone. Antibiotic treatment was started in 87 patients (27%), 51 patients received only antibiotic treatment, while 1 patient received with AH and NS, 1 patient received with anti-GERD treatment, 2 patients received with LTRA, and 8 patients received with NS

Table I: Association of atopic disease history in family and having asthma or wheezy

	Asthma or wheezy infant n (%)	Other etiologies n (%)	p
Having atopic disease history in family	144 (65.75)	35 (33.65)	<0.001

Table II: Association of smoke exposure history and having wheezy in patients under 6 years

	Wheezy infant n (%)	Other etiologies n (%)	p
Having smoke exposure history	58 (77.3)	21 (53.85)	<0.010

treatment. Nasal steroid treatment was started on 45 patients. While 12 patients received only NS treatment, 18 patients received NS and AH, and 2 patients received NS with LTRA. Three patients were treated with anti-GERD treatment alone, and four patients were treated with LTRA only.

One hundred seventy-nine (55.4%) patients had a family history of atopic diseases such as asthma and/or allergic rhinitis. Prick test to show aeroallergen sensitivity was not performed on 101 patients. The presence of aeroallergen sensitivity was demonstrated in 127 (57.2%) of 222 patients who underwent a Prick test. Aeroallergen sensitivities of the patients are shown in Figure 3.

The immunoglobulin levels of 109 patients who described recurrent infections were also examined. Among these patients, one patient was found to have a partial IgA deficiency, and 18 patients had hypogammaglobulinemia. A patient with hypogammaglobulinemia was 11 months old, and immunoglobulin replacement therapy was initiated due to a serum IgG level of <200 mg/dl. The results of a genetic mutation analysis to identify the patient's primary immunodeficiency are awaited.

Of the 219 patients diagnosed with asthma or as wheezy infant, 144 had an atopic disease in the family. This rate was statistically higher in patients followed up with the diagnosis of asthma and/or wheezing compared to other patients (p : <0.001) (Table I). It was found that one hundred and eighty-five patients (57.3%) had domestic smoke exposure. Furthermore, smoke exposure was observed in 58 (77.3%) of 75 patients under the age of 6 years who were followed up with the diagnosis of wheezing. This rate was statistically higher in patients under the age of 6 who were followed up with other diagnoses compared to the rate of smoking exposure (p = 0.010) (Table II.).

DISCUSSIONS

Coughing can be the first symptom of many diseases or conditions that affect the respiratory tract as it is more than

a defense mechanism. Almost all respiratory diseases, as well as some extrapulmonary diseases in some cases, can cause chronic cough. It is critical for the physician to detect serious illnesses that require immediate treatment (24). However, an inadequate definition of the disease that causes chronic cough results in patients receiving inappropriate treatments, which can be harmful to both patient health and the national economy by causing unnecessary drug use.

In our study, asthma, which is one of the most common causes of chronic cough in the literature, was found to be the most common cause. Chronic cough in asthma can occur in a variety of clinical settings and is not always associated with airflow obstruction, wheezing, or dyspnea. Asthma can manifest itself mostly as nocturnal cough, and the diagnosis is supported by the presence of bronchial hypersensitivity (11, 25).

Asthma pathogenesis is influenced by both genetic and environmental factors, and the majority of children with asthma have an allergic component of the disease. Allergen sensitivity plays a role as an important risk factor in the development of asthma. Allergen sensitivity in asthma patients has been reported to range between 44% and 60% (26-28). In another allergen evaluation conducted in Gaziantep with patients who applied with the complaint of chronic cough, 57.1% of the patients were observed to have at least one allergen sensation. However, food allergens and aeroallergens were evaluated together in this study (29). An aeroallergen evaluation was performed in our study, and the presence of aeroallergen sensitivity was found in 127 (57.2%) of 222 patients.

In our study, 16.7% of the patients were diagnosed with post-infectious cough. Cough reflex hypersensitivity, which begins with an airway viral or bacterial infection, can last for weeks and is a common cause in people of all ages (30-32). It often causes dry cough and no other symptoms are seen. Recovery takes time in most patients with post-infection cough and is associated with hypersensitivity (6).

Gastro-esophageal reflux disease should be considered in children with prolonged cough and recurrent ear infections. The cough is both long-term and usually non-productive in these patients. Studies have emphasized that 75% of patients may have cough as the only symptom of GERD (33, 34). In our study, 7 patients were diagnosed with GERD.

Immune deficiencies cause frequent recurrent lung infections, diarrhea, aphtha, and other infections. Along with sibling stories, it is a disease that should be kept in mind in Turkey, where consanguineous marriages are common (35). In our study, 19 patients were followed up for immunodeficiency, and immunoglobulin replacement therapy was started in 1 patient. Chronic cough can be a warning sign of many underlying diseases. Therefore, these diseases should also be kept in mind.

Exposure to smoke is an important cause of cough in children. Passive smoking has been shown to increase the risk of lung infection and to weaken pulmonary functions (2, 35). In our study, it was found that 57.3% of the patients had domestic smoke exposure. It was observed that there was a significant difference in smoke exposure between the children under the age of 6 with wheezing and the patients who were followed up due to other chronic coughs, and that smoke exposure could be a facilitating factor for wheezing in children. Moreover, the presence of atopic disease in the family was found to be significantly different in patients diagnosed with asthma or wheezing compared to other patient groups when all age groups were examined.

In conclusion, it is important to provide disease-specific treatment in pediatric patients with chronic cough if the underlying cause is determined. Among the preventable factors, reasons such as avoiding smoke exposure and allergens causing sensitization should be reviewed. For a correct approach when making a differential diagnosis in pediatric patients presenting with chronic cough, the patient's history, physical examination, laboratory tests, and risk factors should be evaluated as a whole with systematic evaluation.

REFERENCES

- de Jongste JC, Shields MD. Cough. 2: Chronic cough in children. *Thorax* 2003;58:998-1003.
- Chang AB, Oppenheimer JJ, Irwin RS, Panel CEC. Managing Chronic Cough as a Symptom in Children and Management Algorithms: CHEST Guideline and Expert Panel Report. *Chest* 2020;158:303-29.
- rwin RS, Boulet LP, Cloutier MM, Fuller R, Gold PM, Hoffstein V, et al. Managing cough as a defense mechanism and as a symptom. A consensus panel report of the American College of Chest Physicians. *Chest* 1998;114:133S-81S.
- Hay AD, Heron J, Ness A, team As. The prevalence of symptoms and consultations in pre-school children in the Avon Longitudinal Study of Parents and Children (ALSPAC): a prospective cohort study. *Fam Pract* 2005;22:367-74.
- Cornford CS, Morgan M, Ridsdale L. Why do mothers consult when their children cough? *Fam Pract* 1993;10:193-6.
- Kantar A, Marchant JM, Song WJ, Shields MD, Chatziparasidis G, Zacharasiewicz A, et al. History Taking as a Diagnostic Tool in Children With Chronic Cough. *Front Pediatr* 2022;10:850912.
- Munyard P, Bush A. How much coughing is normal? *Arch Dis Child* 1996;74:531-4.
- Kogan MD PG, Yu SM, Kotelchuck M. Over-the-counter medication use among preschool-age children. *JAMA* 1994; 272:1025-30.
- Leonardi GS, Houthuijs D, Nikiforov B, Volf J, Rudnai P, Zejda J, et al. Respiratory symptoms, bronchitis and asthma in children of Central and Eastern Europe. *Eur Respir J* 2002;20:890-8.
- Song DJ, Song WJ, Kwon JW, Kim GW, Kim MA, Kim MY, et al. KAAACI Evidence-Based Clinical Practice Guidelines for Chronic Cough in Adults and Children in Korea. *Allergy Asthma Immunol Res* 2018;10:591-613.
- Chung KF, Pavord ID. Prevalence, pathogenesis, and causes of chronic cough. *Lancet* 2008;371:1364-74.
- Mukerji SS, Yenduri NJS, Chiou E, Moonnumakal SP, Bedwell JR. A multi-disciplinary approach to chronic cough in children. *Laryngoscope Investig Otolaryngol* 2022;7:409-16.
- Asilsoy S, Bayram E, Agin H, Apa H, Can D, Gulle S, et al. Evaluation of chronic cough in children. *Chest* 2008;134:1122-8.
- Karabel M, Kelekci S, Karabel D, Gurkan MF. The evaluation of children with prolonged cough accompanied by American College of Chest Physicians guidelines. *Clin Respir J* 2014;8:152-9.
- Gedik AH, Cakir E, Torun E, Demir AD, Kucukkoc M, Erenberk U, et al. Evaluation of 563 children with chronic cough accompanied by a new clinical algorithm. *Ital J Pediatr* 2015;41:73.
- Usta Guc B, Asilsoy S, Durmaz C. The assessment and management of chronic cough in children according to the British Thoracic Society guidelines: descriptive, prospective, clinical trial. *Clin Respir J* 2014;8:330-7.
- Marchant JM, Newcombe PA, Juniper EF, Sheffield JK, Stathis SL, Chang AB. What is the burden of chronic cough for families? *Chest* 2008;134:303-9.
- Thomson F, Masters IB, Chang AB. Persistent cough in children and the overuse of medications. *J Paediatr Child Health* 2002;38:578-81.
- Chang AB, Oppenheimer JJ, Weinberger M, Grant CC, Rubin BK, Irwin RS, et al. Etiologies of Chronic Cough in Pediatric Cohorts: CHEST Guideline and Expert Panel Report. *Chest* 2017;152:607-17.
- Chang AB, Landau LI, Van Asperen PP, Glasgow NJ, Robertson CF, Marchant JM, et al. Cough in children: definitions and clinical evaluation. *Med J Aust* 2006;184:398-403.
- Chang AB, Glomb WB. Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129:260S-83S.
- www.info4pi.org date of access: 01.11.2022
- Tezcan İ BAİ, Ersoy F, Sanal Ö. Sağlıklı Türk çocukları ve erişkinlerde turbidometrik yöntemle bakılan serum immunoglobulin düzeyleri. *Çocuk Sağlığı ve Hastalıkları Dergisi* 1996; 32: 649-56.
- Chang AB. Causes aamociclCK, Widdicombe JG, Boushey HA, Eds. *Cough: causes, mechanisms and therapy*. Oxford, UK: Blackwell Publishing Ltd 2003; pp. 57-73.
- Corrao WM, Braman SS, Irwin RS. Chronic cough as the sole presenting manifestation of bronchial asthma. *N Engl J Med* 1979;300:633-7.
- Dibek Misirlioglu E, Reha Cengizlier M. Skin prick test results of child patients diagnosed with bronchial asthma. *Allergol Immunopathol (Madr)* 2007;35:21-4.
- Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics* 2001;108:E33.
- Kunt Uzunaslın E, Gürdal Yüksel E, Özyardımcı N. Astma polikliniğimizde izlenmekte olan atopik bronşiyal astmalı olgularda prick, intradermal deri testleri ve Rast yöntemi sonuçlarının değerlendirilmesi. *Van Tıp Derg* 1999;6:13-8.
- Araz ÇN. Gaziantep yöresinde kronik öksürük şikayeti ile başvuran çocuklarda alerjen dağılımı. *Düzce Üniversitesi Tıp Fakültesi Dergisi* 2009;11:21-7
- Chang AB, Robertson CF, Van Asperen PP, Glasgow NJ, Mellis CM, Masters IB, et al. A multicenter study on chronic cough in children

- :burden and etiologies based on a standardized management pathway. *Chest* 2012;142:943-50.
31. Udem BJ, Zacccone E, McGarvey L, Mazzone SB. Neural dysfunction following respiratory viral infection as a cause of chronic cough hypersensitivity. *Pulm Pharmacol Ther* 2015;33:52-6.
32. Shields MD, Thavagnanam S. The difficult coughing child: prolonged acute cough in children. *Cough* 2013;9:11.
33. Özdemir Ö. Çocuklarda gastroözefageal reflü-ilişkili öksürük (reflü öksürüğü): Güncel yaklaşım. *Asthma Allergy Immunol* 2013;11:1-14.
34. Yıldız Y, İçde M. Çocuklarda kronik öksürüğün nedenlerinin incelenmesi. *Cukurova Med J* 2017;42: 66-72.
35. Pekcan S, Kiper N. Chronic cough. *Cocuk Sağlığı ve Hastalıkları Dergisi* 2006;49: 247-55.

Comparison of Language Development, Emotional and Behavioral Problems, Parental Attitude Characteristics, Parental Stress Level and Related Factors in Preschool Period, Between Preterm and Term-Born Children

Preterm ve Term Doğan Çocuklarda Dil Gelişimi, Duygusal ve Davranışsal Sorunlar, Ebeveyn Tutum Özellikleri, Ebeveyn Stres Düzeyi ve İlişkili Faktörlerin Okul Öncesi Dönemde Karşılaştırılması

Barış GÜLLER¹, Erbu YARCI², Ferhat YAYLACI¹

¹Department of Child and Adolescent Psychiatry, Dörtçelik Child Hospital, Bursa, Türkiye

²Department of Neonatology, Dörtçelik Child Hospital, Bursa, Türkiye



ABSTRACT

Objective: We aimed to investigate language development, emotional and behavioral problems, parental attitudes, parental stress levels, and related factors in preschool period between children who were born preterm and term.

Material and Methods: We included 176 children, of whom 90 were born preterm and 86 term, and their mothers. Mothers filled out the sociodemographic data form, Child Adjustment and Parent Efficacy Scale (CAPES-TR), Parenting Stress Index-Short Form (PSI-SF), and Parenting Styles and Dimensions Questionnaire – Short Version (PSDQ) scales. Denver II Developmental Screening Test (DDST) and Test of Early Language Development - Third Edition (TELD-3) were applied to children.

Results: The mean age was 37.97±3.62 months for the preterm children, and 38.77±3.28 months for the term children. The scores of preterm children were lower in the TELD-3 subtests. The rates of children with abnormal development regarding personal social development and language development were significantly higher in preterm children ($p=0.007$ for personal social development and <0.001 for language development, respectively). CAPES-TR emotional and behavioral problems scores were higher in preterm children. CAPES-TR Parental Self-Efficacy Subscale was lower in preterm children ($p<0.001$). PSI-SF total score and PSDQ permissive parenting subscale score were higher in mothers of preterm children ($p=0.005$ and $p<0.001$, respectively). The preterm-born children were more commonly diagnosed with language disorder and global developmental delay ($p=0.006$ and $p=0.019$, respectively). A positive correlation was found between the week of birth, maternal education level and monthly income level and TELD-3 scores, DENVER personal social and language development level ($p<0.050$).

