E-ISSN 1308-6308

The Journal of Current Pediatrics

Güncel Pediatri

Cilt/Volume: 24 Sayı/Issue: 2 Ağustos/August 2026

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Dergi çevrimiçi olarak yayınlanmaktadır.

İmtiyaz Sahibi: Özlem Mehtap Bostan, Bursa Uludağ Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Çoçuk Kardiyoloji Bilimdalı, Bursa, Türkiye

Please refer to the journal's webpage (https://www.guncelpediatri.com/) for "**Aims and Scope**", "**Instructions to Authors**" and "**Ethical Policy**".

The editorial policies are based on the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2013, archived at http://www.icmje.org/) rules.

The Journal of Current Pediatrics is indexed in **Emerging Sources Citation Index (ESCI), Scopus, DOAJ, TÜBİTAK ULAKBİM TR Index, EBSCO, CINAHL, Embase, Gale, Proquest, J-GATE, Türk Medline** and **Turkish Citation Index**.

The journal is published online.

Owner: Özlem Mehtap Bostan, Bursa Uludağ University Faculty of Medicine, Department of Child Health and Diseases, Division of Pediatric Cardiology, Bursa, Türkiye

Online Yayınlanma Tarihi/Online Printing Date: Ağustos 2026 / August 2026
E-ISSN: 1308-6308

Yılda üç kez yayımlanan süreli yayındır.
International periodical journal published three times in a year.

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Güncel Pediatri

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Social Relations and Self-esteem After Leukemia Treatment Among Adolescent Survivors

Lösemi Tedavisini Tamamlayan Ergenlerde Sosyal İlişkiler ve Kendilik Saygısı

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Cite this article as: Çırpan Kantarcıoğlu A, Sezgin MS, Social relations and self-esteem after leukemia treatment among adolescent survivors. J Curr Pediatr. 2026;24(2):59-68

Abstract

Introduction: This study aimed to examine the variables related to leukemia treatment with age, gender, and perceived parental attitudes that may affect adolescent leukemia survivors' peer relations, social support, and self-esteem when they return to school.

Materials and Methods: ALL and AML survivors between 12-17 years of age were recruited if they completed treatment (in remission) and are schooling. Participants' treatment duration is 1 to 2 years. Some survivors are treated with cranial radiation, but none have a bone marrow transplant. Dependent variables were obtained from, The Parent Attitude Scale, Self-Esteem Rating Scale-Short Form, Peer Relations Scale, and Social Support Assessing Scale for Children and Adolescents.

Results: The female participants had more negative self-esteem, received less support from their teachers, less trust and identification, and commitment to peers, and received their fathers more autocratic than male participants. The results show that none of the leukemia-related variables (leukemia type, duration of treatment, duration of schooling, and receiving radiation treatment) differ through self-esteem, peer relations, and perceived social support. The results also show that the perception of the father as authoritative, lower teacher support, and lower commitment to peers could predict self-esteem.

Conclusion: The study's findings might point out that not only do leukemia treatment characteristics affect social functioning. Perceived authoritarian parenting, teacher support, and peer relations such as commitment are essential, especially in self-esteem.

Keywords
Leukemia, social relations, parenting, self-esteem

Anahtar kelimeler
Lösemi, sosyal ilişkiler, ebeveynlik, benlik saygısı

Received/Geliş Tarihi : 15.08.2024
Accepted/Kabul Tarihi : 08.01.2025
Epub : 17.01.2025
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2025.24444

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Öz

Giriş: Bu çalışma, lösemili ergenlerin okula döndüklerinde akran ilişkilerini, sosyal desteğini ve benlik saygısını etkileyebilecek yaş, cinsiyet, algılanan ebeveyn tutumları ile lösemi tedavisi özelliklerini incelemeyi amaçlamıştır.

Gereç ve Yöntem: ALL ve AML tanısı almış, 12-17 yaşları arasında ergenler, tedavilerini tamamlamış (remisyonda) ve okula gidiyorlarsa çalışmaya alınmıştır. Katılımcıların tedavi süresi 1 veya 2 yıldır. Ergenlerden bazıları kraniyal radyasyonla tedavi edilmiş, ancak hiçbirinde kemik iliği nakli yapılmamıştır. Bağımlı değişkenler, Ebeveyn Tutum Ölçeği, Benlik Saygısı Ölçeği-Kısa Form, Akran İlişkileri Ölçeği ve Çocuk ve Ergenler İçin Sosyal Desteği Değerlendirme Ölçeğinden elde edilmiştir.

Bulgular: Kız ergenlerin, erkek ergenlere göre daha fazla olumsuz benlik saygısı olduğu, öğretmenlerinden daha az sosyal destek algıladığı, akranlarıyla daha az

güven ve özdeşleşme ile bağlılık geliştirdikleri ve babalarını daha otoriter algıladıkları bulunmuştur. Lösemi ile ilgili değişkenlerin benlik saygısı, akran ilişkileri ve algılanan sosyal destek açısından farklılık göstermediğini bulunmuştur. Sonuçlar ayrıca babanın otoriter olarak algılanmasının, algılanan düşük öğretmen desteğinin ve akranlara düşük bağlılığın benlik saygısını yordadığını göstermektedir.

Sonuç: Çalışmanın bulguları, sadece lösemi tedavi özelliklerinin sosyal işlevselliği etkilemediğini gösterebilir. Algılanan otoriter ebeveynlik, öğretmen desteği ve bağlılık gibi akran ilişkileri, özellikle benlik saygısında önemli olabilmektedir.

Introduction

Acute leukemia treatments in childhood and adolescence brought the 5-year survival rate to more than 80%, leading some psychologically oriented studies to examine the adaptation of the survivors to their lives after treatment (1).

Although these studies yield different results, likely due to differences in design, study interval, or sample size, they generally show a decrease in quality of life (2-4), an increase in psychiatric problems (5,6), and a decline in neurocognitive abilities (7-9).

Some of the problems reported before may be due to the treatment itself. The treatment characteristics of leukemia are receiving a high dose of cortisol, and intravenous and intra-cranial chemotherapies might cause prolonged hospitalization due to neutropenia with oral mucous. Whether or not to receive radiation during the treatment (as are t-cell acute lymphoblastic leukemia (ALL) patients), receive high-risk treatment protocol (as are acute myeloid leukemia (AML), or have a bone marrow transplant (among high relapse risk patients) may impose an extra burden on patients. Getting radiation therapy prolongs the treatment duration by a few months, and having bone marrow transplants is up to one year in some cases. These treatment characteristics bring more social isolation due to side effects and prolonged treatment duration.

In our country, Berlin-Frankfurt-Münster Chemotherapy (10) protocol is used to treat ALL and AML widely. According to these protocols, treating ALL takes approximately two years, and AML takes at least one year. During this treatment period, leukemia patients experience severe social isolation (the patients cannot go to school, spend very little time with their peers, and cannot attend social activities or courses) primarily due to neutropenia.

After the treatment period, adolescents in return to school and social life soon. However, both their classes and possibly their friend group have changed. When they return to social life, the side effects of the treatment (weakness, baldness, malaise) might continue, which could expect this situation to affect self-esteem, as identify "a set of self-attitudes that reflects a description and an evaluation of one's behavior and attributes'", negatively (11).

The quality of the relationship with parents in early life shapes self-esteem dominantly. Self-esteem is a mental self-representation first built from early relations with parents. The relationship with parents is generally studied as parenting styles (authoritarian, indulgent, authoritative, and neglectful) are differently associated with positive or negative impacts on developmental outcomes, including personal and social adjustment (12). The authoritative style has been associated with the best socialization outcomes, but the authoritarian style is most closely associated with externalizing problems (13). Cross-sectional studies found small to moderate positive associations of authoritative parenting with self-esteem, while authoritarian and neglectful parenting was related to lower self-esteem (14).

Social development issues occur through social interaction with family and society, but leukemia treatment might affect them negatively. Can those survivors quickly return to social life? Some recent studies show that this is not the case. A study shows that by increasing age and when pediatric patients have received a hematopoietic stem cell transplantation at the stop-therapy time, their perception of relationships at school and academic performance decreases (15). Experiences of social isolation evolved as survivors grew through childhood, adolescence, and young adulthood (16). Feelings of alienation from friends, difficulty in studying, being stuck being different from others, apologetic feelings for family, and feelings of uncertain future (17). Survivors' global self-worth scores were significantly lower than those of sibling controls (18). Higher treatment severity is often associated with more late effects, which can be physical, somatic, or psychological (19). Survivors with more aggressive therapy, including cranial radiation (as are AML and ALL-HR treatment), would report lower self-esteem scores, as suggested in the study of Hill et al. (20).

Thus, might perceived parental attitudes and leukemia treatment characteristics impact survivors' social relations and self-esteem at the end of the treatment? What awaits adolescents who return to social life? Should we expect adolescents to have positive social functions? Could the types of leukemia and different treatment characteristics (duration of treatment and getting radiation treatment,

etc.), parental attitudes, or how long they have been attending school (or schooling time) have a predictive effect on social relations and self-esteem among survivors? We expect that exposure to radiation during treatment, having AML-type leukemia because of a more extended hospital stay, might cause more infectious diseases and high-risk treatment, the prolongation of the total duration of treatment, and less time spent at school will negatively affect self-esteem, peer relations and perceived social support. Besides, gender, age, and perceived parenting attitudes contribute to these variables examined. Based on that, we developed the following research questions, are gender, age, perceived parenting attitudes, leukemia type, duration of treatment, duration of schooling, and receiving radiation treatment make a difference in peer relations and perceived social support and self-esteem? (research question 1)

Which gender, age, perceived parenting attitudes, leukemia type, duration of treatment, duration of schooling, and received radiation might predict leukemia survivors' peer relations, perceived social support, and self-esteem? (research question 2)

Materials and Methods

This study was conducted in the Pediatric Oncology-Hematology Hospital in Bursa, Turkiye, in the 2022 late autumn and 2023 early spring.