Conclusion: Our study revealed closer follow-up is important for preterm children to plan special education support when it is necessary.

Key Words: Behavioral problems, Language development, Parenting attitude, Parenting stress, Prematurity

0000-0001-7911-4614 : GÜLLER B
0000-0003-4434-0958 : YARCI E
0000-0002-1360-7771 : YAYLACI F

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. Ethics committee approval was obtained from Uludag University with the date 26.05.2021 and number 2021-6/8.

Contribution of the Authors / Yazarların katkısı: **GÜLLER B:** 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. **YARCI E:** Constructing the hypothesis or idea of research and/or article, Reviewing the article before submission scientifically besides spelling and grammar. **YAYLACI F:** 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 necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Güller B, Yarci E and Yaylaci F. Comparison of Language Development, Emotional and Behavioral Problems, Parental Attitude Characteristics, Parental Stress Level and Related Factors in Preschool Period, Between Preterm and Term-Born Children. Turkish J Pediatr Dis 2023;17:233-242.

Correspondence Address / Yazışma Adresi:

Barış GÜLLER
Department of Child and Adolescent Psychiatry,
Dörtçelik Child Hospital, Bursa, Türkiye
E-posta: drbarisguller@gmail.com

Received / Geliş tarihi : 23.09.2022

Accepted / Kabul tarihi : 16.01.2023

Online published : 01.03.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1179344

ÖZ

Amaç: Çalışmamızın amacı yeni doğan yoğun bakım ünitesinde yatmış olan preterm ve term doğan çocuklarda okul öncesi dönemde dil gelişimi, duygusal ve davranışsal sorunlar, ebeveyn tutumları, ebeveyn stres düzeyleri ve ilişkili faktörleri araştırmaktır.

Gereç ve Yöntemler: Çalışmamız 90 preterm ve 86 term olmak üzere 176 çocuk ve annesi ile yapıldı. Anneler sosyodemografik veri formu, Çocuk Uyumu ve Anne baba Yeterlik Ölçeği (CAPES-TR), Anne Baba Stres Ölçeği-Kısa Form (ABSÖ-KF) ve Anne babalık Stilleri ve Boyutları Ölçeği-Kısa Form ölçeklerini doldurdu. Tüm çocuklara Denver II Gelişimsel Tarama Testi (DGTT) ve Türkçe Erken Dil Gelişim Testi (TEDİL) uygulandı.

Bulgular: Preterm çocukların yaş ortalaması 37.97 ± 3.62 ay, term çocukların 38.77 ± 3.28 aydı. TEDİL alt testlerinde preterm çocukların skorları daha düşüktü. Erken doğmuş çocuklarda kişisel sosyal gelişim ve dil gelişimi açısından anormal gelişim gösteren çocukların oranı daha yüksekti (kişisel sosyal gelişim için $p=0.007$, dil gelişimi için $p < 0.001$). Preterm çocuklarda CAPES-TR duygusal ve davranışsal sorunlar ölçek puanları daha yüksekti. CAPES-TR Ebeveyn Özyeterliliği puan ortalaması preterm çocuklarda daha düşüktü ($p=0.000$). ABSÖ-KF toplam puanı ile ABSÖ-KF izin verici anne babalık alt ölçek puanı preterm çocuk annelerinde daha yüksekti ($p = 0.005$ ve $p < 0.001$). Dil Bozukluğu ve genel gelişimsel gecikme tanısı konma oranları preterm çocuklarda daha yüksekti (sırasıyla $p=0.006$ ve $p=0.019$). Doğum haftası, anne eğitim düzeyi ve aylık gelir düzeyi ile TEDİL skorları, DENVER kişisel sosyal ve dil gelişim düzeyi arasında pozitif korelasyon saptandı ($p < 0.050$).

Sonuç: Çalışmamız preterm çocuklarda erken dönemde yakın takip ve gerekli olduğunda özel eğitim desteği planlamasının önemli olduğunu göstermektedir.

Anahtar Sözcükler: Davranış sorunları, Dil gelişimi, Anne baba tutumu, Ebeveynlik stresi, Prematüre

INTRODUCTION

Long-term results show that preterm babies are at the risk for neurodevelopmental problems and psychiatric disorders. In literature, retardation in fine and gross motor skills, speech delay, difficulties in learning, problems in social and emotional life, hyperactivity, attention deficit, and behavioral problems are often reported as problems that preterm-born children may face (1). In a meta-analysis examining the frequency of anxiety and depressive disorders in children born preterm, it was found that preterm birth was associated with higher levels of anxiety disorder in the period from 3 to 19 years of age (2). In another meta-analysis, low gestational age, low birth weight, neonatal morbidities, and low maternal education levels were associated with lower intelligence scores in young adulthood (3).

The increase in the quality and number of intensive care units has led to an increase in the survival rates of preterm babies. The increase in survival rates has brought the problems of care of preterm babies, who are at high risk in terms of neurodevelopmental, gastrointestinal and respiratory problems. It has been reported that mothers, one of the most important elements of this care, may experience more stress, financial difficulties, and relationship difficulties than those who give birth at term (4). Being more anxious than other parents may cause parents of preterm children to display a more controlling style of parenting (5,6). The high levels of stress in mothers of preterm babies and using control strategies may lead to decreased interactive play with their child and deterioration in the self-regulation capacity of the child. As a result, it has been reported that difficulties in social areas, internalization and externalization problems may appear in the child (7-9).

One of the hypotheses of the study is that there is retardation in language development and general development is more common in preterm-born children during the preschool period

compared to term-born children, and also there is a higher rate of emotional and behavioral problems in preterm-born children. Besides, it was assumed that the stress level of caregivers of preterm-born children is higher, parental self-efficacy is lower, and education level and socioeconomic level are factors associated with these risks. It is important to carry out the regular follow-up of children born preterm in the early period and to identify problems in developmental and behavioral areas. The impacts of preterm birth on the child and family can be reduced by identifying the children in need and ensuring that they benefit from the support systems such as special education in the early period. Although follow-up studies on children preterm-born are common in the literature, these children are compared with term children. There are limited studies, that compare general development and language development in the pre-school period, and also the mental health, attitude characteristics and stress levels of the parents, who have the greatest impact on the development of the children, especially in the pre-school period. The aim of our study is to investigate the neurodevelopmental, emotional and behavioral problems, parental attitudes, parental stress levels and related factors in pre-school period in preterm and term-born children who were hospitalized in the neonatal intensive care unit.

MATERIALS and METHODS

Our study was conducted with 176 pre-school children, at least 30 months old during the study and their mothers, who were born preterm and term and were hospitalized between 2017 and 2019 in the secondary neonatal intensive care unit of a regional pediatric hospital during the neonatal period. Ninety children were born prematurely and 86 children were born at term. The parents were reached through the contact information in the hospital records. The number of preterm children who met the

inclusion criteria and could be reached via registered phone numbers was 117, and the number of term children was 122. Twenty-seven of the parents of preterm children and 36 of the parents of term children were excluded from the study because they did not agree to participate in the study or did not attend the scheduled appointment. Parents who agreed to participate in the study were given an appointment to be evaluated in the child and adolescent psychiatry outpatient clinic.

For both preterm and term-born children, being at least 30 months old at the time of the study, treatment with hospitalization in the neonatal intensive care unit of our hospital during the newborn period for both groups, their parents agreeing to participate in the study, and being literate at a level to fill the assessment tools were accepted as inclusion criteria. When evaluating the results of the study, in order to avoid bias, children who were born both preterm and term were excluded from the study, who are known to have a significant risk factor that affect general development and language development, and who have severe congenital, genetic diseases that have high risk of affecting the stress level of parents, or children who were reported to have severe neurological sequelae. Besides, parents who did not agree to participate in the study and were illiterate to understand and fill in the scales were not included in the study.

Mothers completed the sociodemographic data form, Child Adjustment and Parent Efficacy Scale (CAPES-TR), Parenting Stress Index-Short Form (PSI-SF), and Parenting Styles and Dimensions Questionnaire – Short Version (PSDQ). Denver II Developmental Screening Test (DDST) was applied to all children by an experienced child development specialist, and the Test of Early Language Development - Third Edition (TELD-3) was applied by a speech and language therapist. All children born preterm and term were evaluated by a child and adolescent psychiatry specialist in the child and adolescent psychiatry outpatient clinic. In the diagnostic evaluation of children, TELD-3 and DDST results were examined, and a psychiatric interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was performed.

Ethics committee approval was obtained from Uludag University with the date 26.05.2021 and number 2021-6/8.

Evaluation tools

Sociodemographic data form

In this form, there are questions to investigate the birth week of children, hospitalization history, pregnancy background of mothers, education level and economic condition of parents, and family structure.

Child Adjustment and Parent Efficacy Scale (CAPES-TR)

The scale consists of 27 items and is filled by the parents. The child adjustment subscale consists of two factors: behavioral problems and emotional problems. The other subscale of CAPES-TR is the parent efficacy subscale. Higher scores in the

child adjustment subscale indicate an increase in problematic behaviors related to child adjustment. An increase in the scores in the parent efficacy subscale means that parents have got high self-efficacy in coping with behaviours of their child (10).

Parenting Styles and Dimensions Questionnaire – Short Version (PSDQ)

It was developed to evaluate parenting attitudes. It is filled by the mothers or fathers. The scale includes three subscales that measure democratic, authoritarian, and permissive parenting attitudes. Each subscale is evaluated within itself. The total score obtained from the items which form the subscales includes information about that attitude (11).

Parenting Stress Index-Short Form (PSI-SF)

The scale consists of parental stress, unsuccessful parent-child interaction and difficult child sub-dimensions. A high score on a sub-dimension indicates that parents are experiencing stress on that sub-dimension. An increase in the total scale score means an increase in the stress level of the parents (12).

Denver Developmental Screening Test (DDST)

It provides data on personal-social development, fine motor development, language development and gross motor development of children aged 0-6. It is also a test that helps clinical interviews to detect developmental problems and monitor development (13).

Test of Early Language Development - Third Edition (TELD-3)

It was developed to measure the language skills of children between 2 years 0 months and 7 years 11 months. It is used for purposes such as diagnosing children with language disorders in the early period and providing information about the developmental process (14).

Statistical analysis:

Data were uploaded to and analyzed using SPSS version 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY). Data obtained by measurement are shown as arithmetic mean \pm standard deviation, and data obtained by counting as a percentage (%). Kolmogorov Smirnov test was used to evaluate the fit of numerical variables to normal distribution. Categorical variables such as DDST, socio-demographic variables such as child gender, educational status of parents, employment status of parents, monthly income level and diagnoses made with evaluation based on DSM-5 in preterm and term children were compared with Chi-square analysis and Fisher's Exact Test. Child age, mean age of mother, mean age of father, TELD-3, CAPES-TR, PSI-SF and PSDQ scores in children born preterm and term were compared with the Mann-Whitney U test because the data were not normally distributed. Spearman correlation analysis was used for non-normally distributed data while comparing the relationships between birth week of children, income level of family, education level of mother, CAPES-TR,

PSI Short form, DDST and TELD-3. Statistical significance was accepted as $p < 0.050$ at the 95% confidence interval.

RESULTS

The mean age of the preterm children when they were included in the study was 37.97 ± 3.62 months, and the mean age of the term children was 38.77 ± 3.28 months. The age range of both preterm and full term children ranged from 33 to 46 months. Regarding gender, 58.9% ($n=53$) of preterm children and 58.1% ($n=50$) of term children were male. There was no significant difference between the two groups for the mean age and gender ratios of the children ($p=0.087$ and $p=0.920$, respectively). The mean birth week was 32.96 weeks (minimum 25-maximum 36 weeks) in preterm children, and 38.79 weeks

(minimum 37-maximum 42 weeks) in term children. The hospital stay was 19.45 ± 14.55 days in preterm children and 7.09 ± 4.75 days in term children. Preterm children had a significantly longer hospital stay ($p < 0.001$). Birth weight was found to be 1981.22 grams (± 611.20) in preterm children and 3420 grams (± 482.09) in term children. Birth weight was significantly lower in preterm children ($p < 0.001$). Again, 77.8% ($n=70$) of the children born preterm were delivered by cesarean section, while the rate of delivery by cesarean section was found to be 58.1% ($n=50$) in term babies. Cesarean section rate was significantly higher in preterm children ($p=0.005$) (Table I). When the reasons for hospitalization in the neonatal period were examined, 54.4% ($n=49$) of the preterm children had respiratory distress syndrome, 40% ($n=36$) had transient tachypnea of the newborn, 2.2% ($n=2$) had congenital pneumonia, 2.2% ($n=2$) had indirect hyperbilirubinemia and 1.1% ($n=1$) due to early neonatal sepsis.

Table I: Sociodemographic Characteristics.

	Preterm n (%)	Term n (%)	p
Child Age (Month \pm SD)	37.97 (± 3.62)	38.77 (± 3.28)	0.087*
Birth week	32.96 (± 2.40)	38.79 (± 0.99)	0.000*
Birth weight (grams)	1981.22 (± 611.20)	3420.34 (± 482.09)	0.000*
Birth method			
Normal	20 (22.2)	36 (41.9)	0.005†
Cesarean	70 (77.8)	50 (58.1)	
Duration of hospital stay	19.45 (± 14.55)	7.09 (± 4.75)	0.000*
Child Gender			
Girl	37 (41.1)	36 (41.9)	0.920†
Boy	53 (58.9)	50 (58.1)	
Mean age of mother (year \pm sd)	32.03 (± 5.96)	31.96 (± 4.95)	0.956*
Mean age of father (year \pm sd)	36.94 (± 6.75)	35.58 (± 5.34)	0.212*
Educational Status of Mother			
Secondary School and below	61 (67.8)	41 (47.7)	0.007†
High School and above	29 (32.2)	45 (52.3)	
Educational Status of Father			
Secondary School and below	50 (55.6)	33 (38.4)	0.022†
High School and above	40 (44.4)	53 (61.6)	
Employment Status of Mother			
Works	11 (12.2)	22 (25.6)	0.023†
Does not work	79 (87.8)	64 (74.4)	
Employment Status of Father			
Works	82 (91.1)	81 (94.2)	0.436†
Does not work	8 (8.9)	5 (5.8)	
Monthly income level			
Minimum wage and below	43 (47.8)	24 (27.9)	0.007†
More than minimum wage	47 (52.2)	62 (72.1)	
Any siblings			
Yes	78 (86.7)	69 (80.2)	0.250†
No	12 (13.3)	17 (19.8)	
Who gives care for the child?			
Mother	86 (95.6)	76 (88.4)	0.078†
Baby-sitter or family elder	4 (4.4)	10 (11.6)	
What is the family structure like?			
Nuclear family	69 (76.7)	70 †(81.4)	0.442†
Extended family	21 (23.3)	16 (18.6)	

*:Mann Whitney U Test, †:Chi Square Tests,

Table II: Comparison of DDST and TELD-3 results in children born preterm and term.

	Preterm	Term	p
DDST personal social development*			
normal	71 (78.9)	80 (93.0)	0.007 [‡]
abnormal	19 (21.1)	6 (7.0)	
DDST language development*			
normal	60 (66.7)	79 (91.9)	0.000 [‡]
abnormal	30(33.3)	7 (8.1)	
DDST fine motor development*			
normal	86 (95.6)	84 (97.7)	0.683 [§]
abnormal	4 (4.4)	2 (2.3)	
DDST gross motor development*			
normal	83 (92.2)	85 (98.8)	0.065 [§]
abnormal	7 (7.8)	1 (1.2)	
TELD-3 Receptive Language [†]	31.45 (±8.41)	37.51(±4.84)	0.000
TELD-3 Expressive Language [†]	28.27 (±7.83)	35.72 (±5.57)	0.000

*:n(%), †:Mean ±SD, ‡:Pearson Chi-Square Test, §:Fisher's Exact Test, ||:Mann Whitney U Test, **DDST**: Denver Developmental Screening Test, **TELD-3**: Test of Early Language Development-Third Edition

When hospitalization indications of children born at term were examined, 44.2% (n: 38) had indirect hyperbilirubinemia, 23.3% (n: 20) had early neonatal sepsis, 16.3% (n: 14) had transient tachypnea of the newborn, and 16.3% (n: 14) had congenital pneumonia.

The mean age of the mothers was 32.03±5.96 years in preterm children, 31.96 ±4.95 years in term children. The mean age of the fathers was 36.94±6.75 years in preterm children, 35.58±5.34 years in term children. No significant difference was found between the two groups in the comparison made for the mean age of the mother and father (p-value mean age of mother p=0.956; for father p=0.212). Rates of having a secondary school or lower education level were significantly higher for both mothers and fathers in preterm children than term children (the was p=0.007 for mothers and p=0.022 for fathers). The rate of having a minimum wage or lower income level in the families of preterm children was significantly higher (p=0.007) (Table I).

According to the TELD-3 results, subtest scores evaluating both receptive and expressive language development in preterm children were significantly lower than in term children (p <0.001 for both receptive and expressive language skills). According to DDST results, the rate of children with abnormal development in preterm children regarding the personal social development was 21.1% (n:19), while this rate was 7.0% (n:6) in term children. Also, the rate of children with abnormal development in preterm children regarding the language development was 33.3% (n:30), while this rate was 8.1% (n:7) in term children.

The rates of children with abnormal development regarding personal social development and language development were significantly higher in preterm children (p=0.007 for personal social development and p<0.001 for language development, respectively). Besides, according to DDST results, although rates of abnormal development were higher in preterm children in fine motor and gross motor development than in term children, these differences were not statistically significant (p=0.683 for fine motor development, p<0.065 for gross motor development) (Table II).

Preterm and term children were compared according to the scores obtained from the CAPES-TR subscales filled by the mothers. CAPES-TR emotional problems (p=0.015), behavioral problems (p=0.009), and child adjustment subscale total score (p=0.005) were higher in preterm children (Table III). Comparisons were made for parenting self-efficacy, parenting stress, and parenting attitudes of the mothers. The mean score of the Parental Self-Efficacy Sub-Scale, which is included in the CAPES-TR scale and evaluates the self-confidence of the parents, was lower in mothers of preterm children (p<0.001). The mean PSI-SF Total Score, which evaluates the stress level of parents in child care, was higher in mothers of preterm children (p=0.005). There was no significant difference between the groups in the mean scores of the PSDQ democratic and authoritarian parenting subscales (p=0.159 and 0.408, respectively). The mean score of the permissive parenting subscale was higher in preterm children (p<0.001) (Table III).

A psychiatric interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was done for the psychiatric diagnostic evaluation of the children. A total of 26.7% (n:24) of preterm children were diagnosed with language disorder, while the rate of children diagnosed with language disorder in term children was 10.5% (n:9). The rate of diagnosis of global developmental delay was 18.9% (n:17) in preterm children, while it was 7.0% (n:6) in term children. The rates of having language disorder and global developmental delay diagnosis were higher in preterm children (p=0.006 for language disorder, p=0.019 for global developmental delay). Furthermore, while two children were diagnosed with ASD in the preterm group, no child was diagnosed with ASD in the term group. ASD was defined in a limited number of patients, thus, no statistical comparison was made between the two groups.

We also examined the relationship between CAPES-TR, PSI-SF, scores of TELD-3 and DDST subtests. There was a negative correlation between the difficulty score of CAPES-TR Child Adjustment subscale and TELD-3 receptive (r=-0.171, p=0.023) and expressive language (r=-0.232, p=0.002), DDST personal social (r=-0.252, p=0.001), language (r=-0.210, p=0.005), and fine motor development levels (r=-0.170, p=0.024). There was a positive correlation between the mean score of CAPES-TR Parental Self-Efficacy Sub-Scale and TELD-3 receptive (r=0.226, p=0.003) and expressive language

Table III: Comparison of CAPES-TR, PSI-SF, PSDQ scores in preterm and term children.

	Preterm	Term	p [†]
CAPES_TR Child Adjustment Subscale Emotional Problems*	3.00 (±2.53)	1.98 (±1.58)	0.015
CAPES_TR Child Adjustment Subscale Behavioral Problems*	27.65 (±11.51)	22.63 (±10.05)	0.009
CAPES_TR Child Adjustment Subscale Total Score*	30.65 (±13.12)	24.62 (10.99)	0.005
CAPES_TR Parental Self-Efficacy Subscale*	135.17 (±31.96)	160.33 (±20.30)	0.000
PSDQ democratic parenting attitude*	60.56 (±8.88)	62.82 (±7.15)	0.159
PSDQ authoritarian parenting attitude*	19.05 (±5.18)	18.62 (±5.28)	0.408
PSDQ permissive parenting attitude*	13.92 (±3.84)	11.27 (±3.50)	0.000
Parenting Stress Index-Short Form Total Score*	78.31 (±23.54)	68.18 (±18.02)	0.005

*:Mean±SD, †:Mann Whitney U Test, **CAPES_TR**: Child Adjustment and Parent Efficacy Scale, **PSDQ**: Parenting Styles and Dimensions Questionnaire–Short Version

Table IV: Correlations between birth week of children, income level of family, education level of mother, CAPES-TR, PSI Short form, DDST and TELD-3.

	1	2	3	4	5	6	7	8
1. CAPES_TR Child Adjustment Total Score								
2. CAPES_TR Parental Self-Efficacy Subscale	-0.666 *							
3. PSI Short Form Total Score	0.663*	-0.587*						
4. TELD-3 Receptive language	-0.171 (p=0.023)	0.226 (p=0.003)	-0.192 (p=0.011)					
5. TELD-3 Expressive Language	-0.232 (p=0.002)	0.229 (p=0.002)	-0.228 (p=0.002)	0.893*				
6. DDST personal social development	-0.252 (p=0.001)	0.227 (p=0.002)	-0.169 (p=0.025)	0.613*	0.607*			
7. DDST language development	-0.210 (p=0.005)	0.247 (p=0.001)	-0.189 (p=0.012)	0.876*	0.929*	0.655*		
8. DDST Fine Motor development	-0.170 (p=0.024)	0.221 (p=0.003)	-0.155 (p=0.041)	0.514*	0.452*	0.808*	0.552*	
9. Birth week	-194 (p=0.010)	0.357*	-155 (p=0.040)	0.369*	0.423*	0.178 (p=0.018)	0.468*	0.174 (p=0.021)
10. Monthly income level	-0.259 (p=0.001)	0.274 *	-0.212 (p=0.005)	0.227 (p=0.002)	0.316*	0.203 (p=0.007)	0.291*	0.127 (p=0.094)
11. Education level of mother	-0.196 (p=0.009)	0.237 (p=0.002)	-0.216 (p=0.004)	0.190 (p=0.011)	0.209 (p=0.005)	0.159 (p=0.035)	0.194 (p=0.010)	0.008 (p=0.918)

Spearman's correlation analysis, *p<0.001 statistically significant, **CAPES_TR**: Child Adjustment and Parent Efficacy Scale, **PSDQ**: Parenting Styles and Dimensions Questionnaire–Short Version, **DDST**: Denver Developmental Screening Test, **TELD-3**: Test of Early Language Development - Third Edition

(r=0.229, p=0.002), DDST personal social (r=0.227, p=0.002), language (r=0.247, p=0.001), and fine motor development levels (r=0.221, p=0.003). A negative correlation was found between PSI-SF and TELD-3 receptive (r=-0.192, p=0.011) and expressive language scores (r=-0.228, p=0.002) and DDST personal social (r=-0.169, p=0.025), language (r=-0.189, p=0.012), and fine motor development level (r=-0.155, p=0.041) (Table IV).

A positive correlation was determined between birth week, education level of mother, and monthly income level of family and CAPES-TR Parental Self-efficacy, TELD-3 receptive and expressive language scores, DDST personal social and language development level of all children. A negative correlation was found between birth week, education level of the mother, monthly income of the family, and CAPES-TR Child Adjustment Total Difficulty score and PSI-SF total score (p<0.050) (Table IV).

In our study, preterm children were also divided into two groups as early preterm (gestational age less than 32 weeks) and, moderate and late preterm (gestational age between 32 and 37 weeks). The statistical analysis were performed for the groups separately. Between these two groups, there was no significant difference in the comparisons made in terms of maternal education levels and monthly income levels (p=0.218 for maternal education level, p=0.737 for monthly income level). According to the DDST results, there was no statistically significant difference between the early preterm and, moderate/late preterm children in terms of personal social development, fine motor development and language development (p values for personal social development p=0.604, fine motor development p=0.292, language development p=1.000). Also according to the TELD-3 results, there was no statistically significant difference between groups (p-value for receptive

Table V: Comparisons made for children born early preterm and moderate or late preterm.

	Early Preterm	Moderate or Late Preterm	p
Educational Status of Mother*			
Secondary School and below	25 (75.8)	36 (63.2)	0.218 [‡]
High School and above	8 (24.2)	21 (36.8)	
Monthly income level*			
Minimum wage and below	15 (45.5)	28 (49.1)	0.737 [‡]
More than minimum wage	18 (54.5)	29 (50.9)	
DDST personal social development*			
normal	27 (81.8)	44 (77.2)	0.604 [‡]
abnormal	6 (18.2)	13 (22.8)	
DDST language development*			
normal	22 (66.7)	38 (66.7)	1.000 [‡]
abnormal	11 (33.3)	19 (33.3)	
DDST fine motor development*			
normal	33 (100)	53 (93.0)	0.292 [§]
abnormal	0 (0)	4 (7.0)	
CAPES_TR Child Adjustment Subscale Total Score [†]	31.54 (±13.21)	30.14 (±13.16)	0.503
CAPES_TR Parental Self-Efficacy Subscale [†]	131.60 (±33.82)	137.24 (±30.95)	0.456
Parenting Stress Index-Short Form Total Score [†]	76.66 (±21.03)	79.26 (±25.01)	0.706
TELD-3 Receptive Language [†]	31.87 (±8.59)	31.21 (±8.37)	0.807
TELD-3 Expressive Language [†]	28.84 (±7.18)	27.94 (±8.24)	0.613

*: n (%), †Mean ±SD, ‡: Chi Square Tests, §: Fisher's Exact Test, ||: Mann Whitney U Test

language: $p=0.807$, expressive language: $p=0.613$). In addition, no significant difference was found in terms of the CAPES-TR child adjustment subscale total score ($p=0.503$), the CAPES-TR parental self-efficacy subscale mean score ($p=0.456$) and the PSI-SF total mean score ($p=0.706$) were compared with early preterm and moderate/late preterm children (Table V).

DISCUSSION

Despite the improvements in neonatal intensive care units, infants and children born preterm are still likely to experience delays in cognitive, language, and motor development. In our study, in which we evaluated preterm and term children who were hospitalized in the neonatal intensive care unit, we had important findings such as language development and general development retardation, more emotional and behavioral problems, higher rate of diagnosis of neurodevelopmental disorder, decrease in parenting self-efficacy and increase in the level of parental stress in preterm children.

In our study, TELD-3 receptive language and expressive language scores were lower in preterm children and the rate of children with abnormal development in the areas of personal social development and language development from DDST subtests was higher in preterm children. As a result of DSM-5 based psychiatric interviews, both language disorder and global developmental delay diagnoses were higher in preterm children. In a review of studies evaluating language development in children with prematurity and low birth weight, retardation in both receptive and expressive language development of

children was found in four of 11 studies (15). In another study comparing neurodevelopmental problems, mental index scores and psychomotor index scores were found to be lower in preterm children (1). Literature and our study results show that preterm children are at risk of retardation in many areas of development.

In our study, CAPES-TR emotional problems, behavioral problems, and child adjustment subscale scores were higher in preterm children. In a study conducted in the Netherlands, more attention and behavior problems, retardation in cognitive development, and emotional regulation difficulties were determined in children born between 32nd-36th weeks compared to term children (16). In the same study based on the reports of both mothers and teachers, more attention problems and hyperactivity were reported in middle/late preterm children when they were 8 years old compared to term children (16). In a review in which 28 studies were examined, it was reported that psychiatric disorders, especially ADHD, were more common in preterm children, but there were inconsistent findings regarding the frequency of ASD (17). Considering the prevalence of emotional and behavioral problems in premature children, especially the evaluation of neurodevelopmental disorders and the arrangement of appropriate treatments in the early period may increase the capacity of these children to adapt to school against the risk of lowering their school success.