Participants

ALL and AML survivors between 12-17 years of age were recruited through follow-up clinics in our hospital. All the participants have completed treatment (in remission) and are schooling. Participants' treatment duration is 1 to 2 years. Some survivors treat with cranial radiation, but none have a bone marrow transplant. Participants matched with the exact socio-economic (middle) background. See Table 1 for information on the participants.

Data Collection Procedures

All participants and guardians provided written informed consent to participate in the study. Those willing to participate, which totaled 54 individuals, were directed to informed consent obtained from all participants in the study. The study was approved by Ethics Committees in Uludağ University Medical University Ethical Committee (date: 08.06.2022 approval number: 2022-12/9).

One psychologist conducted data collection. Participants were individually invited to the hospital interview room and responded to all measures using Likert-type scales. All data for the study were collected in one session. Socio-demographic characteristics were assessed through a short questionnaire.

Data Collections

The scales evaluate mother-father parenting attitudes, self-esteem, peer relations, and perceived social support assessment.

The Parent Attitude Scale

The Parent Attitude Scale was developed by Lamborn, Mounts, Steinberg, and Dornbush (21). The scale has three dimensions; support, control, and psychological autonomy. The support dimension aims to measure how children perceive their parents as caring, involved, and involved. The size of control seeks to measure how controlling both parents are separate. Finally, the measurement of psychological autonomy aims to estimate how much they apply the mother's and father's democratic attitude and to what extent they encourage their individuality. According to the answers given to the three sub-dimensions, parental perspectives are evaluated from authoritarian to democratic styles. It is a 5-point Likert-type scale with responses ranging from strongly disagree (1 point) to agree (5 points) completely. When reverse-coded items are changed, low scores indicate authoritarian parenting style perception. Yılmaz (22)

Table 1. Participant characteristics

Characteristics	N	Percentile
Age		
14-15	15	27,8%
12-13	17	31,5%
16-17	22	40,7%
Gender		
Female	22	40,7%
Male	32	59,3%
Leukemia type		
ALL	40	74,1%
AML	14	25,8%
Cranial radiation therapy		
No	40	74,1%
Yes	14	25,8%
Treatment duration		
1 year	12	22,2%
2 years	42	78,8%
Schooling duration		
Up to 6 months	12	22,2 %
6 months- 1 year	19	35,2 %
1-2 years	23	42,6%

conducted a validity and reliability study of the scale in our country (22).

Self-Esteem Rating Scale-Short Form

The scale reliability and validity studies were carried out by Çuhadaroğlu (23). The Turkish validity and reliability study of the RBSS points to high self-esteem, 2-4 points to medium self-esteem, and 5-6 points to low self-esteem. The positively and negatively charged items are listed sequentially. 1. 2. 4. 6. 7. items positive, 3. 5. 8. 9. 10. items are negatively loaded. 4-point Likert-type scale with responses ranging from strongly agree (1 point) to disagree (5 points) completely strongly. When reverse-coded items are changed, a low score on the scale scores high self-esteem; a high score indicates low self-esteem.

Peer Relations Scale

The scale was developed to evaluate peer relationships in our country by Kaner (24) and has four subscales. The commitment subscale assesses adolescents' feelings of closeness and love for each other. The trust and identification subscale measures the degree of trust and identification that adolescents have with each other, and the self-disclosure subscale measures how well they can express themselves with their friends. The loyalty subscale measures their loyalty to their friends even if they are in trouble. The Cronbah-alpha value of the subscales ranged from 0.58 to 0.86. On the other hand, test-retest reliability ranged from 0.77 to 0.93, a 5-point Likert-type scale with responses ranging from strongly agree (1 point) to disagree (5 points) completely. A low score on the ranking points to high friendship relations.

Social Support Assessing Scale for Children and Adolescents

The scale developed by Dubow and Ullman (25) assesses children's family, friends (close friends and class friends), and teachers perceived perceptions of social support. The items measure the extent to which the child evaluates themself as someone loved, cared for, valued, and accepted by their social network. The items measure the time to which the child considers themself as someone loved, cared for, valued, and accepted by their social network. The scale consists of 3 subtests; perceived friend, family, and teacher support, and consists of 41 items. A low score on the ranking points means high perceived support from friends, family, and teachers. Gökler (26) carried out reliability and validity studies in our country.

Statistical Analysis

In this study, gender, age, perceived parental attitudes, leukemia type, receiving radiation therapy, duration of treatment, and duration of schooling were used as independent variables. The dependent variables were self-esteem, peer relations, and perceived social support (perceived family, peers, and teacher support; commitment, trust and identification, loyalty, and self-closure to peers). We ran the analysis with IBM SPSS version 22 and used $p \leq 0.05$ for the significance level. Descriptive statistics characterized the demographic and clinical characteristics of the sample. The data observed was customarily distributed and homogeneous (according to Skewness and Kurtosis analysis). Univariable testing (e.g., Pearson correlation, ANOVA) and linear regression analysis assessed associations with scores among variables of interest.

Results

The mean and standard deviation values of the study are shown in Table 2.

According to the results of the correlation analysis performed to evaluate which independent variables have a significant relationship with the dependent variables, gender and self-esteem scores (r= -,050; p ≤.001), teacher support (r= ,438; p≤.001), commitment (r= -,482; p ≤.000), trust and identification (r= -,442; p≤.001) and the father's attitude (r = ,269; p ≤ 0.05) were significantly correlated. There is a positive correlation between the father's perception of autocratic and low support from teachers and the female gender. Being female negatively correlates with self-esteem, commitment, trust and identification to peers Table 3.

To answer our first research question (are gender, age, perceived parenting attitudes, leukemia type, duration of treatment, duration of schooling, and receiving radiation treatment make a difference in peer relations and perceived social support and self-esteem?) we conducted an ANOVA analysis.

According to results, gender and self-esteem (F=17,22; df (1); p≤.000) teacher support (F=12,32; df (1); p ≤ .001) commitment to peers (F=15,75; df (1); p≤.000) trust and identification to peers (F= 12,65; df (1); p≤.001) and perceived father attitude (F=4,05; df (1); p≤.05) were significantly different. The female participants had more negative self-esteem, received less support from their teachers, less trust and identification, and commitment to peers, and received their fathers more autocratic than male participants. The results show that none of the leukemia-related variables

Table 2. Means and standart deviations of variables											
		Self-esteem	Peer support	Family support	Teacher support	Mother attitude	Father attitude	Peer commitment	Peer trust	Peer Self-disclosure	Peer loyalty
Female	Mean	24,63	56,95	33,22	29,00	190,45	154,22	22,36	12,13	9,50	11,27
	N	22	22	22	22	22	22	22	22	22	22
	Std. Deviation	7,75	5,70	3,76	4,20	16,41	19,67	6,79	3,10	2,220	2,99
Male	Mean	17,59	57,21	31,90	32,28	182,06	164,75	14,96	8,96	10,53	11,68
	N	32	32	32	32	32	32	32	32	32	32
	Std. Deviation	4,71	6,38	2,037	2,66	24,78	18,33	6,68	3,28	2,89	2,71
12-13 years	Mean	19,40	58,20	31,46	30,93	186,13	165,20	18,73	10,33	10,80	12,20
	N	15	15	15	15	15	15	15	15	15	15
	Std. Deviation	6,28	7,27	2,82	3,91	17,79	12,71	7,74	3,39	2,30	2,33
14-15 years	Mean	22,00	56,47	33,52	29,76	193,70	167,47	17,64	10,29	10,05	11,88
	N	17	17	17	17	17	17	17	17	17	17
	Std. Deviation	8,04	5,25	2,55	4,73	17,52	14,44	8,75	3,70	2,38	2,42
16-17 years	Mean	20,00	56,86	32,27	31,86	178,68	151,81	17,72	10,18	9,68	10,77
	N	22	22	22	22	22	22	22	22	22	22
	Std. Deviation	6,71	5,93	3,07	2,35	25,91	23,48	6,86	3,69	3,09	3,29
ALL	Mean	20,37	56,65	32,40	30,87	185,52	160,12	17,40	10,07	9,90	11,42
	N	40	40	40	40	40	40	40	40	40	40
	Std. Deviation	6,98	5,77	2,89	3,74	21,60	17,63	8,09	3,65	2,68	2,79
AML	Mean	20,71	58,42	32,57	31,14	185,35	161,42	19,64	10,78	10,71	11,78
	N	14	14	14	14	14	14	14	14	14	14
	Std. Deviation	7,30	6,89	3,05	3,75	23,90	24,58	5,95	3,30	2,61	2,96
CRT Yes	Mean	21,20	56,27	32,55	30,52	184,12	159,50	18,27	10,50	10,15	11,25
	N	40	40	40	40	40	40	40	40	40	40
	Std. Deviation	7,36	5,53	3,02	4,05	22,22	20,66	7,89	3,46	2,27	3,00
No	Mean	18,35	59,50	32,14	32,14	189,35	163,21	17,14	9,57	10,00	12,28
	N	14	14	14	14	14	14	14	14	14	14
	Std. Deviation	5,54	7,04	2,62	2,21	21,61	15,68	6,90	3,83	3,67	2,09

Table 2. Continued

		Self-esteem	Peer support	Family support	Teacher support	Mother attitude	Father attitude	Peer commitment	Peer trust	Peer Self-disclosure	Peer loyalty
Treatment duration 1 year	Mean	20,25	58,25	32,66	30,75	186,83	160,00	19,25	10,83	10,58	12,08
	N	12	12	12	12	12	12	12	12	12	12
	Std. Deviation	8,17	4,73	3,31	4,07	25,87	26,06	5,84	3,58	2,81	3,23
2 years	Mean	20,52	56,78	32,38	31,00	185,09	160,59	17,61	10,09	9,97	11,35
	N	42	42	42	42	42	42	42	42	42	42
	Std. Deviation	6,74	6,40	2,82	3,66	21,08	17,47	8,063	3,56	2,64	2,70
Schooling Time 6 months	Mean	17,66	57,08	31,41	30,91	189,83	166,08	17,25	9,66	10,41	12,58
	N	12	12	12	12	12	12	12	12	12	12
	Std. Deviation	6,34	7,52	1,92	2,67	19,34	14,26	7,43	2,99	3,14	2,27
6 -12 months	Mean	21,78	56,47	32,15	30,89	183,84	153,57	18,42	10,47	10,15	11,21
	N	19	19	19	19	19	19	19	19	19	19
	Std. Deviation	7,46	6,10	3,46	3,79	17,04	20,99	7,86	4,37	3,14	3,15
12-24 months	Mean	20,82	57,65	33,21	31,00	184,56	163,21	18,00	10,39	9,91	11,21
	N	23	23	23	23	23	23	23	23	23	23
	Std. Deviation	6,82	5,39	2,72	4,23	26,94	19,50	7,78	3,15	1,99	2,74

CRT: Cranial radiation therapy

(leukemia type, duration of treatment, duration of schooling, and receiving radiation treatment) differ through self-esteem, peer relations, and perceived social support.

Our second research question was, which gender, age, perceived parenting attitudes, leukemia type, duration of treatment, duration of schooling, and received radiation might predict leukemia survivors' peer relations, perceived social support, and self-esteem?

Since we could not find any meaningful relationship between leukemia treatment characteristics and self-esteem, peer relationships, and social support, we investigated what might be predictors of survivors' self-esteem.

Regarding which variables could predict self-esteem, regression analysis was performed with correlated variables such as perceived family and teacher support, perceived father's parenting attitude, commitment, and trust and identification with peers. The variables that predicted self-esteem were determined when trust and identification to peers and perceived family support were removed in the 3rd step with the linear regression backward method. The results show that the perception of the father as authoritative (β= -,088, p< .021), perceived lower teacher support (β= -,366, p< .051), and lower commitment to peers (β= ,510, p< .000) could predict (R^2 =, 459) self-esteem (Durbin-Watsons; 2,48).

In other words, the results of the regression analyses showed that perceived authoritative fathers, lower teacher support, and lower commitment to peers significantly explained 46% of leukemia survivors' self-esteem variance (F=16.96, p≤=.000).

Discussion

This study aimed to examine the variables related to leukemia treatment characteristics (leukemia type, receiving radiation during the treatment, treatment duration, and high-risk treatment protocol) with age, gender and perceived parental attitudes that may affect adolescent leukemia survivors' peer relations, social support, and self-esteem when they return to school.

Prolonged treatment duration, receiving cranial radiation, and high-risk protocol mean staying away from social environments more. It was expected that

Tablo 3. Results of linear regression analysis predicting the self-esteem			
Model 3	**β**	**t**	**Sig.**
Constant	36,763	3,873	0,000
Father attitude	-,088	-2,377	0,02*
Teacher support	-,366	-1,872	0,51*
Peer commitment	,510	5,272	0,000*
p≤ .05			

shorter schooling time, longer treatment received, high-risk protocol, and radiotherapy would adversely affect these social relations.

Some previous research found no difference in self-esteem scores among adolescent leukemia survivors between control groups (27) or only differed in favor of the female gender (28). Still, other studies found significantly lower self-esteem scores among leukemia survivors (2,29).

However, the current study found differences explicitly based on gender, not leukemia treatment characteristics. Girls received lower self-esteem, teacher support, commitment, trust and identification to peers and perceived their fathers as more authoritarian. The girls' low self-esteem was predicted by the perception of an authoritarian father, low perceived teacher support, and low commitment to their peers.

It has been reported in the literature that girls may have lower self-esteem during adolescence, which may be observed more frequently in societies where gender roles are dominant. At the same time, considering that body image is highly effective on self-esteem, the appearance characteristics of girls (shorter hair, cracks in the skin, physical weakness, etc.) during their return to school may have affected their self-esteem more negatively. A study conducted in Turkiye found that high school female students' dissatisfaction with their body image was positively associated with low self-esteem (30).

Why is the effect of perceiving the father as more authoritarian on self-esteem more effective in girls? As is known, uncompromising, insensitive parenting attitudes are associated with low self-esteem (31,32). Adolescents with warm, caring parents are more likely to develop positive self-esteem (33). According to a study, adolescent girls think that their families have an authoritarian parental attitude; male adolescents have a democratic parental attitude toward their families. The results show that the democratic parenting style and high self-esteem are highly related (34). In this study, we observe that female adolescents perceived more authoritarian fathers and low self-esteem, regardless of the characteristics of leukemia treatment, similar to earlier studies.

Our study also observed that self-esteem is predicted by the perception of the father as authoritarian, low perceived support from the teacher, and low commitment to friends.

Perceived attitudes from parents significantly predict self-esteem throughout adolescence (35). Multiple studies have found that authoritative parents, who maintain high expectations for their children in the context of a close and affectionate relationship, tend to have better-adjusted adolescents in several areas, including self-esteem (36). Caring, supportive relations with non-related adults, such as teachers, can be fundamental to the development of adolescents' self-esteem and reflects the totality of the individual's thoughts and emotions regarding the self. Besides family and friends, teachers are essential sources of support for the adolescent. Teachers need to deal with the students' problems, play a supportive role, and be models for the children in developing their self-esteem. The supportive attitude of the teacher can also increase the support of friends. Self-esteem is positively shaped by the support received from these social support sources, essential for adolescents. Perceived teachers' support is critical for boys' and girls' positive self-esteem (37,38). A study found that, for both boys and girls, changes in perceptions of teachers' support reliably predicted changes in both self-esteem and depression. In particular, those students perceiving increasing teacher support showed corresponding decreases in depressive symptoms and increases in self-esteem (39).

Two recent studies on peer commitment among adolescents in our country found that female adolescents had more commitment than males (40,41), which differs from our study. According to Patrick et al. (42), although female adolescents have the same level of commitment to peers, they mentioned receiving negative peer attention more frequently than males and more often cited social dissatisfaction as a significant contributor to decreased involvement or quitting. Perhaps, returning to school with treatment visible side effects, female adolescents feel more uncomfortable and have the anxiety to fear being different from males of the same gender. Those results may also

explain why their loyalty, trust and identification with peers scores were significantly lower than that of males.

Although there were differences in the current study of social and peer relationships according to gender and perceived parenting attitudes, leukemia treatment characteristics did not affect these variables. Previous studies, for example, Tremolada et al. (15) report that childhood AML survivors with a high-risk treatment were more at risk in their self-esteem. Some survivors expressed that they encountered peer rejection in school. It has been reported that survivors have low self-esteem, especially in terms of interpersonal relationships, and suffer from anxiety about peer relationships (43). Negative experiences with peers (bullying related to cancer, physical appearance, and chronic problems) may make it difficult for the survivors to adapt to school. Continuing education at a lower level compared to their peers can be disturbing. In addition, they are worried about the possible attitude of their teachers and friends. The support of friends, teachers, and the healthcare team ensures a positive experience returning to school.

The reasons for experiencing problems in social relations and returning to social life at the end of the treatment have been reported such as discrimination (44), low self-esteem, especially in terms of interpersonal relationships, suffering from anxiety about peer relationships, and negative experiences with peers (bullying related to cancer, physical appearance, and chronic problems) may make it difficult for the survivors to adapt to school (15).

Generally, in our country, making fun of or humiliating people who have had something terrible happen to them is perceived as horrible behavior and is avoided. The idea that making fun of it happens to you is shared. For this reason, adolescents treated for leukemia are less likely to be excluded in social settings or schools for only that situation, which might have prevented them from having trouble with social relations.

According to Arpaci et al. (45), adolescents who are not included in the disease and treatment process and are not adequately informed feel worthless. However, doctors and psychologists in our hospital give adolescents continuous information about their disease and treatment process. That approach might lessen the treatment burden reported.

Additionally, theater/art performances, birthday celebrations, sharing experiences when they return to school, celebrations on New Year's, and religious holidays are held regularly for pediatric patients undergoing cancer treatment. There is a group activity hall and play therapy unit in our hospital. Patients often receive gifts, which might let less effect on treatment.