In our study, the mean score of the Parental Self-Efficacy Subscale was lower in mothers of preterm children. Preterm infants behave less reactive in parent-infant interactions. Moreover, they are observed as less rewarding social partners

in reciprocal relationships. Therefore, parents of preterm infants may experience difficulties in acquiring a sense of self-efficacy regarding parenting tasks more commonly (18). In addition, the mean PSI-SF Total Score was higher in the mothers of preterm children. Studies have reported higher levels of post-traumatic stress disorder, anxiety, and depression in the first 6 months, 5th and 7th years after birth in parents who gave preterm birth (19,20). Considering our findings and the literature, it can be commented that preterm birth carries risks not only for the child but also for the mental health of the parents and the quality of parenting. Therefore, while planning the intervention programs, the needs of the parent should be taken into account as well as the preterm child.

There was no significant difference in the mean scores of democratic and authoritarian parenting subscales, while the mean score of permissive parenting was higher in preterm children. Premature birth can cause stress for parents. It has been reported that having such a child negatively affects parenting behavior and the development of the child (21). In a meta-analysis, parents with preterm children were found to be more controlling than those with full-term births. Also, studies were reporting that mothers of preterm babies may start to behave less controlling after the first 6 months of life (22). In another meta-analysis, no difference was found in terms of attitude towards children (23). Compared with other studies, the different results regarding parental attitudes in our study can be explained by the heterogeneity of samples related to characteristics such as gestational age, birth weight, the age range of children, and socioeconomic status, compared to other studies.

Another finding of our study is that there is a negative correlation between CAPES-TR Child Adjustment total difficulty score and TELD-3 receptive and expressive language, DDST personal social, language, and fine motor development levels. In a study conducted with 386 preschool children, a negative correlation was found between language skills and behavioural problems (24). On the other hand, a positive correlation was reported between language skills and social skills. In a study examining the relationship between self-regulation skills and language development from the pre-school period to the second grade, it was reported that children who showed self-regulation skills in the early stages had better language and reading comprehension skills in the forthcoming periods (25). Considering their interrelationships, it is important to provide appropriate guidance for the solution of emotional and behavioral problems that may adversely affect their benefit from education, while planning education for developmental problems in preterm children.

There was a positive correlation between the mean score of the CAPES-TR Parental Self-Efficacy Subscale and the TELD-3 and DDST subtests (except for gross motor development). Besides, there was a negative correlation between PSI-SF Total Score and TELD-3 and DDST subtests (except for gross

motor development). The effects of the mother's stress and self-efficacy on language development can be explained by the fact that the interaction between mother and child is not good enough. In studies, delays in the language development of the child have been reported in cases in which the mother is less sensitive to the child (26). It has been reported that children of depressed mothers have fewer number of words at the age of 1-3 years compared to children of non-depressed mothers (27). It is important to evaluate the relationship with the mother in detail, especially while planning education for children with retardation in global and language development. In the presence of insufficient and inappropriate mother-child relationships, making the necessary arrangements will increase the benefit of special education.

In our study, the education level of the mother and the monthly income level of the family were lower in preterm children. Also a positive correlation was found between the birth week, education level of the mother, monthly income level of the family, TELD-3 receptive and expressive language scores, DDST personal social and language development level. Also, a negative correlation was found with the CAPES-TR Child Adjustment Total Difficulty Score. In a study in which 101 preterm and 44 term children at an average age of 12.5 years were evaluated, it was shown that low socioeconomic levels have a negative effect on the cognitive development of preterm adolescents (28). In another study investigating the effect of socioeconomic differences on the language development of premature children, language scores of premature children who were at a low socioeconomic level were found to be lower than those with a high socioeconomic level when they reached the age of 2 (29). In a study investigating the effect of mothers' education level on language, cognitive, and motor skills of 177 children who were born preterm, the Bayley Infant Development Scale was used at the corrected age of 20 months. The study found that as the education level of the mother increased, preterm babies got higher scores (30). Having a low socioeconomic level increases these risks even more for the preterm babies born with many risks. In this context, the necessity of supporting families with low socioeconomic levels who have preterm babies comes into sight.

In our study, no significant difference was found in comparisons made for socioeconomic factors, DDST, TELD-3 and CAPES-TR for children born early preterm and moderate and late preterm. In another study comparing the neurodevelopmental prognosis of late preterm children with early preterm children in the preschool period, no significant difference was found between the two groups in terms of personal social development and gross motor development. In the same study, it was reported that the mean scores of both groups were similar in terms of socioeconomic and cultural level scoring (31). The fact that no significant differences were found in the comparisons between children born early and late preterm in our study suggests that the family structure is mostly similar, and that parents at all levels continue to support their children.

Limitations:

In our study, focusing only on mother-child interactions rather than evaluating father-child interactions is among the limitations. Again, the fact that the study was single-centered can be considered as another limitation. In the future, multicenter studies that also evaluate father-child interaction will contribute to the literature.

CONCLUSION

Early evaluation of children born preterm, who are at risk of having problems in many developmental areas, can be helpful for interferences such as special education support. Early education support for those in need can reduce the difficulties they may experience during the school period. Our findings prove that the difficulties experienced in many areas by preterm children are also closely related to socioeconomic factors. Therefore, in addition to the special education support which will be planned for preterm children, it is also important to include initiatives for the social environment, especially parental education, into the process.

REFERENCES

- Woythaler MA, McCormick MC and Smith VC. Late preterm infants have worse 24-month neurodevelopmental outcomes than term infants. *Pediatrics* 2011;127:622-9.
- Fitzallen GC, Sagar YK, Taylor HG, Bora S. Anxiety and depressive disorders in children born preterm: a meta-analysis. *J Dev Behav Pediatr* 2021;42:154-62.
- Eves R, Mendonça M, Baumann N, Ni Y, Darlow BA, Horwood J, et al. Association of very preterm birth or very low birth weight with intelligence in adulthood: an individual participant data meta-analysis. *JAMA pediatr* 2021;175:e211058-e211058.
- Vigod SN, Villegas L, Dennis CL, Ross LE. Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. *BJOG* 2010;117:540-50.
- Potharst ES, Houtzager BA, van Wassenaer-Leemhuis AG, Kok JH, Koot HM, Last BF. Maternal and paternal perception of child vulnerability and behaviour problems in very preterm born children. *Infant and Child Development* 2015;24:489-505.
- Wightman A, Schluchter M, Drotar D, Laura A, Gerry TH, Nancy K, et al. Parental protection of extremely low birth weight children at age 8 years. *J Dev Behav Pediatr* 2007;28:317-26.
- Reijneveld SA, De Kleine MJK, van Baar AL, Kollee LAA, Verhaak CM, Verhulst FC, et al. Behavioural and emotional problems in very preterm and very low birth weight infants at age 5 years. *Arch Dis Child Fetal Neonatal Ed* 2006;91:423-28.
- Essex MJ, Klein MH, Cho E, Kalin NH. Maternal stress beginning in infancy may sensitize children to later stress exposure: effects on cortisol and behavior. *Biol Psychiatry* 2002;52:776-84.
- Muller-Nix C, Forcada-Guex M, Pierrehumbert B, Jaunin L, Borghini A, Ansermet F. Prematurity, maternal stress and mother-child interactions. *Early Hum Dev* 2004;79:145-58.
- Morawska A, Sanders MR, Haslam D, Filus A, Fletcher R. Child adjustment and parent efficacy scale: Development and initial validation of a parent report measure. *Australian Psychologist* 2014;49:241-52.
- Robinson CC, Mandleco B, Olsen SF, HartCHPerlmutter BF, Touliatos J, Holden GW. The parenting styles and dimensions questionnaire (PSDQ). *Handbook of family measurement techniques* 2001;3:319-21.
- Abidin R. (Ed.). *Parenting stress index: Professional manual* (3rd ed.). Lutz, FL: Psychological Assessment Resources, Inc 1995.
- Frankenburg WK, Dodds J and Archer P, Denver II: screening manual: Denver Developmental Materials, Incorporated 1990.
- Hresko WP, Reid DK and Hammill DD. *Test of Early Language Development (TELD)*. Third ed. PRO-ED, Austin: Texas 1999.
- Zerbeto AB, Cortelo FM and C Filho ÉB. Association between gestational age and birth weight on the language development of Brazilian children: a systematic review. *J Pediatr (Rio J)* 2015;91:326-32.
- van Baar AL, Vermaas J, Knots E, de Kleine MJK, Soons P. Functioning at school age of moderately preterm children born at 32 to 36 weeks' gestational age. *Pediatr* 2009;124:251-7.
- de Jong M, Verhoeven M and Van Baar AL. School outcome, Cognitive functioning and behavior problems in moderate and late preterm children and adults: A Review. *Semin Fetal Neonatal Med* 2012;17:163-9.
- Harrison MJ and Magill-Evans J. Mother and father interactions over the first year with term and preterm infants. *Res Nurs Health* 1996;19:451-59.
- Feeley N, Hayton B, Gold I, Zerkowitz P. A comparative prospective cohort study of women following childbirth: mothers of low birthweight infants at risk for elevated PTSD symptoms. *J Psychosom Res* 2017;101:24-30.
- Barkmann C, Helle N and Bindt C. Is very low infant birth weight a predictor for a five-year course of depression in parents? A latent growth curve model. *J Affect Disord* 2018;15:415-20.
- Singer LT, Fulton S, Kirchner HL, Eisengart S, Lewis B, Short E, et al. Longitudinal predictors of maternal stress and coping after very low-birthweight birth. *Arch Pediatr Adolesc Med* 2010;164:518-24.
- Toscano C, Soares I and Mesman J. Controlling Parenting Behaviors in Parents of Children Born Preterm: A Meta-Analysis. *J Dev Behav Pediatr* 2020;230-41.
- Bilgin A and Wolke D. Maternal Sensitivity in Parenting Preterm Children: A Meta-analysis. *Pediatrics* 2015;136:177-93.
- Qi CH, Van Horn ML, Selig JP, Kaiser AP. Relations between language skills and problem behaviour in preschool children. *Early Child Development and Care* 2019;1-12.
- Skibbe LE, Montroy JJ, Bowles RP, Morrison FJ. Self-regulation and the development of literacy and language achievement from preschool through second grade. *Early Child Res Q* 2019;46:240-51.
- Delaney EM and Kaiser AP. The effects of teaching parents blended communication and behavior support strategies. *Behavioral Disorders* 2001;26:93-116.
- Pan BA, Rowe ML, Singer JD, Snow CE. Maternal correlates of growth in toddler vocabulary production in low-income families. *Child Dev* 2005;76:763-82.
- Schneider LA, Burns NR, Giles LC, Higgins RD, Nettelbeck TJ, Ridding MC, et al. Cognitive abilities in preterm and term-born adolescents. *J Pediatr* 2014;165:170-7.

29. Wild KT, Betancourt LM, Brodsky NL, Hurt H. The effect of socioeconomic status on the language outcome of preterm infants at toddler age. *Early Hum Dev* 2013;89:743-6.
30. Patra K, Greene MM, Patel AL, Meier P. Maternal Education Level Predicts Cognitive, Language, and Motor Outcome in Preterm Infants in the Second Year of Life. *Am J Perinatol* 2016;33:738-44.
31. Akar S, Kavuncuođlu S, Aldemir ES, Öztüregen E, Arslan G. Okul öncesi dönemde geç prematürelere nörogelişimselprognozunun erken prematürelere karşılaştırılması: Prospektif Kohort Çalışması. *İKSSTD* 2020;12:159-68.

Determination of the Relationship Between Self-Esteem and Social Anxiety in Adolescents with Burns

Yanığı Olan Adölesanlarda Benlik Saygısı ile Sosyal Anksiyete Arasındaki İlişkinin Belirlenmesi

Derya SULUHAN¹, Ecem SAĞIROĞLU², Sabri DEMİR³, Dilek YILDIZ¹, Merve ONAT⁴, Emrah ŞENEL³

¹Gülhane Faculty of Nursing, University of Health Sciences Turkey, Ankara, Turkey

²Department of Pediatric Surgery Intensive Care, Ankara Bilkent City Hospital, Ankara, Turkey

³Department of Pediatric Surgery, Ankara Bilkent City Hospital, Ankara, Turkey

⁴Department of Child Psychiatry and Diseases, Ankara Bilkent City Hospital, Ankara, Turkey



ABSTRACT

Objective: Burns are complex, traumatic incidents including significant morbidity and impairment of psychological, emotional, and physical well-being. This study aimed to determine the relationship between self-esteem and social anxiety in adolescents with burns.

Material and Methods: A cross-sectional, descriptive research design was used. The research was carried out in the 12-bed Pediatric Burn Center with 86 adolescents. The data collection form, Rosenberg Self-Esteem Scale and the Social Anxiety Scale for Children was used. Comparisons were made at the $p<.05$ significance level for statistical analyses.

Results: Hot liquid (31.4%), chemicals (22.1%), flames (17.4%), electricity (16.3%), and contact with hot objects (12.8%) were burn factors. It was determined that 81.4% of the participants had a scar/mark. The total body surface area of the burn was determined as 1%-10% (61.6%), 10%-25% (32.6%), $\geq 50\%$ (3.5%), and 25%-50% (2.3%). The multiple linear regression model established according to the effects of self-esteem scores and socio-demographic variables on children's social anxiety was statistically significant ($F(20.65)=2.384$, $p<.05$). In the study, 42.6% of the variance in the scores on the social anxiety scale for children was explained by self-esteem scores and socio-demographic variables. Self-esteem scores predicted children's social anxiety scores statistically positively and significantly ($B=4.413$, $t=4.139$, $p<.05$).

Conclusion: The study revealed that there was relation between low self-esteem and high social anxiety in adolescents with burns in line with our study question, while there is no relation between characteristics of children and burn history in children.