As the reasons for this, we suggest that humiliating leukemia patients are sporadic in our country, adolescents are informed about the disease and treatment from the moment of diagnosis, and their participation in treatment and social activities during treatment in the hospital can alleviate the treatment burden. It can be said that according to our research results, the gender of the girl and the authoritarian perception of the father, not the treatment itself only, harm social relations and self-esteem after leukemia treatment. Especially adolescent girls survivors may need to be supported in social and peer relations, as well as their physical examinations and psychological review regularly.

Conclusion

Leukemia treatment characteristics might burden patients' mental health and social life even after the end of the treatment. Especially in adolescence, when social development areas proliferate, being away from the social environment due to neutropenic isolation could affect social ability negatively. However, our findings might point out that not only do leukemia treatment characteristics affect social functioning. Perceived authoritarian parenting, perceived teacher support, and peer relations such as commitment are essential, especially in self-esteem. Future research with more participants may include more variables (the total length of hospital stay or socialization times, the duration of mucositis or other infections experienced by the patients), which may also affect the results.

To the best of our knowledge, this is the first study in our country to evaluate the post-treatment self-perceptions and social relationships of adolescents treated for leukemia in relation to treatment characteristics. our study may contribute to increased interest in the fact that returning to normal life after serious treatments may be full of difficulties and lead to other studies.

Ethics

Ethics Committee Approval: The study was approved by Ethics Committees in Uludağ University Medical University Ethical Committee (date:08.06.2022, approval number: 2022-12/9).

Acknowledgments

We would like to thank all the participants for their involvement.

Footnotes

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

Financial Disclosure: The author declared that this study received no financial support.

References

1. Pui CH, Campana D, Pei D, Bowman WP, Sandlund JT, Kaste SC, et al. Treating childhood acute lymphoblastic leukemia without cranial irradiation. N Engl J Med. 2009;360:2730-41.
2. Baytan B, Aşut Ç, Çırpan Kantarcıoğlu A, Sezgin Evim M, Güneş AM. Health-related quality of life, depression, anxiety, and self-image in acute lymphocytic leukemia survivors. Turk J Haematol. 2016;33:326-330.
3. Rodgers CC, Hooke MC, Taylor OA, Koerner KM, Mitby PA, Moore IM, et al. Childhood cancer symptom cluster: leukemia and health-related quality of life. Oncol Nurs Forum. 2019;46:228-37.
4. Vetsch J, Wakefield CE, Robertson EG, Trahair TN, Mateos MK, Grootenhuis M, et al. Health-related quality of life of survivors of childhood acute lymphoblastic leukemia: a systematic review. Qual Life Res. 2018;27:1431-43.
5. Abadie A, Massoubre C, Casagranda L, Protière A, Buisson-Papet G, Trombert-Paviot B, et al. Prevalence of psychiatric complications in young adults after childhood cancer treatment: results of the long-term follow-up studies in oncology. J Adolesc Young Adult Oncol. 2020;9:247-55.
6. Heo J, Park JE, Noh OK, Shin Y. Psychiatric disorders among children with acute lymphoblastic leukemia in South Korea: a nationwide population-based longitudinal study. J Int Med Res. 2022;50:3000605221075223.
7. Liu W, Cheung YT, Conklin HM, Jacola LM, Srivastava D, Nolan VG, et al. Evolution of neurocognitive function in long-term survivors of childhood acute lymphoblastic leukemia treated with chemotherapy only. J Cancer Surviv. 2018;12:398-406.
8. Partanen M, Phipps S, Russell K, Anghelescu DL, Wolf J, Conklin HM, et al. Longitudinal trajectories of neurocognitive functioning in childhood acute lymphoblastic leukemia. J Pediatr Psychol. 2021;46:168-78.
9. Stefanski KJ, Anixt JS, Goodman P, Bowers K, Leisenring W, Scott Baker K, et al. Long-term neurocognitive and psychosocial outcomes after acute myeloid leukemia: a childhood cancer survivor study report. J Natl Cancer Inst. 2021;113:481-95.
10. Niemeyer CM, Reiter A, Riehm H, Donnelly M, Gelber RD, Sallan SE. Comparative results of two intensive treatment programs for childhood acute lymphoblastic leukemia: The Berlin-Frankfurt-Münster and Dana-Farber Cancer Institute protocols. Ann Oncol. 1991;2:745-9.
11. Orth U, Robins RW. Is high self-esteem beneficial? Revisiting a classic question. Am Psychol. 2022;77:5-17.
12. Gimenez-Serrano S, Garcia F, Garcia OF. Parenting styles and its relations with personal and social adjustment beyond adolescence: Is the current evidence enough? Eur J Dev Psychol. 2021;19:1-21.
13. Durbin DL, Darling N, Steinberg L, Brown BB. Parenting style and peer group membership among European-American adolescents. J Res on Adolesc. 1993;3:87-100.
14. Pinquart M, Gerke DC. Associations of parenting styles with self-esteem in children and adolescents: a meta-analysis. Journal of Child and Family Studies. 2019;28:2017-35.
15. Tremolada M, Taverna L, Bonichini S, Pillon M, Biffi A, Putti MC. Pediatric patients treated for leukemia back to school: a mixed-method analysis of narratives about daily life and illness experience. Behav Sci (Basel). 2020;10:107.
16. Howard AF, Goddard K, Tan de Bibiana J, Pritchard S, Olson R, Kazanjian A. Adult childhood cancer survivors' narratives of managing their health: the unexpected and the unresolved. J Cancer Surviv. 2016;10:711-25.
17. An H, Lee S. Difficulty in returning to school among adolescent leukemia survivors: a qualitative descriptive study. Eur J Oncol Nurs. 2019;38:70-75.
18. Andrés-Jensen L, Larsen HB, Johansen C, Frandsen TL, Schmiegelow K, Wahlberg A. Everyday life challenges among adolescent and young adult survivors of childhood acute lymphoblastic leukemia: an in-depth qualitative study. Psychooncology. 2020;29:1630-7.
19. Andrés-Jensen L, Skipper MT, Mielke Christensen K, Hedegaard Johnsen P, Aagaard Myhr K, Kaj Fridh M, et al. National, clinical cohort study of late effects among survivors of acute lymphoblastic leukaemia: the ALL-STAR study protocol. BMJ Open. 2021;11:e045543.
20. Hill JM, Kornblith AB, Jones D, Freeman A, Holland JF, Glicksman AS, et al. A comparative study of the long term psychosocial functioning of childhood acute lymphoblastic leukemia survivors treated by intrathecal methotrexate with or without cranial radiation. Cancer. 1998;82: 208-18.
21. Lamborn SD, Mounts NS, Steinberg L, Dornbusch SM. Patterns of competence and adjustment among adolescents from authoritative, authoritarian, indulgent, and neglectful families. Child Dev. 1991;62:1049-65.
22. Yılmaz, A. Anne-baba tutum ölçeğinin güvenirlik ve geçerlik çalışması. Çocuk ve Gençlik Ruh Sağlığı Dergisi. 2000;7:160-172.
23. Çuhadaroğlu F. Adölesanlarda benlik saygısı. [master's thesis]. Hacettepe University. 1986.
24. Kaner S. Peer relations scale and peer deviation scale development study. Ankara University Journal of Faculty of Educational Sciences (JFES). 2000; 33:77-89.
25. Dubow EF, Ullman DG. Assessing social support in elementary school children: the survey of children's social support. Journal of Clinical Child Psychology. 1989;18: 52-64.
26. Gökler I. Çocuk ve ergenler için sosyal destek değerlendirme ölçeği Türkçe formunun uyarlama çalışması: Faktör yapısı, geçerlik ve güvenirliği. Çocuk ve Gençlik Ruh Sağlığı Dergisi. 2007;14: 90-9.
27. Maggiolini A, Grassi R, Adamoli L, Corbetta A, Charmet GP, Provantini K, et al. Self-image of adolescent survivors of long-term childhood leukemia. J Pediatr Hematol Oncol. 2000;22:417-21.
28. Zebrack BJ, Chesler M. Health-related worries, self-image, and life outlooks of long-term survivors of childhood cancer. Health Soc Work. 2001;26:245-56.
29. Sherief LM, Kamal NM, Abdalrahman HM, Youssef DM, Alhady MAA, Ali S, et al. Psychological impact of chemotherapy for childhood acute lymphoblastic leukemia on patients and their parents. Medicine (Baltimore). 2015;94:e2280.
30. Oktan V, Şahin M. Examination of the relationship between the body image and self-esteem of female adolescents. Journal of Human Sciences. 2010; 7:543-56.

31. Haktanır G, Baran G. Gençlerin benlik saygısı düzeyleri ile anne baba tutumlarını algılamalarının incelenmesi. Çocuk ve Gençlik Ruh Sağlığı Dergisi. 1998;5:134-41.
32. Kındap Y, Sayıl M, Kumru, A. Anneden algılanan kontrolün niteliği ile ergenin psikososyal uyumu ve arkadaşlıkları arasındaki ilişkiler: benlik değerinin aracı rolü. Türk Psikoloji Dergisi. 2008; 23:92-107.
33. Rångtell FH, van Egmond L, Karamchedu S, Boukas A, Moulis A, Ilemosoglou M, et al. Praise and competence-based self-esteem alter offline gains in motor skills. Digitala Vetenskapliga Arkivet. 2019. urn: nbn: se: uu: diva-382099.
34. Dokuyan M. 12. Sınıf öğrencilerinde algılanan anne-baba tutumları ile benlik saygısı arasındaki ilişkinin incelenmesi. Ahi Evran Üniversitesi Sosyal Bilimler Enstitüsü Dergisi. 2016;2:1-21.
35. Harter S. Issues in the assessment of the self-concept of children and adolescents. In: La Greca AM, editor. Through the eyes of the child: Obtaining self-reports from children and adolescents, Allyn & Bacon, Needham Heights. 1990. 292-325.
36. Baumrind D. Effective parenting during the early adolescent transition. In Cowan PA, Hetherington EM, editors. Family transitions. Lawrence Erlbaum Associates, Inc. 1991.111-63
37. Arslan C. Anger, self-esteem, and perceived social support in adolescence. Social Behavior and Personality: an international journal. 2009;37:555-64.
38. Erkman F, Caner A, Sart HZ, Börkan B, Şahan K. Influence of perceived teacher acceptance, self-concept, and school attitude on the academic achievement of school-age children in Turkey. Cross-Cultural Research. 2010; 44:295-309.
39. Reddy R, Rhodes JE, Mulhall P. The influence of teacher support on student adjustment in the middle school years: a latent growth curve study. Dev Psychopathol. 2003;1:119-38.
40. Atalay D, Özyürek A. Ergenlerde arkadaşlık ilişkileri ve akran sapması. Journal of Humanities and Tourism Research. 2020;10:249-61.
41. Günaydın B, Yöndem ZD. Ergenlerde akran bağlılığının bazı değişkenler açısından incelenmesi. Abant İzzet Baysal Üniversitesi Eğitim Fakültesi Dergisi. 2007;7:129-39.
42. Patrick H, Ryan AM, Alfeld-Liro C, Fredricks JA, Hruda LZ, Eccles JS. Adolescents' commitment to developing talent: the role of peers in continuing motivation for sports and the arts. Journal of youth and adolescence. 1999;28:741-63.
43. Yi J, Kim MA, Hong JS, Akter J. Childhood cancer survivors' experiences in school re-entry in South Korea: focusing on academic problems and peer victimization. Child Youth. 2016;67:263-9.
44. Kim Y, Lee KS, Koh KN. Difficulties faced by long-term childhood cancer survivors: A qualitative study. Eur J Oncol Nurs. 2018; 36:129-34.
45. Arpaci T, Altay N, Yozgat AK, Yaralı HN, Özbek NY. 'Trying to catch up with life': the expectations and views of adolescent survivors of childhood acute lymphoblastic leukemia about long-term follow-up care: a qualitative research. Eur J Cancer Care (Engl). 2022;31:e13667.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Esophageal Atresia: Comparison of Mortality Classifications and Factors Affecting Mortality

Trakeoözofageal Fistül/Özofageal Atrezili Hastalarda Mortalite Skorlarının ve Mortaliteye Etki Eden Faktörlerin Karşılaştırılması

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Cite this article as: Kocael F, Sivrikaya Yıldırım C, Üstün Elmas K, Gürpınar AN, Parlak A, Köksal N. Esophageal atresia: comparison of mortality classifications and factors affecting mortality. J Curr Pediatr. 2026;24(2):69-76

Abstract

Introduction: Esophageal atresia (EA) is a disease that is accompanied by other concomitant systemic anomalies in 30-70% of cases. In this study, we aimed to evaluate the antenatal and postnatal factors that influence mortality in patients with EA, examine the relationship between these factors and mortality and compare the effectiveness of mortality classification defined in the literature in assessing mortality.

Materials and Methods: This retrospective study examined records of patients diagnosed with EA who were hospitalized between 2010 and 2020 in the NICU. Patient demographics, additional congenital anomalies, and Montreal, Bremen, and Spitz mortality classifications were evaluated.

Results: A total of 71 patients were included in the study. The mean gestational week of the patients was 35.7 ± 2.5, and the mean birth weight was 2382 ± 715 g. The mortality rate was 29.5% (21/71).

All patients with three or more concomitant anomalies had died. All mortality classifications were significant in predicting mortality. Low birth weight, prematurity, low APGAR score, presence of preoperative pneumonia, and presence of preoperative intubation were concluded to be significant in predicting mortality. The highest correlation between mortality and classification systems was found for the Montreal classification.

Conclusion: The identification of risk factors determining mortality remains controversial. Prematurity, a low APGAR score, the presence of more than three anomalies, preoperative pneumonia, and the need for invasive mechanical ventilation have been found to increase mortality in EA. In conclusion, there is a need for new classification systems that evaluate various parameters that affect mortality, including multiple congenital anomalies.

Keywords
Esophageal atresia (EA), tracheoesophageal fistula, mortality, neonates, mortality classification

Anahtar kelimeler
Özafagus atrezisi, trakeoözofageal fistül (TÖF), mortalite, yenidoğan, mortalite skorlaması

Received/Geliş Tarihi : 09.10.2024
Accepted/Kabul Tarihi : 06.03.2025
Epub : 02.03.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026
DOI:10.4274/jcp.2025.70846

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Öz

Giriş: Trekeo-özofagial fistül (TÖF), %30-70'inde eşlik eden başka sistem anomalileri olan bir hastalıktır. Hastalarda mortaliteyi belirlemek için farklı risk skorlamaları kullanılmaktadır. Bu çalışmada, TÖF olan hastalarda mortaliteyi etkileyen prenatal ve postnatal faktörleri, bu faktörler ile mortalite ve morbiditeler arasındaki ilişkiyi değerlendirmeyi, literatürde tanımlanmış mortalite skorları ile bu skorların mortalite ve morbiditenin değerlendirilmesinde ne kadar etkin oldukları ve birbirlerine üstünlüklerinin karşılaştırılması amaçlandı.

Gereç ve Yöntem: Bu retrospektif çalışmaya 2010 ile 2020 yılları arasında yenidoğan yoğun bakım ünitesine yatırılarak izlenen TÖF tanısı alan hastaların kayıtları

incelenmiştir. Hastaların demografik özellikleri, ek konjenital anomalileri yanında Montreal, Bremen ve Spitz mortalite skorları kaydedildi.
Bulgular: Çalışmaya toplam 71 hasta dahil edildi. Hastaların ortalama gestasyon haftası 35.7 ± 2.5, doğum ağırlığı 2382 ± 715 gr idi. Mortalite oranı %29.5 (21/71) idi.
Eşlik eden anomali sayısı üç ve üzeri olan tüm hastalar kaybedildi. Düşük doğum ağırlığı, prematürite, APGAR skorunun düşük olması, operasyon öncesi pnömoni ve invaziv mekanik ventilasyon ihtiyacı mortaliteyi öngörmede anlamlı saptandı (p<0.001, p= 0,035, p=0.03, p<0,001, p<0.001). Mortalite skorlarının hepsi mortaliteyi ön görmede anlamlı saptandı. Mortalite ve skorlama sistemleri arasında en yüksek korelasyon ise Montreal sınıflamasında bulundu (r=0.71, p <0,001).
Sonuç: TÖF'lü hastalarda, mortaliteyi belirleyen risk faktörlerinin tanımlanması tartışmalı olmaya devam etmektedir. Prematüre doğum, düşük APGAR skoru, üçten fazla konjenital anomalinin varlığı, ameliyat öncesi pnömoni ve invaziv mekanik ventilasyon ihtiyacının TÖF'te mortaliteyi arttırdığı bulunmuştur. Sonuç olarak, çoklu konjenital anomaliler dahil olmak üzere mortaliteyi etkileyen çeşitli parametreleri değerlendiren yeni sınıflandırma sistemlerine ihtiyaç vardır.

Introduction

Esophageal atresia (EA)/tracheoesophageal fistula (TEF) is a disease first described in 1670 and can present with multiple anomalies (1). Its etiology is largely unknown; however, it is thought to be multifactorial (2). Although different incidences are reported in different countries, it is considered to occur in 1 in 2500 live births (2).

There are other concomitant systemic anomalies in 30-70% of infants with TEF. These are congenital heart disease (CHD), urinary system anomalies, gastrointestinal system anomalies, neurological system anomalies, and skeletal system anomalies (2). One of the most common associated congenital anomalies is VACTERL association (vertebral, anorectal, cardiac, tracheoesophageal, renal, and limb anomalies). Various mortality risk classifications have been used to determine patient mortality (3).

The Waterston classification was first defined in 1962, after which the Montreal, Bremen, and Spitz classifications were introduced (4). These classifications evaluate the patient's birth weight, cardiac pathology, congenital anomalies, and inability to wean from the ventilator and may sometimes fail to adequately predict mortality in most patients. In this study, in addition to these parameters, we also assessed the effectiveness of antenatal and postnatal characteristics of patients, operative time, clinical conditions such as preoperative pneumonia and sepsis, duration of invasive mechanical ventilation before and after surgery, and concomitant neonatal morbidities in predicting mortality.

We aimed to evaluate the aforementioned factors that influence mortality in patients with TEF, examine the relationship between these factors and mortality and morbidity, and compare the mortality classifications defined in the literature. Thus, we aimed to establish what parameters could be considered when creating a novel mortality classification.

Materials and Methods

This retrospective study included patients diagnosed with EA who were hospitalized between January 2010 and September 2020 in the Neonatal Intensive Care Unit (NICU) of the Pediatrics and Pediatric Surgery Departments of Bursa Uludag University Faculty of Medicine.

The study received approval from the institution's ethics committee (Bursa Uludağ

University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2011-KAEK-26/620, date: 13.11.2020).