Key Words: Adolescent, Burn, Self-esteem, Social anxiety



0000-0002-7358-7266 : SULUHAN D
0000-0002-1403-9569 : SAĞIROĞLU E
0000-0003-4720-912X : DEMİR S
0000-0001-8757-4493 : YILDIZ D
0000-0002-1970-672X : ONAT M
0000-0002-0383-4559 : ŞENEL E

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 Ankara City Hospital, Clinical Research Ethics Committee No. 2 (dated 06/07/2022 and decision number E2-22-2056).

Contribution of the Authors / Yazarların katkısı: **SULUHAN D:** 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. **SAĞIROĞLU E:** 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. **DEMİR S:** Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar, Organizing, supervising the course of progress and taking the responsibility of the research/study. **YILDIZ D:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Reviewing the article before submission scientifically besides spelling and grammar. **ONAT M:** 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. **ŞENEL E:** Organizing, supervising the course of progress and taking the responsibility of the research/study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf yazım şekli : Suluhan D, Sağiroğlu E, Demir S, Yıldız D, Onat M and Şenel E. Determination of the Relationship Between Self-Esteem and Social Anxiety in Adolescents With Burns. Turkish J Pediatr Dis 2023;17: 243-249.

Additional information / Ek bilgi: This study was presented as an oral presentation at the 25th Congress of Pediatric Surgery Nursing on November 2-5, 2022 in Kuşadası.

Correspondence Address / Yazışma Adresi:

Derya SULUHAN
Gülhane Faculty of Nursing, University of Health Sciences Turkey, Ankara, Turkey
E-posta: dsuluhan@gmail.com

Received / Geliş tarihi : 18.02.2023

Accepted / Kabul tarihi : 28.03.2023

Online published : 10.04.2023

Elektronik yayın tarihi

DOI: 10.12956/tchd.1254730

ÖZ

Amaç: Yanıklar, önemli morbidite ve psikolojik, duygusal ve fiziksel refahın bozulması dahil olmak üzere karmaşık, travmatik olaylardır. Bu çalışma, yanık olan adölesanlarda benlik saygısı ile sosyal anksiyete arasındaki ilişkiyi belirlemeyi amaçlamıştır.

Gereç ve Yöntemler: Kesitsel, tanımlayıcı bir araştırma tasarımı kullanılmıştır. Araştırma, 86 adölesan ile 12 yataklı Pediatrik Yanık Merkezinde gerçekleştirildi. Veri toplama formu, Rosenberg Benlik Saygısı Ölçeği ve Çocuklar için Sosyal Anksiyete Ölçeği kullanılmıştır. İstatistiksel analizler için karşılaştırmalar $p<0.05$ anlamlılık düzeyinde yapılmıştır.

Bulgular: Sıcak sıvı (%31.4), kimyasallar (%22.1), alevler (%17.4), elektrik (%16.3) ve sıcak cisimlerle temas (%12.8) yanık faktörleriydi. Katılımcıların %81.4'ünde skar/iz olduğu belirlenmiştir. Yanık toplam vücut yüzey alanı sırasıyla, %1-%10 (%61.6), %10-%25 (%32.6), \geq %50 (%3.5), ve %25-%50 (%2.3). Benlik saygısı puanlarının ve sosyo-demografik değişkenlerin çocukların sosyal kaygısı üzerindeki etkilerine göre oluşturulan çoklu doğrusal regresyon modeli istatistiksel olarak anlamlıydı ($F(20.65)=2.384$, $p<.05$). Çalışmada, çocuklar için sosyal anksiyete ölçeğindeki puanlardaki varyansın %42.6'sı benlik saygısı puanları ve sosyo-demografik değişkenler ile açıklanmıştır. Benlik saygısı puanları, çocukların sosyal kaygı puanlarını istatistiksel olarak olumlu ve anlamlı olarak öngörmüştür ($B=4.413$, $t=4.139$, $p<.05$).

Sonuç: Çalışmamız, çalışma sorumuz doğrultusunda yanık olan adölesanlarda düşük benlik saygısı ile yüksek sosyal anksiyete arasında ilişki olduğunu, çocuklarda yanık öyküsü ile çocukların özellikleri arasında ilişki olmadığını ortaya koymuştur.

Anahtar Sözcükler: Adölesan, Yanık, Benlik saygısı, Sosyal anksiyete

INTRODUCTION

Burn injuries occur following direct contact with surfaces, fire, hot liquids, chemicals, gases, electricity, or radiation, which cause tissue damage inside or outside the body (1). While burns can be seen as simple injuries, they can turn into a life-threatening trauma that causes physical, psychological, sociological, and economic problems depending on their degree (2). Although burns lead to a trauma that affects individuals of all age groups, they are more common in children. They are the fifth most common cause of non-fatal childhood trauma (3). Every day, around 300 children aged between 0 and 19 are treated in emergency services due to burn-related injuries (6).

Burn injuries may suddenly disrupt normal life in children. They may threaten the health and body integrity of the child and may require prolonged hospitalization, multiple surgical procedures, intense and long-term physical therapy, and lifelong rehabilitation. Children are likely to have permanent scars and, in some cases, limited functionality (7). Self-esteem, which plays a critical role in the development of adolescents, is how the individual feels in various components of self-concept, such as social identity, personal identity, and body image (8). Self-esteem has a huge impact on health. It has been proven that individuals with low self-esteem cannot cope with difficulties in daily life and that they face negative psychological and physical consequences (9-11).

Social anxiety is one of the main variables that affect the child's social interaction process and is characterized by fear of negative evaluation and discomfort/distress in social environments (12). Social relations are highly important for the child's emotional development. Burn marks in visible areas are associated with social anxiety, isolation, exclusion, and avoidance. Therefore, visible burn scars may hinder the individual's social activities and lead to social isolation (11, 13, 14). Accordingly, this study was planned to determine the relationship between self-esteem and social anxiety in adolescents with burns.

MATERIALS and METHODS

A cross-sectional, descriptive research design was used. In this study, it was aimed to determine the relationship between self-esteem and social anxiety in adolescents with burns.

Research population and sample

The population of the study consisted of patients admitted for burn treatment to Ankara City Hospital, Children's Hospital Pediatric Burn Center. The research was carried out in the 12-bed Pediatric Burn Center of Ankara City Hospital Children's Hospital. The sample of the study consisted of 86 children who met the inclusion criteria and were selected by using the slice sampling method between the dates of the study.

Inclusion criteria for the study were determined as volunteering to participate in the study, admission to the Ankara City Hospital, Children's Hospital Pediatric Burn Center for burn treatment, being between the ages of 12 and 18, and not having any mental or developmental disorders. The exclusion criteria were being a migrant child and not volunteering to participate in the study.

Research questions

Is there a relationship between self-esteem and social anxiety in adolescents with burns?

Is there a relationship between the independent variables of adolescents with burns and their social anxiety?

Data collection tools

A data collection form prepared by the researcher consisted of a total of 25 questions about age, gender, number of siblings, family type, place of residence, income status, age of parents, job, education level, burn characteristics, and the effects of the burn on the adolescent. The Rosenberg Self-Esteem Scale was used to determine the self-esteem levels of the adolescents,

and the Social Anxiety Scale for Children was used to determine their social anxiety levels.

The data collection form

This form includes a total of 25 questions about some socio-demographic characteristics of adolescents with burns, such as age, gender, number of siblings, birth order, the place where the family lives, family type, mother's age, education level, and job, father's age, education level, and job, and school grade; information about the burn, such as age at burn injury, the burn site, degree of the burn, the total body surface area of the burn, having received education-consultancy on burn care at discharge, having a burn-related amputation, and having a visible scar after the burn; information about the effects of the burn on the adolescent, such as the status of having a school break, changes in daily life due to burns/treatment process, changes in the attitudes and behaviors of family/friends during the illness/treatment, and the status of receiving support from a psychologist or psychiatrist.

The Rosenberg Self-Esteem Scale (RSES): This scale was developed by Rosenberg to assess self-esteem, especially in the adolescent age group. It consists of ten negative or positive multiple-choice items with four options, namely 'very true', 'true', 'false', and 'very false'. Total scores are interpreted as follows: 0-1, high self-esteem; 2-4, moderate self-esteem; 5-6, low self-esteem. Çuhadaroğlu performed the validity and reliability study of the scale in our country (15). In the study by Çuhadaroğlu, the validity and reliability coefficients were found as 0.71 and 0.75, respectively. Cronbach's alpha internal consistency coefficient was 0.69 in our study.

Social Anxiety Scales for Children (SASC): This scale was developed by La Greca et al. and its Turkish validity and reliability study was conducted by Demir et al. (12). It is a 5-point Likert-type self-report scale and is one-dimensional. It is evaluated on the basis of total scores. The scores that can be obtained from the scale are between 18 and 90, and the higher the scores are, the higher the level of social anxiety is. In the study by Demir, Cronbach's α was found to be 0.81, and it was found as 0.87 in our study.

Implementation of the research

The Data Collection Form, the Rosenberg Self-Esteem Scale, and the Social Anxiety Scale for Children were applied to the children who met the inclusion criteria and volunteered to participate in the study in Ankara City Hospital, Children's Hospital Pediatric Burn Center after their consent and parents' approval were obtained.

Statistical Analysis

The data were analyzed on the SPSS 24.0 (IBM, Armonk, NY: IBM Corp.) software package. Descriptive statistics were presented using frequency and percentage distribution

values. Multiple linear regression analysis method was used to determine the relationship between the variables. The normality of the data was examined with skewness and kurtosis values. The skewness and kurtosis values of the scale scores were between ± 1.5 , which showed that the data had a normal distribution (16, 17). For multiple linear regression analysis, each of the sociodemographic variables was transformed into two categories (1 and 0), and the reference values of each group were indicated in the linear regression table. Comparisons were made at the $p < .05$ significance level for statistical analyses.

Ethical permissions

The study was approved by Ankara City Hospital, Clinical Research Ethics Committee No. 2 (dated 06/07/2022 and decision number E2-22-2056). Participation in the study was on a voluntary basis. An informed consent forms were obtained from participants and their parents.

RESULTS

A total of 86 adolescents receiving treatment for burns were included in the study. Of the participants, 67.4% were male, and 83.7% had a nuclear family. It was found that 37.2% of the mothers were primary school graduates, 83.7% did not have a job, 33.7% of the fathers were primary school graduates, and 77.9% had a job. Also, 66.3% of the participants had less income than their expenses. According to the findings, 64% of the participants had a school break, 53.5% stated that having a school break had no effect, 64% thought that it had an effect on daily life, and 62.8% thought that there was no change in the attitudes and behaviors of family/friends. The majority of the participants (80.2%) stated that they did not receive psychiatrist/psychologist support. The distribution of the burn factors was found as hot liquid (31.4%), chemicals (22.1%), flames (17.4%), electricity (16.3%), and contact with hot objects (12.8%), respectively. It was determined that 81.4% of the participants had a scar/mark while 18.6% did not. When analyzed by site, 10.5% of the participants had a burn scar on the face/neck, 31.4% on the body/back, 30.2% on the arms, 26.7% on the hands, 30.2% on the legs, 20.3% on the feet, and 5.8% on the genitals. The distribution of the degree of the burn was found as second-degree (66.3%), third-degree (23.3%), and first-degree (10.5%), respectively. The distribution of the total body surface area of the burn was determined as 1%-10% (61.6%), 10%-25% (32.6%), $\geq 50\%$ (3.5%), and 25%-50% (2.3%), respectively. Finally, it was determined that 96.5% of the participants did not have an amputation, while 3.5% of them had been amputated (Table I).

Descriptive statistics for the self-esteem scale and the social anxiety scale for children are given in Table II. The scores on the total RSES ranged from 0 to 6, with the mean score being 1.47

Table I : The descriptive characteristics of the participants and the family (n=86).

Variable	n (%)
Gender	
Female	28 (32.6)
Male	58 (67.4)
Location	
City	36 (41.9)
District	43 (50)
Village	7 (8.1)
Family Type	
Nuclear family	72 (83.7)
Extended family	14 (16.3)
Education state of mother	
Illiterate	8 (10.5)
Primary school	32 (37.2)
Secondary school	22 (25.6)
High school	19 (22.1)
University	4 (4.7)
Working state of mother	
No	72 (83.7)
Yes	14 (16.3)
Education state of father	
Illiterate	5 (5.8)
Primary school	29 (33.7)
Secondary school	22 (25.6)
High school	25 (29.1)
University	5 (5.8)
Working state of father	
No	19 (22.1)
Yes	67 (77.9)
Income status	
Income less than expenses	57 (66.3)
Income equals expense	27 (31.4)
Income higher than expenses	2 (2.3)
Take a break from school	
No	31 (36.1)
Yes	55 (64)
Effect of school break	
No	46 (53.5)
Yes	40 (46.5)
Daily life effects	
No	31 (36)
Yes	55 (64)
Attitude and behavior changes to family/friends	
No	54 (62.8)
Yes	32 (37.2)
Psychiatry/psychologist support	
No	69 (80.2)
Yes	17 (19.8)
Burn factor	
Warm Liquid	27 (31.4)
Fire	15 (17.4)
Electric	14 (16.3)
Chemical	19 (22.1)
Contact with hot objects	11 (12.8)
Condition of scar/mark	
No	16 (18.6)
Yes	70 (81.4)

Variable	n (%)
Face / neck	
No	77 (89.5)
Yes	9 (10.5)
Body / back	
No	59 (68.6)
Yes	27 (31.4)
Arms	
No	60 (69.8)
Yes	26 (30.2)
Hands	
No	63 (73.3)
Yes	23 (26.7)
Legs	
No	60 (69.8)
Yes	26 (30.2)
Feet	
No	66 (76.7)
Yes	20 (23.3)
Genitals	
No	81 (94.2)
Yes	5 (5.8)
Degree of burn	
Linear	9 (10.5)
Second degree	57 (66.3)
Third degree	20 (23.3)
The total surface area of the burn	
1%-10%	53 (61.6)
10%-25%	28 (32.6)
25%-50%	2 (2.3)
50% and above	3 (3.5)
Amputation	
No	83 (96.5)
Yes	3 (3.5)

Table II: The RSES and SASC scores in adolescents with burns

Scale	References (min-max)	min	max	mean	SD	Skewness	Kurtosis
RSES total	0-6	0	6	1.47	1.48	1.236	1.233
SASC total	18-90	18	84	42.47	14.09	0.566	0.096

RSES: Rosenberg Self-Esteem Scale, **SASC:** Social Anxiety Scales for Children, **SD:** Standard Deviation, **min:** minimum, **max:** maximum

(SD=1.48). The total SASC scores ranged between 18 and 84, with the mean score being 42.47 (SD=14.09).