Gestational age, birth height-weight-head circumference and percentiles, mode of delivery, sex, multiple pregnancies, number of pregnancies, number of births, maternal age, antenatal steroid history, maternal diabetes history, prolonged premature rupture of the membranes, pre-eclampsia/eclampsia, presence of chorioamnionitis, polyhydramnios, oligohydramnios, antenatal diagnosis, and in vitro fertilization information were recorded for all patients.

At clinical follow-up of the infants, APGAR scores of the 1st and 5th minute, sepsis findings, pneumonia findings, oxygen requirement, mechanical ventilation requirement, day of transition to full enteral feeding, length of hospital stay, height-weight-head circumference and percentiles at discharge, CHD, central nervous system anomaly, presence of coloboma, urinary system anomaly, gastrointestinal tract anomaly, ear anomaly, choanal atresia, genital anomaly, chromosomal anomaly, esophageal atresia type, status of intraventricular hemorrhage, presence and stage of retinopathy of prematurity, presence and stage of bronchopulmonary dysplasia, presence of necrotizing enterocolitis, operative day (time), presence of preoperative pneumonia and intubation, and presence and day of mortality were recorded.

The mortality classification systems of the patients according to Waterston, Montreal, Bremen, and Spitz were calculated (4). The effectiveness of these scores in assessing mortality and morbidity was compared.

Statistical Analysis

Characteristics, mortality classifications of discharged and deceased (exitus) patients, and their relationship to mortality were calculated using the SPSS version 22 program (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The Shapiro-Wilk test was used to examine the fit of the data to the normal distribution. Comparisons between two groups were performed with t-tests for normally distributed parameters. For parameters that did not have a normal distribution, comparisons between the two groups were made using the Mann-Whitney U test, and multiple comparisons were made using the Kruskal-Wallis test. Data with a normal distribution are shown as the mean ± standard deviation (SD), and those without a normal distribution are shown as a percentage (%). Pearson chi-square analysis was used to analyze the cross-tabulations. Spearman correlation analysis was performed for the variables that did not have a normal distribution to determine the strength and direction of the relationship between the variables. Multivariate logistic regression analysis was applied to identify risk factors for mortality. A p-value of <0.05 was considered statistically significant for all tests.

Results

During the ten years studied, a total of 71 infants with a diagnosis of EA were admitted to the NICU. The mean gestational age was 35.7±2.5, and the mean birth weight was 2382 g ± 715. Nine (12.6%) patients had a birth weight below 1500 g, and 41 (57.7%) patients were premature. Only 6 (8.5%) patients had an antenatal diagnosis (Table 1). Thirty (42%) patients were diagnosed after admission to the NICU, 27 (38%) patients were diagnosed by radiography after suspicion in the delivery room, and 6 (8.5%) patients were diagnosed by the onset of symptoms after handover to the mother. The most common EA type was EA+distal TEF (Type C) in 66 (93%) patients.

Concomitant Anomalies

Fifty-seven (80.3%) patients had additional concomitant anomalies, with the most common concomitant anomaly being cardiovascular in 52 (73.2%) patients. The most common cardiac anomalies were patent ductus arteriosus (PDA), atrial septal defect (ASD), and ventricular septal defect. The most common skeletal anomalies were butterfly vertebrae and hemivertebrae (5/71). Anal atresia was present in 7 (9.8%) patients, undescended testis in 3 (4.2%) patients, and diaphragmatic hernia in 2 patients. Two (2.8%) patients had VACTERL association, 1 (1.4%) patient had CHARGE syndrome, 4 (5.6%) patients had trisomy 18, and 3 (4.2%) patients had trisomy 21 (Table 2). Among the patients who died following the operation, 3 had trisomy 18, 1 had Down syndrome, 1 had a diaphragmatic hernia, 2 had anal atresia, and 1 had VACTERL association. A common feature among all these patients was the presence of a congenital heart anomaly.

Mortality

Of the 71 patients, 21 (29.5%) died in the neonatal period. Seven (9.8%) of the exitus patients died before they could be operated on. Of the 64 operated patients, 51 (71.8%) were discharged after successful surgery. The characteristics of the exitus and discharged patients are given in Table 2. Of the 21 patients who died, 20 (28.1 %) had type C esophageal atresia and 1 (1.4 %) had type H esophageal atresia. All patients who died before the operation had severe congenital heart anomalies.

Birth weight and 1-minute APGAR scores were lower ($p<0.001$, $p=0.03$) in exitus patients than in discharged

Table 1. Patients' demographic and clinical characteristics

Birth weight (gr), mean ± SD	2382 ± 715
Gestational week, mean ± SD	35.7 ± 2.5
Birth weight < 1500 gr n (%)	9 (12.6)
Prematurity n (%)	41 (57.7)
Male n (%)	34 (47.8)
Caesarean n (%)	46 (64.8)
APGAR 1st minute, median (min-max)	6.5 (1-10)
APGAR 5th minute, median (min-max)	8 (1-10)
Antenatal diagnosis n (%)	6 (8.5)
Polyhydramnios n (%)	25 (35)
Presence of preoperative pneumonia n (%)	19 (26.8)
Presence of preoperative intubation n (%)	16 (22.5)
Operated patients n (%)	64 (90.1)
The age at which the operation was done (day), median (min-max)	3 (1-16)
Duration of invasive mechanical ventilation (day), median (min-max)	3 (0-166)
Mortality n (%)	21 (29.5)

patients. In addition, prematurity and birth weight less than 1500 grams were identified as factors that increased mortality (p=0.035, p=0.016). Among the exitus patients, 14 (87.5%) had preoperative intubation, and 15 (78.9%) had preoperative pneumonia. In addition, it was found that the presence of preoperative intubation and pneumonia and the long duration of invasive mechanical ventilation (before and after surgery) were among the important factors that significantly increased mortality (p<0.001 for each parameter) (Table 2).

When all anomalies associated with TEF were evaluated, it was concluded that concomitant isolated CHD did not increase mortality, whereas the number of concomitant anomalies of two or more significantly increased mortality. While all 4 patients with trisomy 18 anomaly and all patients diagnosed with CHARGE and VACTERL died, only one of the 3 patients diagnosed with Down syndrome died (Table 3). The most common cause of mortality was infection in 13 (65%) patients. The patient with type H esophageal atresia had severe congenital heart disease, specifically type 4 truncus arteriosus, along with choanal atresia, hemivertebrae, various skeletal anomalies, and cerebral ischemic infarction. Unfortunately, this patient passed away before surgery could be performed.

Mortality Classification Systems

The distribution of patients by group within the Waterston, Montreal, Bremen, and Spitz classification systems is given in Table 4. All mortality classification systems were significant in predicting mortality (Tables 5, 6). The highest correlation between mortality and classification systems was found for the Montreal classification (Table 5, 6) (p <0.001, r=0.70).

Discussion

TEF is a congenital anomaly that requires early diagnosis, surgical treatment, and a multidisciplinary approach (5). Mortality rates vary between 9-59.7% in the literature (4,6-9). Of the 71 patients included in our study, 21 (29.5%) died in the neonatal period. The wide range of mortality rates by country suggests that they vary according to the level of a country's development.

The mean birth weight of the exitus patients in the current study was 2400.9±639.4 g. Birth weight below 1500 g and prematurity were found to be significant risk factors for mortality, similar to those reported in the literature (p 0.001) (10-12). Moreover, the APGAR scores of the exitus patients were calculated as 5-8 in the 1st and 5th minutes, respectively, and the low APGAR score was determined to be significant in predicting mortality (p=0.03, p=0.02). Similar studies in the literature reported that a low APGAR score was significant in predicting mortality (10,13).

Additional congenital anomalies may accompany TEF. The most common accompanying congenital anomalies are anomalies of the cardiovascular system. In two retrospective

Table 2. Comparison of demographic-characteristics of death and discharged patients

	Death n=21 (%29.5)	**Discharged n=50 (%70.4)**	**p**
Birth weight (gr) mean ± SD	2400.9±639.4	2661.04±665.2	**<0.001**[a]
Birth weight <1500 gr n (%)	6 (28.5)	3 (6)	**0.016**[a]
Gestational week mean ± SD	34.5±2.2	36.2±2.5	0.1[a]
Prematurity n (%)	16 (76)	25 (50)	**0.035**[b]
Male n (%)	7 (35)	27 (52.9)	0.197[b]
Caesarean n (%)	14 (70)	32 (62)	0.783[b]
APGAR 1st minute, median (min-max)	5 (1.9)	8 (1.10)	**0.03**[c]
APGAR 5th minute, median (min-max)	8 (3.10)	8 (1.10)	**0.02**[c]
Antenatal diagnosis n (%)	3 (15)	3 (5.8)	0.118[b]
Polyhydramnios n (%)	10 (50)	15 (29)	0.258[b]
Presence of preoperative pneumonia n (%)	15 (78.9)	4 (21)	**<0.001**[b]
Presence of preoperative intubation n (%)	14 (87.5)	2 (12.5)	**<0.001**[b]
Operated patients n (%)	16 (25)	48 (75)	**0.021**[b]
The age at which the operation was done, median (min-max)	5 (1-16)	3 (2-10)	0.06[c]
Duration of invasive mechanical ventilation (day), median (min-max)	15 (2-59)	3 (0-166)	**<0.001**[c]