The multiple linear regression model established according to the effects of self-esteem scores and socio-demographic variables on children's social anxiety was statistically significant ($F(20.65)=2.384, p<.05$). The R square value expresses how much of the variance in the predicted variable is explained by independent variables (Pallant, 2007). In the study, 42.6% of the variance in the scores on the social anxiety scale for children was explained by self-esteem scores and socio-demographic variables. Self-esteem scores predicted children's social anxiety scores statistically positively and significantly ($B=4.413, t=4.139, p<.05$). A 1-unit increase in self-esteem scores resulted in a 4.413-unit increase in children's social anxiety scores (Table III).

Table III: Multiple linear regression of variables associated with SASC score

	B	Std. Error	Beta	t	p
Constant	32.273	5,669		5.693	.000
RSES total	4.413	1.066	0.463	4.139	.000
Gender (ref: male)	0.751	4.177	0.025	0.18	0.858
Education state of mother (ref: primary school)	4.11	3.099	0.142	1.326	0.189
Working state of mother (ref: no)	4.834	3.739	0.131	1.293	0.201
Education state of father (ref: primary school)	3.27	3.254	0.11	1.005	0.319
Working state of father (ref: no)	7.61	3.955	0.216	1.924	0.059
Income (ref: income less than expenses)	0.579	3.606	0.02	0.16	0.873
Take a break from school (ref: no)	-3.696	4.154	-0.126	-0.89	0.377
Effect of school break (ref: yes)	2.195	3.753	0.078	0.585	0.561
Daily life effects (ref: yes)	-2.506	3.794	-0.086	-0.66	0.511
Attitude and behavior changes to family/friends (ref: yes)	1.773	3.613	0.061	0.491	0.625
Psychiatry/psychologist support (ref: yes)	-6.635	4.059	-0.189	-1.635	0.107
Burn factor (ref: warm liquid)	-1.96	4.131	-0.065	-0.474	0.637
Condition of scar/mark (ref: yes)	-4.366	4.002	-0.121	-1.091	0.279
Face / Neck (ref: yes)	2.454	4.898	0.054	0.501	0.618
Body / Back (ref: yes)	5.019	3.311	0.166	1.516	0.134
Arms (ref: yes)	1.93	3.997	0.063	0.483	0.631
Degree of burn (ref: third degree)	-1.595	4.484	-0.048	-0.356	0.723
The total surface area of the burn (ref: 10% and above)	-1.158	3.643	-0.04	-0.318	0.752
Amputation (ref: yes)	3.211	8.978	0.042	0.358	0.722

RSES: Rosenberg Self-Esteem Scale, **SASC:** Social Anxiety Scales for Children. $F_{(20,65)}=2.384$, $p=0.004$, $R=0.651$, $R^2=0.426$, **β :** Beta coefficient, **R^2 :** coefficient of determination

In other words, an increase in self-esteem increased children's social anxiety scores. The effect of sociodemographic variables on children's social anxiety scores was not significant ($p>.05$).

DISCUSSION

Burn injuries cause life-changing events for both children and their families (18,19). The European Burns Association recommends that health professionals in burn centers should provide the treatment of all aspects of burns and that burn centers should provide comprehensive and continuous burn care, including both physical and psychosocial care in patients with burns (20). In our study, we evaluated the relationship between self-esteem and social anxiety in adolescents with burns. Accordingly, the outcomes of this study indicated that adolescents with burns suffered from psychosocial problems such as low self-esteem and social anxiety.

Numerous studies have investigated the clinical characteristics of children with burns (20-27). The demographic characteristics and burn history of children with burns were similar to our results. Santos et al. (20) reported that burn injuries were found higher among boys and that most burns were due to hot liquid or objects in Portugal. In studies by Han et al. (21) conducted in Central China and by Nthumba (24) conducted in sub-Saharan Africa, it was shown that boys had higher burn

injuries than girls. A review study indicated that burns were more prevalent among low socioeconomic populations and undeveloped regions (27). A study by Öztörün indicated that the majority of patients with burns were male children and that the primary reason for burns was hot liquid (26). Moreover, in our study children with burns had low income families. Smolle et al. (27) emphasized that burn injuries were more common in populations with lower socioeconomic status. These results are important as they show the burn risks of healthy children to health professionals.

When the cases were examined according to the total body burn percentages, the most common type was a burn area of 10%-25%. Similar to the study of Chen, our study showed that the mean percentage of total damaged body surface area was 32.6% (25). The burn center where this study was carried out admitted more complicated children with burns as it is an important burn center of Ankara in Turkey.

Burns are complex, traumatic incidents including significant morbidity and impairment of psychological, emotional, and physical well-being (27). Scars are common in burn cases. They require comprehensive treatment and care. This long-term treatment causes impairment of psychological and emotional well-being (28). Russell et al. (10) reported that poorer self-concept was associated with emotional problems in children with burns. In two studies in which the self-esteem

of children and adolescents who had experienced a burn injury were determined by Russell et al. (10) and Riobueno-Naylor et al. (29), appearance concerns related with self-esteem were associated with lower self-worth. Another impairment of psychological well-being is anxiety which is most commonly reported as psychological problem in children and adolescents following a burn injury. Rimmer et al. (30) indicated that children reported high anxiety levels.

In our study, the adolescents with burn injuries had social anxiety. Moreover, the adolescents who had low self-esteem had social anxiety and 42.6% of the variance in scores obtained from the social anxiety scale for children was explained by self-esteem scores in this study. According to Hall, physical appearance could be associated with social anxiety due to societal stresses on attractiveness (31). In our study, four of five children had burn scars and near half of the children, it was stated seeing changes in family/friend attitudes and behaviors after burn injury. Given these results, health professionals need to be aware of the psychological outcomes of adolescents with burns.

CONCLUSION

In conclusion, we found that there was relation between low self-esteem and high social anxiety in adolescents with burns in line with our study question, while there is not a relation between characteristics of children and burn history in children. Health professionals should be aware of the fact that burn management of adolescents requires a comprehensive approach provided by members of multidisciplinary team including a pediatric surgeon, pediatric nurse, psychiatrist and psychologist. Healthcare professionals should consult to adolescents who low self-esteem and high social anxiety to psychiatrist and psychologist. Thanks to this multidisciplinary team approaches holistic care will be ensured to adolescents in burn unit or centers.

REFERENCES

1. Wanjeri JK, Kinoti M, Olewe THAM. Risk factors for burn injuries and fire safety awareness among patients hospitalized at a public hospital in Nairobi, Kenya: A case control study. *Burns* 2018; 44:962-8.
2. Sarıgöl OY, Sütsünbuloğlu E. Yanık yaraları ve hemşirelik bakımı. *Türkiye Klinikleri J Surg Nurs-Special Topics* 2017; 3:216-23.
3. World Health Organization. Erişim Tarihi: 29 Ekim 2022. Available from: <https://www.who.int/news-room/fact-sheets/detail/burns>.
4. American Burn Association. Erişim tarihi: 20 Ekim 2022. Available from: Education – American Burn Association (ameriburn.org)
5. Türkiye İstatistik Kurumu. Erişim tarihi: 18 Ekim 2022. Available from: <http://www.tuik.gov.tr/PreHaberBultenleri.do?id=24572>.
6. National Safe Kids Company. Erişim Tarihi: 18 Eylül 2022. Available from: <https://www.safekids.org/embed/1829>
7. Bakker A, Maertens KJ, Van Son MJ, Van Loey NE. Psychological consequences of pediatric burns from a child and family perspective: a review of the empirical literature. *Clin Psychol Rev* 2013; 33:361-71.
8. Kim LM, Manion AB. Improving self-esteem and building self-confidence in adolescent mothers: implementation of self-efficacy-focused activity sessions. *J Psychosoc Nurs Ment Health Serv* 2019; 57:11-5.
9. Mehrabi A, Falakdami A, Mollaei A, Takasi P, Ghorbani VP, Jafari H, et al. A systematic review of self-esteem and related factors among burns patients. *Ann Med Surg (Lond)* 2022; 84:104811.
10. Russell W, Robert RS, Thomas CR, Holzer CE, Blakeney P, Meyer WJ. Self perceptions of young adults who survived severe childhood burn injury. *J Burn Care Res* 2013; 34:394-402.
11. Gorbani A, Rezaiee Moradali M, Shabanloei R. Relationship between self-esteem and perceived social support in burn patients in Sina Hospital of Tabriz. *Nurs Open* 2021; 8:1194-1200.
12. Demir T, Demir ED, Türksoy N, Özmen E, Uysal Ö. Çocuklar için sosyal anksiyete ölçeğinin geçerliliği ve güvenilirliği. *Düşünen Adam* 2000; 13:42-8.
13. Jain M, Khadilkar N, De Sousa A. Burn-related factors affecting anxiety, depression and self-esteem in burn patients: an exploratory study. *Ann Burns Fire Disasters* 2017; 30:30-4.
14. do Amaral Zorita L, Blanes L, Francescato Veiga D, da Silva Augusto F, Masako Ferreira L. Health-related quality of life and self-esteem among burn patients. *Wounds: a Compendium of Clinical Research and Practice*. *Wounds* 2016; 28:27-34.
15. Çuhadaroğlu F. Adölesanlarda Benlik Saygısı, Hacettepe Üniversitesi Tıp Fakültesi Psikiyatri Ana Bilim Dalı, Uzmanlık Tezi, Ankara, 1986.
16. Pallant J. SPSS Survival Manual: A step by step guide to data analysis using SPSS for Windows (Version 12). 2nd ed. New York: Open University Press, 2007.
17. Tabachnick BG, Fidell LS. Using Multivariate Statistics. 6th ed. Boston: Pearson, 2013.
18. Patterson KN, Beyene TJ, Lehman K, VerLee SN, Schwartz D, et al. Evaluating effects of burn injury characteristics on quality of life in pediatric burn patients and caregivers. *Burns* 2023; S0305-4179(23)00011-6.
19. European Burns Association (EBA): European practice guidelines for burn care – Minimum level of burn care provision in Europe, Version 4, Barcelona/Spain 2017; 1-147.
20. Santos JV, Viana J, Oliveira A, Ramalho A, Sousa-Teixeira J, et al. Hospitalisations with burns in children younger than five years in Portugal, 2011-2015. *Burns* 2019; 45:1223-30.
21. Han D, Wei Y, Li Y, Zha X, Li R, et al. epidemiological and clinical characteristics of 5,569 pediatric burns in Central China from 2013 to 2019. *Front Public Health* 2022; 10:751615.
22. Zheng Y, Lin G, Zhan R, Qian W, Yan T, Sun L, et al. Epidemiological analysis of 9,779 burn patients in China: An eight-year retrospective study at a major burn center in southwest China. *Exp Ther Med*. 2019; 17:2847-54.
23. Dinesh A, Polanco T, Khan K, Ramcharan A, Engdahl R. Our inner-city children inflicted with burns: A retrospective analysis of pediatric burn admissions at Harlem Hospital, NY. *J Burn Care Res* 2018; 39:995-9.
24. Nthumba PM. Burns in sub-Saharan Africa: A review. *Burns* 2016; 42:258-66.

25. Chen B, Hou J, Song H, Gao Q, Xu M, Wang F, et al. Using rational strategies for children's scars based on more than 5 years assessment after burn. *Burns* 2021; 47:190-7.
26. Öztörün Cİ, Demir S, Azılı MN, Şenaylı A, Livanelioğlu Z, Şenel E. The outcomes of becoming a pediatric burn center in Turkey. *Ulus Travma Acil Cerrahi Derg* 2016; 22:34-9.
27. Smolle C, Cambiaso-Daniel J, Forbes AA, Wurzer P, Hundeshagen G, Branski LK, et al. Recent trends in burn epidemiology worldwide: A systematic review. *Burns* 2017; 43:249-57.
28. Simons M, Kimble R, McPhail S, Tyack Z. The longitudinal validity, reproducibility and responsiveness of the Brisbane Burn Scar Impact Profile (caregiver report for young children version) for measuring health-related quality of life in children with burn scars. *Burns* 2019; 45:1792-809.
29. Riobueno-Naylor A, Williamson H, Canenguez K, Kogosov A, Drexler A, Sadeq F, et al. Appearance concerns, psychosocial outcomes, and the feasibility of implementing an online intervention for adolescents receiving outpatient burn care. *J Burn Care Res* 2021; 42:32-40.
30. Rimmer RB, Bay RC, Sadler IJ, Alam NB, Foster KN, Caruso DM. Parent vs burn-injured child self-report: contributions to a better understanding of anxiety levels. *J Burn Care Res* 2014; 35:296-302.
31. Hart TA, Flora DB, Palyo SA, Fresco DM, Holle C, Heimberg RG. Development and examination of the social appearance anxiety scale. *Assessment* 2008; 15:48-59.

A Novel Double Homozygous *BTD* Gene Mutation in a Case of Profound Biotinidase Deficiency

Ağır Biotinidaz Eksikliği Olgusunda Yeni Çift Homozigot *BTD* Gen Mutasyonu

Kübra DEVECİ¹, Halil Tuna AKAR², Yılmaz YILDIZ², R. Köksal ÖZGÜL^{2,3}

¹ Department of Pediatrics, Hacettepe University Medical School, Ankara, Turkey

² Department of Pediatrics, Division of Pediatric Metabolism and Nutrition, Hacettepe University Medical School, Ankara, Turkey

³ Department of Pediatric Metabolism and Nutrition Hacettepe University Medical School, Institute of Child Health, Ankara, Turkey



ABSTRACT

Biotinidase deficiency is a rare autosomal recessive inherited metabolic disorder. If not treated in the early neonatal period, profound biotinidase deficiency can cause serious neurological defects, metabolic abnormalities, coma and death. Screening for biotinidase deficiency in newborns and early treatment with free biotin supplementation can prevent all symptoms from occurring. The biotinidase enzyme is encoded by the *BTD* gene. More than 165 mutations have been identified in the *BTD* gene. In this case report; a rare case with homozygous double mutation in the *BTD* gene is presented; and a new allelic variant and genotype is defined. Especially in societies where consanguineous marriages are common; it should be kept in mind that apart from common mutations, different genetic variants may also be seen.

Key Words: Inborn errors of metabolism, Biotinidase deficiency, Newborn screening

ÖZ

Biotinidaz eksikliği, nadir görülen otozomal çekinik olarak kalıtılan bir hastalıktır. Erken yenidoğan döneminde tedavi edilmezse ciddi nörolojik kusurlara, metabolik bozukluklara, komaya ve ölüme neden olabilir. Yenidoğanlarda biotinidaz eksikliği taraması ve biyotin takviyesi ile erken tedavi, semptomların çoğunun ortaya çıkması engellenebilir. Biotinidaz enzimi, *BTD* geni tarafından kodlanır. *BTD* geninde 165'ten fazla mutasyon tanımlanmıştır. Bu olgu bildiriminde Ulusal Yenidoğan Tarama programında tespit edilen, *BTD* geninde homozigot çift mutasyon saptanan nadir bir tablo sunulmuş olup yeni bir allelik varyant ve genotip bildirilmiştir. Özellikle akraba evliliklerinin sık rastlandığı toplumlarda; yaygın görülen mutasyonlar haricinde farklı genetik tabloların da görülebileceği akılda tutulmalıdır.

Anahtar Kelimeler: Doğumsal metabolik hastalıklar, Biotinidaz eksikliği, Yenidoğan taraması

INTRODUCTION

Biotinidase is the enzyme that separates vitamin biotin from its biocytin and sources bound to dietary proteins, thereby recycling biotin. Free biotin can enter the biotin pool directly and is used to convert four human carboxylase enzymes from apocarboxylases to active holocarboxylase forms (1). Biotin-dependent carboxylases catalyze the fixation of bicarbonate in organic acids and are involved in fatty acid, amino acid and

glucose metabolism. Carboxylase activities are significantly reduced in biotin deficiency resulting from biotinidase deficiency (2).

Biotinidase deficiency is a rare autosomal recessive inherited disease. The incidence of biotinidase deficiency has been reported to be approximately 1/60 000 in the world. In a study conducted in Turkey in 1998, the incidence of biotinidase deficiency was reported as 1/1100 (3). Clinical manifestations include sensorineural hearing loss, lactic acidosis, and neurological (acute

0000-0003-2097-9757 : DEVECİ K
0000-0003-1982-8046 : AKAR HT
0000-0001-9076-1388 : YILDIZ Y
0000-0002-0283-635X : ÖZGÜL RK

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

Financial Disclosure / Finansal Destek: The authors declared that this case has received no financial support.

Confirmation / Onay: The written consent was received from the patient who was presented in this study.

How to cite / Atıf Yazım Şekli : Deveci K, Akar HT, Yıldız Y, Özgül RK. A Novel Double Homozygous *BTD* Gene Mutation in A Case of Profound Biotinidase Deficiency. Turkish J Pediatr Dis 2023;17:250-252.

Correspondence Address / Yazışma Adresi :

Kübra DEVECİ
Department of Pediatrics,
Hacettepe University Medical School, Ankara, Turkey
E-posta: kubradeveci@hacettepe.edu.tr

Received / Geliş tarihi : 11.03.2022

Accepted / Kabul Tarihi : 23.06.2022

Online published : 15.09.2022

Elektronik yayın tarihi

DOI: 10.12956/tchd.1082479

metabolic encephalopathy, neurodevelopmental delay, refractory epilepsy, myelopathy, hypotonia, myelopathy), dermatological (eczematous skin rash, seborrheic dermatitis, alopecia), immunological (T cell abnormalities) and ophthalmological (infections, optic neuropathies and visual disturbances, motility disturbances, retinal pigment changes and pupillary findings) abnormalities (4).

If biotinidase deficiency is not treated in the early neonatal period, it can cause serious neurological defects, coma and death (5). Screening for biotinidase deficiency in newborns and early treatment with biotin supplementation can prevent symptoms from occurring (6). The diagnosis of biotinidase deficiency is made by measuring biotinidase activity in plasma (7). In profound biotinidase deficiency, enzyme activity is considered to be less than 10% of the laboratory standard. In partial biotinidase deficiency, enzyme activity is between 10% and 30%. Enzyme activity may also be temporarily low due to indirect hyperbilirubinemia or prematurity (8, 9). Enzymatic assay for biotinidase activity measurement is usually sufficient to determine whether a child has profound biotinidase deficiency. However, enzymatic assays may not always be sufficient to distinguish whether a child has partial deficiency or is a carrier for profound deficiency (9). Therefore, DNA sequencing analysis is important to confirm the diagnosis (10).

The biotinidase enzyme is encoded by the *BTD* gene, which is located on chromosome 3p25 and contains four exons. More than 165 mutations have been identified in the *BTD* gene (11). Biallelic pathogenic variants in *BTD* gene (especially deletion, insertion, or nonsense mutations) usually cause profound or near-profound loss of biotinidase activity. In this case report, a case of biotinidase deficiency detected via the National Newborn Screening Program, who had a novel genotype with a homozygous double mutation in *BTD* gene is presented.

CASE REPORT

A 17-day-old male was referred to our center with a preliminary diagnosis of biotinidase deficiency with the National Neonatal Screening program. He was born as the first child of consanguineous parents, from an 18-year-old mother via spontaneous vaginal delivery at 40 weeks of gestation. Perinatal history was uneventful, and the family history was otherwise unremarkable. The biotinidase activity in the capillary blood sample taken on the second and fourth postnatal days were 1.68 MRU, and 8.31 MRU, respectively (Normal: >65 MRU). The patient's family was alerted by the primary health care center and was referred to the pediatric metabolic diseases department, and he was diagnosed with profound biotinidase deficiency, since the plasma biotinidase activity was 0.28 U/L (3.9% of the laboratory standard) by the spectrophotometric measurement and the enzyme activity was not detectable by

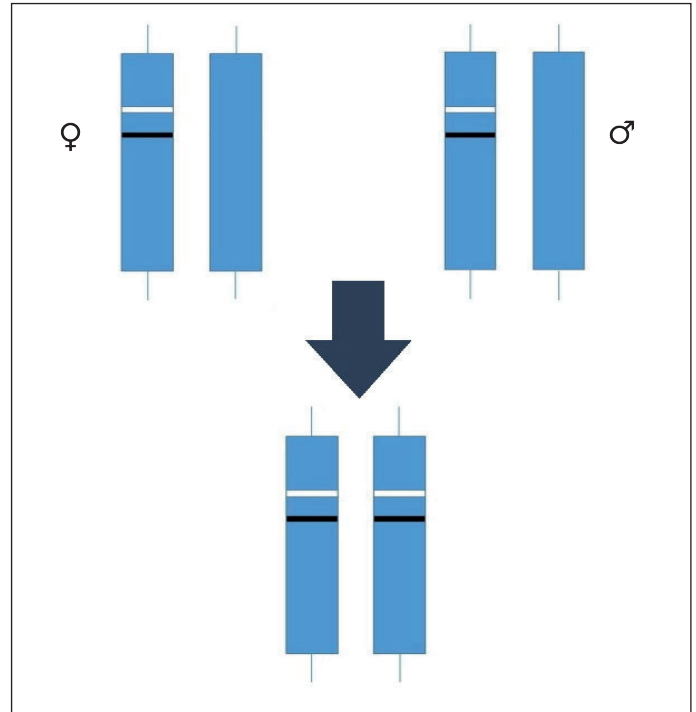


Figure 1: Segregation analysis of the *BTD* gene in the family. Both parents were found heterozygous for .c.499C>T;p.Pro167Ser and c.572 G>A;p.Arg191His mutations (in cis position).

the colorimetric method. Free biotin treatment was started at a dose of 10 mg/day. In the clinical follow-up of the patient, who used the treatment regularly, his examination findings, growth and development were normal, and his routine follow-up visits were continued.

Within the scope of genotyping studies; c.499C>T; p.Pro167Ser and c.572G>A;p.Arg191His mutations in *BTD* gene (RefSeq NM_001370658.1) were determined as homozygous “double mutation” in the patient by Sanger DNA sequencing (Genotype: c.(499C>T;572G>A);(499C>T;572G>A)). Paternal biotinidase activity was 4.12 U/L (58.0%) whereas maternal biotinidase activity was 4.22U/L (59.4%), both consistent with carrier status. Segregation analysis was performed to determine the “cis-trans” positions of nucleotide changes detected in family members. In the segregation analysis, both c.499C>T;p.Pro167Ser and c.572G>A;p.Arg191His mutations were found to be heterozygous for *BTD* gene in both parents; Since biotinidase activities were compatible with carrier status, it was thought that these mutations in the mother and father were in the cis position on the same allele. Segregation analysis is shown in figure 1.

DISCUSSION

Many different point mutations detected in the *BTD* gene to date have been associated with biotinidase deficiency. What makes this patient different is the genetic defect reported at two different

points in the same allele in the mother and father. Literature review did not reveal any reported cases with c.559C>T;p.Pro187Ser and c.572G>A;p.Arg191His mutations detected in the “cis position” on the same allele of the *BTD* gene. However, considering the relevant mutations, it was observed that the c.559C>T; p.Pro187Ser homozygous mutation in the *BTD* gene previously associated with profound biotinidase deficiency (12). Biallelic c.572 G>A; p.Arg191His variant in the *BTD* gene have been reported in ClinVar database, but there are not any case presantations in the literature correlating pathogenicity of this variant. This variant was evaluated as “probably pathogenic” according to the ACMG 2015 criteria. When this variant was examined with the in silico analysis program (“UniProt”), it was observed that it disrupted the three-dimensional structure of the enzyme and was classified as likely pathogenic. Other allelic variations harboring double mutations have also been reported in patients with biotinidase deficiency. The most well-known of these is double homozygosity of the p.Ala171Thr; p.Asp444His allele. This double homozygous genotype (p.(Ala171Thr;Asp444His);(Ala171Thr;Asp444His)) was also reported in six patients in a study conducted in our center. Individuals who are homozygous for the p.Asp444His pathogenic variant are expected to have approximately 45%-50% of mean normal serum biotinidase enzyme activity (which is similar to the activity of heterozygotes for profound biotinidase deficiency) and do not require biotin therapy (13). A double homozygous mutation of p.Phe403Val and p.Asp444His in the *BTD* gene was also reported in a patient from the United Arab Emirates (14).

As a result, considering that consanguineous marriages are common in the Middle East and our region, it is not an extraordinary situation to encounter diverse genetic variations. High rate of consanguineous marriages in a society leads to a rise in the allele frequency of ancestrally inherited disease-causing genotypes and pathogenic alleles in the common gene pool, increasing the chance of co-occurrence of these mutations in future generations. Double mutations can cause synergistic effects on the enzyme that may be more or less severe than the effects caused by either mutation separately. In this study, a rare case homozygous for an allele with two mutations is presented, and a new allelic variant and genotype has been reported. The most important limitations of this case report is lack of functional studies showing the pathogenicity of homozygous c.572 G>A;p.Arg191His variant. Although the presence this double mutation has been associated with the clinical phenotype of profound biotinidase deficiency in this patient, functional studies are required to reveal the individual or combined contributions of the variants to this phenotype. Screening only for common mutations and not sequencing all the coding exons and exon-intron junctions may cause similar situations to be missed. In biotinidase deficiency, in which double-mutated alleles are reported, analysis of the whole coding sequence is important for accurate genotyping.

REFERENCES

1. Canda E, Uçar SK, Çoker M. Biotinidase Deficiency: Prevalence, Impact And Management Strategies. *Pediatric Health Med Ther* 2020;11:127-33.
2. Zemleni J, Hassan YI, Wijeratne SS. Biotin and biotinidase deficiency. *Expert Rev Endocrinol Metab* 2008;3:715-24.
3. Baykal T, Hüner G, Sarbat G, Demirkol M. Incidence of biotinidase deficiency in Turkish newborns. *Acta Paediatr* 1998;87:1102-3.
4. Tomar RPS, Vashisth D, Vasudevan R. Biotinidase deficiency. *Med J Armed Forces India* 2012;68:81-3.
5. Tezel B, Dilli D, Bolat H, Sahman H, Ozbas S, Acican D, et al. The development and organization of newborn screening programs in Turkey. *J Clin Lab Anal* 2014;28: 63- 9.
6. Zengin Akkus P, Ciki K, Mete Yesil A, Bahadur EI, Karahan S, Ozmert EN, et al. Developmental and behavioral outcomes of preschool-aged children with biotinidase deficiency identified by newborn screening. *Eur J Pediatr* 2021;180: 217-24.
7. Kazanasmaz H, Atas N and Karaca M. Specificity and sensitivity of biotinidase activity measured from dried blood spot by colorimetric method. *Ann Med Res* 2019;26:2306-11.
8. Sourmala T,Wick H and Baumgartner E. Low biotinidase activity in plasma of some preterm infants: possible source of false-positive screening results. *Eur J Pediatr* 1988; 147:478-80.
9. Wolf B. Clinical issues and frequent questions about biotinidase deficiency. *Mol Genet Metab* 2010;100:6-13.
10. Wolf B. Biotinidase deficiency:“if you have to have an inherited metabolic disease, this is the one to have”. *Genet Med* 2012;14:565-75.
11. Al-Eitan LN, Alqa qa K, Amayreh W, Khasawneh R, Aljamal H, Al-Abed M, et al. Identification and characterization of *BTD* Gene mutations in jordanian children with biotinidase deficiency. *J Pers Med* 2020;10: 4.
12. Iqbal F, Item CB, Vilaseca MA, Jalan A, Mühl A, Couce ML, et al. The identification of novel mutations in the biotinidase gene using denaturing high pressure liquid chromatography (dHPLC). *Mol Genet Metab* 2010; 100: 42-5.
13. Karaca M, Ozgul RK, Unal O, Yucel Yilmaz D, Kilic M, Hismı B, et al. Detection of biotinidase gene mutations in Turkish patients ascertained by newborn and family screening. *Eur J Pediatr* 2015;174: 1077-84.
14. Hesemann J, Anderson C, Chavey J, Raymond K, Matern D, Hertecant J, et al. Double homozygous mutations in profound biotinidase deficiency: A case study. *Abstracts/Molecular Genetics and Metabolism* 2012;105:273-366.