[a]: T-test, [b]: Chi-square, [c]: Mann-Whitney U Test

Table 3. Concomitant anomalies of death and discharged patients			
Clinical characteristics of patients	**Death n=21 (%29.5)**	**Discharged n=50 (%70.4)**	**p**
Anomaly present	**12 (25)**	**36 (75)**	0.09[a]
CHD*	3 (14.2)	18 (85.7)	**0.048**[a]
Urinary System Anomaly	-	2	
Limb-Vertebra Anomaly	-	1	
Central Nervous System Anomaly	-	1	
Gastrointestinal Tract Anomaly	-	2	
CHD + Limb-Vertebra Anomaly	3	-	
CHD + Genital System Anomaly		2	
CHD + Gastrointestinal Tract Anomaly	1 (50)	1 (50)	
CHD + Urinary System Anomaly	-	2	
Genital System Anomaly + Ear Anomaly	-	1	
CHD + Central Nervous System Anomaly	-	1	
CHD + Urinary System Anomaly + Gastrointestinal Tract Anomaly	-	3	
CHD + Limb-Vertebra Anomaly + Urinary System Anomaly	-	2	
CHD + Urinary System Anomaly + Limb-Vertebra Anomaly + Central Nervous System Anomaly	1	-	
CHD+ Urinary System Anomaly + Limb-Vertebra Anomaly + Gastrointestinal Tract Anomaly	2	-	
Diaphragmatic Hernia +CHD	1	-	
Diaphragmatic Hernia + CHD + Limb-Vertebra Anomaly	1		
Anomaly absent	1 (7.6)	12 (92.3)	
Chromosomal anomaly	5 (71)	2 (29)	
Syndromic patients	3	-	
[a]: Chi-square, *CHD: Congenital heart disease			

cohort studies in the literature, the incidence of cardiac anomalies was reported to be 33-47% (6,14). In our study, the most common concomitant anomaly was cardiovascular system anomaly.

Considering the parameters used to predict mortality when evaluating mortality classification systems in patients with TEF, the presence of cardiac anomalies and concomitant severe anomalies are included in the classifications. Few studies have examined the association between mortality and anomalies, except for CHD. In our study, concomitant anomalies were present in 12 of the 21 exitus patients, and the most common isolated anomaly was severe CHD. It has been reported that when a concomitant systemic anomaly was added to TEF, the mortality rate was 3.2%, but the addition of two or more systems increased mortality up to 40%. Our study also found that the mortality rate was higher in patients with two or more systemic anomalies. In the study by German et al. (15), the presence of two or more anomalies was emphasized to increase mortality.

The presence of preoperative pneumonia was significant for mortality in our study (p 0.001), which is similar to the literature (16). In addition, in line with the literature, the presence of preoperative intubation was also identified as significant for mortality (p <0.001) (17,18).

Syndromes of known genetic etiology with additional malformations are present in approximately half of the cases. A genetic cause is present in 11-12% of patients diagnosed with TEF. Nonsyndromal TEF is generally considered a multifactorial disorder, suggesting that epigenetic and environmental factors also contribute to the disease (2). In our study, 2 (2.8%) patients had VACTERL association, 1 (1.4%) patient had CHARGE syndrome, 4 (5.6%) patients had trisomy 18, and 3 (4.2%) patients had trisomy 21. All patients diagnosed with trisomy 18 died. In the study by Sparey et al. (19), an increased mortality rate was

Table 4. Mortality classifications and their relationships with reported mortality			
Mortality classification	**Discharged n (%)**	**Death n (%)**	**Total**
Waterston			
A	18 (94.7)	1 (5.3)	19
B	23 (92)	2 (8)	25
C	9 (33.3)	18 (66)	27
Montreal			
1	44 (91.6)	4 (8.3)	48
2	6 (26)	17 (73.9)	23
Bremen with complication			
1	1 (50)	1 (50)	2
2	7 (38)	11 (61)	18
3	0	4 (100)	4
Bremen without complication			
1	40 (95.2)	2 (4.7)	42
2	3 (60)	2 (40)	5
0	0	1 (100)	1
Spitz			
1	40 (93)	3 (7)	43
2	10 (43.4)	13 (56.5)	23
3	0	5 (100)	5

Table 5. Correlation of mortality classification with reported mortality					
Mortality	**Waterston**	**Montreal**	**Bremen with complication**	**Bremen without complication**	**Spitz**
p	<0.001	<0.001	0.13	<0.001	<0.001
r	0.55	**0.70**	0.31	0.50	0.62

Table 6. Relative values of mortality classifications in predicting mortality			
	Waterston	**Montreal**	**Spitz**
Odds ratio	0.392	160	14.54
%95 Confidence interval	0.01-0.264	15.2-1683.26	3.48-60.8
p-value	<0.001	<0.001	<0.001

determined in patients with TEF diagnosed with a genetic disease (19).

Perioperative classification systems have been established to determine prognosis in patients with TEF based on preoperative clinical factors and patient characteristics (4). In 1962, Waterson et al. (20) identified the presence of low birth weight, congenital anomalies, and pneumonia as major risk factors and developed a classification system based on these factors. However, this classification system did not take into account the nature of the patients' congenital anomalies, length of stay on the ventilator, or other factors affecting mortality (11). The Montreal classification was developed in 1993 by Poenaru et al. (11) as an alternative to the Waterston classification. This classification system is based on whether the patient is ventilator dependent or not and whether the accompanying congenital anomaly is

mild or severe. On the other hand, in 1994, Spitz et al. (21) created a new classification system based on the patients' birth weight and the degree of CHD. In 2000, Yaygu et al. (16) created a new classification system as an adaptation of the Spitz classification by adding an assessment of the patient's pulmonary status before surgery.

There are few studies in the literature that evaluate each system and its relationship to mortality. A retrospective study by Peters et al. (4) in England, which included 248 patients over a 20-year period, compared the Waterston, Spitz, and Montreal classifications, and all were significant in predicting mortality, similar to our study. The study by Teich et al. (22) compared the Waterston and Montreal classifications and concluded that the Montreal classification was more successful in identifying high-risk patient groups. In our study, the Montreal classification system was found to be the system with the highest correlation scores.

In a study conducted between 1999 and 2012 by Sulkowski et al. (17) in the USA with 3479 patients, the evaluation of mortality factors showed that birth weight, CHD, genetic anomalies, and being on an invasive mechanical ventilator before surgery were factors that increased mortality. Similarly, in our study, the presence of preoperative intubation, low birth weight, and genetic anomalies (urinary system anomaly) were found to be factors that increased mortality.

TEF may be associated with many congenital anomalies, with CHD being the most common (6,17,23). Bremen and Spitz classifications assessed the presence of severe CHD as a parameter that affected mortality (12,16).

In the study by Sulkowski et al. (17), the presence of concomitant anomalies was found to be a factor in predicting mortality. However, there is no study in the literature that evaluates multiple mortality-affecting independent risk factors, including all congenital anomalies. When considering the presence of multiple anomalies in cases diagnosed with TEF, the question of which anomaly is the main factor influencing mortality remains controversial. In our study, all 5 patients who died without surgery had severe congenital heart disease. With the exception of patients with severe CHD or multiple anomalies incompatible with life, the life expectancy of these patients has increased with advances in medicine. Therefore, there is a need for new classification systems that will incorporate patient CHD and other associated risk factors when determining mortality risk. The prenatal factors need to be considered and actually a prenatal score calculated based on the prenatal signs could be a great help to predict the postnatal mortality and decide or not to interrupt the pregnancy.

Study Limitations

The relatively small number of patients and their retrospective evaluation from patient records are the limitations of our study. In addition, surgical techniques that may influence mortality were not evaluated in this study.

Conclusion

The survival rate of patients with TEF/EA has increased in recent years. The identification of risk factors that determine survival remains controversial. We believe that a new system that assesses mortality risk with a scoring system rather than a classification and evaluates birth weight, prematurity, low APGAR score, length of stay on an invasive mechanical ventilator, number of concomitant anomalies, preoperative intubation, presence of preoperative pneumonia, presence of syndromes, and chromosomal anomalies is needed. Large-scale studies may contribute to the development of new mortality classification system.

Ethics

Ethics Committee Approval: The study received approval from the institution's ethics committee (Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2011-KAEK-26/620, date: 13.11.2020).

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. German JC, Mahour GH, Woolley MM. The twin with esophageal atresia. J Pediatr Surg. 1979;14:432–5.
2. Brosens E, Ploeg M, van Bever Y, Koopmans AE, IJsselstijn H, Rottier RJ, et al. Clinical and etiological heterogeneity in patients with tracheo-esophageal malformations and associated anomalies. Eur J Med Genet. 2014;57:440-52.
3. Yamoto M, Nomura A, Fukumoto K, Takahashi T, Nakaya K, Sekioka A, et al. New prognostic classification and managements in infants with esophageal atresia. Pediatr Surg Int. 2018;34:1019-26.
4. Peters RT, Ragab H, Columb MO, Bruce J, MacKinnon RJ, Craigie RJ. Mortality and morbidity in oesophageal atresia. Pediatr Surg Int. 2017;33:989-94.
5. Hunt RW, Perkins EJ, King S. Peri-operative management of neonates with oesophageal atresia and tracheo-oesophageal fistula. Paediatr Respir Rev. 2016;19:3-9.