Unusual Surgical Treatment Option for an Uncommon Disease: Ureterocutaneostomy in an Emphysemateous Pyelonephritis Patient

Nadir Bir Hastalık İçin Olağandışı Cerrahi Tedavi Seçeneği:
Amfizematöz Piyelonefritli Hastada Üreterokutanostomi

Günay EKBERLİ¹, Sevgin TANER², Nevzat Can ŞENER³

¹Department of Pediatric Urology, Ministry of Health, Adana City Training and Research Hospital, Adana, Turkey

²Department of Pediatric Nephrology, Ministry of Health, Adana City Training and Research Hospital, Adana, Turkey

³Department of urology, Ministry of Health, Adana City Training and Research Hospital, Adana, Turkey



ABSTRACT

Emphysematous pyelonephritis (EPN) is severe necrotising inflammation of renal parenchyma. Because of the devastating consequences of the pathology aggressive treatment can prevent permanent renal damage. Fifteen-year-old-girl patient without medical follow-up applied to emergency room with fever and vomiting. Computed Tomography (CT) revealed EPN. After diagnostic procedure minimal invasive procedures like double J catheter and nephrostomy tube insertion failed. While taking into account family's treatment and medical follow-up compliance, also severe dilatation in both ureters made bilateral ureterocutaneostomy (UC) to be considered as a feasible option. UC creation can be thought as a safe and effective alternative surgical procedure. Pediatric neurogenic bladder (NB) population incompatible to treatment and follow-up are candidates for EPN development. We also believe that UC can be beneficial in terms of acute and long-term management of EPN in NB patients who the clinician thinks will not be compatible with complex surgical intervention, follow-up and treatment.

Key Words: Children, Emphysematous Pyelonephritis, Neurogenic Bladder

ÖZ

Amfizematöz piyelonefrit (AP), renal parankimin ileri derece nekrotizan inflamasyondur. Patolojinin yıkıcı sonuçları nedeniyle agresif tedavi kalıcı böbrek hasarını önleyebilir. On beş yaşında takipsiz kız hasta acil servise ateş ve kusma şikayeti ile başvurdu. Bilgisayarlı Tomografi (BT) AP şeklinde rapor edildi. Tanı sürecinden sonra bilateral double J kateter veya nefrostomi gibi minimal invaziv girişimler başarısız oldu. Hastanın postür bozukluğu nedeniyle nefrostomi tüpü ile drenaj yapılamadı. Ailenin tedavisi ve tıbbi takip uyumu dikkate alınarak, her iki üreterde de ciddi dilate olması bilateral üreterokutanostominin (ÜK) uygun bir seçenek olarak düşünülmesine neden oldu. ÜK oluşturulması güvenli ve etkili alternatif bir cerrahi prosedür olarak düşünülebilir. Tedavi ve takibe uyumsuz pediatrik nörojen mesane (NB) popülasyonu, AP gelişimi için adaydır. Klinisyenin karmaşık cerrahi müdahale, takip ve tedavi ile uyumlu olmayacağını düşündüğü NB hastalarında ÜK'nin AP'in akut ve uzun süreli yönetimi açısından faydalı olabileceğine inanıyoruz.

Anahtar Kelimeler: Çocuk, Amfizematöz, Piyelonefrit, Nörojen Mesane

INTRODUCTION

EPN is rare and aggressively progressive urinary tract infection characterized by gas collection within renal parenchyma, collecting system or perirenal tissue (1). The first case of EPN in adults was reported in 1898, and the first case of EPN in a pediatric patient was reported in 1985 (2,3). EPN

is extremely rare in pediatric population (1). EPN is extremely rare in the pediatric population, to date only eight pediatric patients have been reported in the literature, to our knowledge) (1,3,4-9). Most of the cases are documented from adult population (10). Aggressive treatment is mandatory because of the high mortality rate (12-50%) (11). Neurogenic bladder (NB), obstructive pathologies of urinary tract (ureterocele,

0000-0002-0021-5998 : EKBERLİ G
0000-0003-1578-789X : TANER S
0000-0003-3974-187X : ŞENER NC

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

Financial Disclosure / Finansal Destek: The authors declared that this case has received no financial support.

Confirmation / Onay: The written consent was received from the patient who was presented in this study.

How to cite / Atıf Yazım Şekli : Ekberli G, Taner S and Şener NC. Unusual Surgical Treatment Option for an Uncommon Disease: Ureterocutaneostomy in an Emphysematous Pyelonephritis Patient. Turkish J Pediatr Dis 2023;17:253-255.

Correspondence Address / Yazışma Adresi :

Günay EKBERLİ
Department of Pediatric Urology, Ministry of Health,
Adana City Training and Research Hospital, Adana, Turkey
E-posta: gnyekbrl@yahoo.com

Received / Geliş tarihi : 03.11.2022
Accepted / Kabul Tarihi : 09.01.2023
Online published : 01.03.2023
Elektronik yayın tarihi
DOI: 10.12956/tchd.1198673

ectopic ureter, ureteropelvic junction obstruction), acquired immunodeficiency, renal stones or previous history of nephro-urological malformation surgery are reported causes of EPN pediatric population (1,4-9). Treatment could be medical alone or a combination of medical and surgical interventions.

CASE REPORT

Fifteen-year-old-girl patient without medical follow-up applied to emergency room with fever and vomiting. Patient had a history of meningocele operation without shunt. Serious postural disorder secondary to severe scoliosis, club foot deformity and immobility of lower extremity detected in clinical examination of the patient. Abdominal examination was insignificant because of the patient's mental status. Laboratory analyses was as follows: WBC: $30.6 \times 10^3/\text{mm}^3$, HGB: 7 g/dl, PLT: $4696 \times 10^3/\text{mm}^3$, BUN: 59 mg/dL, creatinine: 2.17 mg/dL, Na-122 mmol/L, K-4.36 mmol/L, CRP-367 mg/L. Antibiotics and intravenous fluid resuscitation for electrolyte imbalance started and Foley catheter inserted and purulent drainage of urine observed.

Urinary ultrasound in emergency room revealed parenchymal hyperechogenicity in both kidneys, severe dilatation in pelvicalyceal system – anteroposterior diameter of right and left kidney reported to be 37mm and 45 mm, respectively. Also, severe thickness and mucosal irregularity of bladder wall reported. Because of the inability of patients to express herself and insignificant clinical examination findings abdominal computerized tomography (CT) was planned. Enlarged kidneys, intraparenchymal and intracalyceal gas with an air fluid level confirmed diagnosis EPN as a cause of acute renal failure (Figure 1). Bilateral severe ureteral dilatation and very thick-walled fibrotic bladder detected in CT. *E. coli* isolated from the urine samples of the patient.

After diagnostic procedure bilateral double J catheter insertion for upper urinary tract drainage was planned. Because of the severe trabeculation of mucosa, fibrotic appearance of bladder

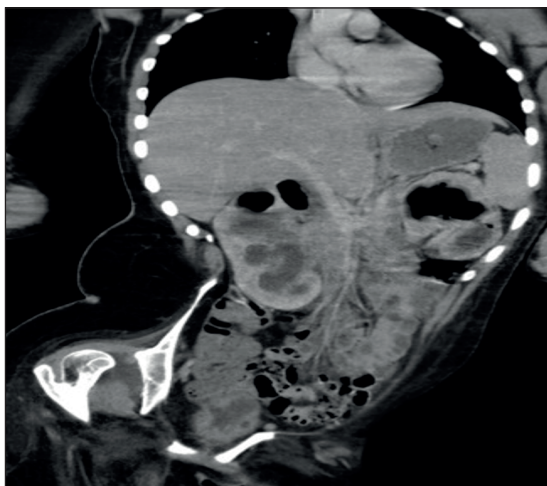


Figure 1: Emphysematous change within renal parenchyma.

that compromised ureteral orifices to be detected, procedure failed. Drainage with nephrostomy tube was impossible because of the postural disorder of the patient. While taking into account family's treatment and medical follow-up compliance, also severe dilatation in both ureters made bilateral led us to consider UC as a feasible option. After discussion with the family operation was completed. On post-operative fifth day, clear urine drainage obtained from UC and blood analyses was completely normal. She discharged from the hospital on postoperative first week. The option of bladder augmentation will be offered to family after full recovery.

DISCUSSION

EPN is rare and aggressively progressive urinary tract infection characterized by gas collection within renal parenchyma, collecting system or perirenal tissue (1). The first case of EPN in adults was reported in 1898, and the first case of EPN in a pediatric patient was reported in 1985 (2,3). EPN is extremely rare in the pediatric population, to date only eight pediatric patients have been reported in the literature, to our knowledge (1,3). Most of the cases are documented from adult population (4). Aggressive treatment is mandatory because of the high mortality rate (12-50%) (5). Neurogenic bladder (NB), obstructive pathologies of urinary tract (ureterocele, ectopic ureter, ureteropelvic junction obstruction), acquired immunodeficiency, renal stones or previous history of nephro-urological malformation surgery are reported causes of EPN pediatric population (1,4-9). Unlike adults, high renal glucose levels secondary to diabetes mellitus (DM) is not detected to be a comorbidity factor in pediatric population (1). There is only one reported case without apparent health issue from Nigeria (6). Comorbidity of the presented case was bilateral functional obstruction due to severe NB.

E. coli is the most common EPN causing pathogen (70%). Especially in patients with DM and urinary tract obstruction *E. coli* and *K. pneumonia*, *Proteus mirabilis*, *Klebsiella pneumoniae*, group D *Streptococcus*, coagulase-negative *Staphylococcus*, and *Enterobacteriaceae* are other causative pathogens (7). Rare organisms such as coagulase negative *Staphylococcus*, *Clostridium*, *Candida species* and *Aspergillus fumigates* have also been reported (8,9). Rare pathogens like *A. schaalii*, *Actinomyces turicensis*, *Prevotella bergensis*, and *Prevotella disiens* isolated from the urine sample of the case reported by Kitano et al. (1) *E. coli* in concordance with the literature isolated from the urine culture of the presented case. There are two speculated mechanisms for EPN development. Presence of gas-producing pathogen in addition to local tissue defect encourage tissue destruction and inhibition of locally produced gas thought to be cause of EPN. Other speculated mechanisms are that the increased levels of glucose in the tissues together with decreased blood supply to the kidneys contributes to the anaerobic metabolism of glucose and lactate

by the organisms and thereafter the production of gases like carbon dioxide, hydrogen, nitrogen, oxygen and methane by the gas-forming organisms (10). CT is a recommended radiological tool for classification of EPN, which was developed by Huang and Seng (8). According to the CT findings, the presented case classified as class 2, which is defined as gas in the renal parenchyma without extension to the extrarenal space.

EPN is a life-threatening condition with 12-50% of mortality (5). There is no consensus regarding treatment options in pediatric population also.

Treatment options for EPN are (9):

1-Fluid and electrolyte replacement, correction of acid-base imbalance, 2-Antibiotic treatment, 3-Percutaneous drainage (PCD), 4-Urgent nephrectomy or subsequent surgical intervention. Especially in a pediatric population conservative treatment should be promptly attempted for prevention of fulminant course and nephrectomy. Treatment options can be combined according to the patient's clinical course. In this case after administration of subsequent intravenous fluid and meropenem initiation (1gr/every 8 hours) surgical intervention was performed. For localized EPN (class 1 or 2) PCD and/or relief of the urinary tract obstruction with antibiotic combination reported to provide good outcome (8). In presented case, bilateral UC was created instead of PCD or other minimal invasive procedures because of the inconvenient bladder and postural appearance of patient. However, unsuccessful PCD, fulminant course of disease or extensive EPN may require nephrectomy (8). As a result of the literature review about EPN in pediatric population, it can be claimed that this is the first case of EPN managed with urinary diversion.

CONCLUSION

Considering kidney's irreplaceable role in growth and development of the pediatric population, UC creation can be thought as a safe and effective alternative surgical procedure. Pediatric NB population incompatible with treatment and follow-up are candidates for EPN development. We also believe that UC can be beneficial in terms of acute and long-term management of EPN in NB patients who the clinician thinks will not be compatible with complex surgical intervention, follow-up and treatment.

A consent form for the use of medical information was signed by patient's parents.

REFERENCES

1. Kitano H, Hieda K, Kitagawa H, Nakaoka Y, Koba Y, Ota K, Shigemoto N, et al. Emphysematous Pyelonephritis with a Congenital Giant Ureterocele. *Front Pediatr* 2021;9:775468.
2. Kelly HA, MacCallum WG. Pneumaturia. *JAMA* 1898;8:375-81.
3. Ambaram PR, Kala UK, Petersen KL. Emphysematous Pyelonephritis in Children. *Pediatr Infect Dis J* 2016;35:1159-61.
4. Arsene C, Saste A, Arul S, Mestrovich J, Kammo R, Elbashir M, et al. A case series of emphysematous pyelonephritis. *Case Rep Med* 2014;2014:587926.
5. Lu YC, Chiang BJ, Pong YH, Chen CH, Pu YS, Hsueh PR, et al. Emphysematous pyelonephritis: clinical characteristics and prognostic factors. *Int J Urol* 2014;21:277-82.
6. Jiya FB, Ibitoye PK, Jiya NM, Amodu-Sanni M, Mohammed Y, Aquib DM, et al. Emphysematous pyelonephritis in an infant from Sokoto, north-western Nigeria. *Afr J Lab Med* 2021;10:1181.
7. Gross IT, Ford R. Emphysematous Pyelonephritis in a Child with Nephrolithiasis. *J Pediatr* 2016;168:250-0.
8. Huang JJ, Tseng CC. Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. *Arch Intern Med* 2000;160:797-805.
9. Mohsin N, Budruddin M, Lala S, Al-Taie S. Emphysematous pyelonephritis: a case report series of four patients with review of literature. *Ren Fail* 2009;31:597-601.
10. Turney JH. Renal conservation for gas-forming infections. *Lancet* 2000;355:770-1.