6. Wang B, Tashiro J, Allan BJ, Sola JE, Parikh PP, Hogan AR, et al. A nationwide analysis of clinical outcomes among newborns with esophageal atresia and tracheoesophageal fistulas in the United States. J Surg Res. 2014;190:604-12.
7. Celayir S, İlce Z, Tekand GT, Emir H, Yeker Y, Kaya G, et al. The experience with esophagus atresia (1978-2000). Cerrahpasa Med J. 2008;33:86-92.
8. Al-Salem AH, Kothari M, Oquaish M, Suzi K, Mohammad D. Morbidity and mortality in esophageal atresia and tracheoesophageal fistula: a 20-year review. Ann Pediatr Surg. 2013:9:93–8.
9. Karaveli C, Aslan A, Akilli A, Karaguzel G, Melikoglu M. Evaluation of the prognostic classifications in esophageal atresia and tracheoesophageal fistula. Turkish J Ped Surgery. 2006:20:75-8.
10. Vukadin M, Savic D, Malikovic A, Jovanovic D, Milickovic M, Bosnic S, et al. Analysis of prognostic factors and mortality in children with esophageal atresia. Indian J Pediatr. 2015;82:586-90.
11. Poenaru D, Laberge JM, Neilson IR, Guttman FM. A new prognostic classification for esophageal atresia. Surgery. 1993;113:426-32.
12. Okamoto T, Takamizawa S, Arai H, Bitoh Y, Nakao M, Yokoi A, et al. Esophageal atresia: prognostic classification revisited. Surgery. 2009;145:675-81.
13. Prato AP, Carlucci M, Bagolan P et al. A cross-sectional nationwide survey on esophageal atresia and tracheoesophageal fistula. J Pediatr Surg. 2015;50:1441-56.
14. Maheshwari R, Trivedi A, Walker K, Holland AJ. Retrospective cohort study of long-gap oesophageal atresia. J Paediatr Child Health. 2013;49:845-9.
15. German JC, Mahour GH, Woolley MM. Esophageal atresia and associated anomalies. J Pediatr Surg. 1976;11:299-306.
16. Yagyu M, Gitter H, Richter B, Booss D. Esophageal atresia in Bremen, Germany--evaluation of preoperative risk classification in esophageal atresia. J Pediatr Surg. 2000;35:584-7.
17. Sulkowski JP, Cooper JN, Lopez JJ, Jadcherla Y, Cuenot A, Mattei P, et al. Morbidity and mortality in patients with esophageal atresia. Surgery. 2014156:483-91.
18. Sugito K, Koshinaga T, Hoshino M, Inoue M, Goto H, Ikeda T, et al. Study of 24 cases with congenital esophageal atresia: what are the risk factors? Pediatr Int. 2006;48:616-21.
19. Sparey C, Jawaheer G, Barrett AM, Robson SC. Esophageal atresia in the Northern Region Congenital Anomaly Survey, 1985-1997: prenatal diagnosis and outcome. Am J Obstet Gynecol. 2000;182:427-31.
20. Waterston DJ, Carter RB, Aberdeen E. Oesophageal atresia: tracheo-oesophageal fistula: a study of survival in 218 infants. The Lancet. 1962;279:819-22.
21. Spitz L, Kiely EM, Morecroft JA, Drake DP. Oesophageal atresia: at-risk groups for the 1990s. J Pediatr Surg. 1994;29:723-5.
22. Teich S, Barton DP, Ginn-Pease ME, King DR. Prognostic classification for esophageal atresia and tracheoesophageal fistula: Waterston versus Montreal. J Pediatr Surg. 1997;32:1075-9; discussion 1079-80.
23. Seo J, Kim DY, Kim AR, Kim DY, Kim SC, Kim IK, et al. An 18-year experience of tracheoesophageal fistula and esophageal atresia. Korean J Pediatr. 2010;53:705-10.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

In Vitro Evaluation of the Effect of Mixing Iron Supplements with Orange Juice on the Surface Properties and Discoloration of Primary Teeth

Demir Takviyelerinin Portakal Suyu ile Karıştırılmasının Süt Dişi Yüzey Özellikleri ve Renk Değişimine Etkisinin Değerlendirilmesi

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Cite this article as: Akçay Güngör E, Güçyetmez Topal B. In vitro evaluation of the effect of mixing iron supplements with orange juice on the surface properties and discoloration of primary teeth. J Curr Pediatr. 2026;24(2):77-88

Abstract

Introduction: Tooth discoloration is a common side effect of liquid iron supplements used in pediatric patients. This in vitro study aimed to evaluate the effects of ferric polymaltose, ferrous sulfate, and Lipofer® iron supplements, when mixed with orange juice, on the color change and enamel surface roughness of primary teeth.
Materials and Methods: Sixty primary canine teeth were embedded in acrylic resin and randomly divided into six groups. Each supplement was diluted with either orange juice or distilled water. Samples were immersed in the solutions for 5 minutes daily over 28 days. Color change (ΔE_{00}) was measured with a spectrophotometer, and surface roughness was assessed using a profilometer on days 0, 7, 14, 21, and 28.
Results: Among the iron supplement groups, the Lipofer® group showed significantly less discoloration effect ($p<0.05$). Mixing iron supplements with orange juice had no statistically significant effect on primary teeth discoloration and enamel surface roughness ($p>0.05$).
Conclusions: Lipofer® supplementation caused less discoloration compared to other iron preparations. Based on the findings of our study, the administration of iron supplements mixed with orange juice may be recommended to enhance taste tolerance in pediatric patients.

Keywords
Primary teeth, iron supplements, tooth discoloration

Öz

Giriş: Diş renklenmesi, çocuk hastalarda kullanılan sıvı demir takviyelerinin yaygın bir yan etkisidir. Bu in vitro çalışma, ferrik polimaltoz, ferröz sülfat ve Lipofer® içerikli demir takviyelerinin portakal suyu ile karıştırıldığında süt dişlerinin renk değişimi ve mine yüzey pürüzlülüğü üzerindeki etkilerini değerlendirmeyi amaçlamıştır.
Gereç ve Yöntem: Altmış adet süt kanin dişi akrilik rezine gömülerek rastgele altı gruba ayrıldı. Her demir takviyesi, portakal suyu veya saf su ile seyreltilerek kullanıldı. Örnekler 28 gün boyunca her gün 5 dakika boyunca bu solüsyonlara daldırıldı. Renk değişimi (ΔE_{00}) spektrofotometre ile, yüzey pürüzlülüğü ise profilometre kullanılarak 0., 7., 14., 21. ve 28. günlerde değerlendirildi.
Bulgular: Demir takviyesi grupları arasında, Lipofer® grubu anlamlı derecede daha az renklenme etkisi gösterdi ($p<0,05$). Demir takviyelerinin portakal suyu ile karıştırılması, süt dişlerindeki renk değişimi ve mine yüzey pürüzlülüğü üzerinde istatistiksel olarak anlamlı bir etki göstermedi ($p>0,05$).
Sonuç: Lipofer® takviyesi, diğer demir preparatlarına kıyasla daha az renk değişimine neden oldu. Çalışmamızın bulgularına dayanarak, demir takviyelerinin portakal suyu ile karıştırılarak verilmesi, çocuk hastalarda tat toleransını artırmak amacıyla önerilebilir.

Anahtar kelimeler
Süt dişi, demir takviyeleri, diş renklenmesi

Received/Geliş Tarihi : 05.02.2026
Accepted/Kabul Tarihi : 22.04.2026
Epub : 04.05.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2025.93609

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Introduction

Iron deficiency and the resultant iron deficiency anaemia represent a considerable public health problem, affecting a substantial segment of the global population (1). Oral iron supplements are widely used for the prophylactic prevention and treatment of iron deficiency anaemia. In children, ferrous (Fe^{+2}) iron salts, ferric polymaltose (FP; Fe^{+3}) iron complexes and supplements containing sucrosomial and liposomal ferric pyrophosphate are most commonly used to treat the condition (2).

Tooth discoloration and erosion that may occur due to the use of iron supplements in the form of drops and syrups constitute a significant adverse effect of these supplements in children (3,4). In vitro studies have shown that iron supplements containing ferrous sulphate (FS) and FP possess the potential to discolour primary teeth (3,5).

Ascorbic acid (vitamin C) increases the absorption of iron supplements. Therefore, it is recommended that iron-containing drops and syrups be consumed with fruit juices containing vitamin C (6,7). Orange juice (OJ) has a high ascorbic acid content and influences iron absorption (8). Studies on the effect of iron supplements on the physical properties of primary teeth are available in the literature (4,9,10). However, no study has evaluated the effect of combining different iron supplements with OJ on the enamel surface properties and discoloration of primary teeth.

This study aimed to evaluate the effect of FP, FS and Lipofer® (LF) iron supplements mixed with fresh OJ and distilled water (DW) on the colour change and enamel surface roughness of primary teeth in vitro. The null hypothesis of this study was that mixing different iron supplements with orange juice would not have a significant effect on enamel discoloration or surface roughness of primary teeth compared to distilled water.

Materials and Methods

Approval for this in vitro experimental study was obtained from the Non-Interventional Clinical Research Ethics Committee of Kütahya Health Sciences University (decision no: E-41997688-050.99-130396, date: 11.03.2024).

The power analysis of the study was performed using the G. Power programme (HHU, Düsseldorf, Germany). As established in a preceding study, it was determined that a minimum of eight samples should be incorporated into each group, in accordance with the 95% confidence level (1-α), 95% test power level (1-β), an effect size (d) of 2.017 and a two-way independent samples t-test power analysis (11). The tooth samples were randomly divided into six groups, with 10 teeth in each group. The distribution of the study groups is illustrated in Figure 1.

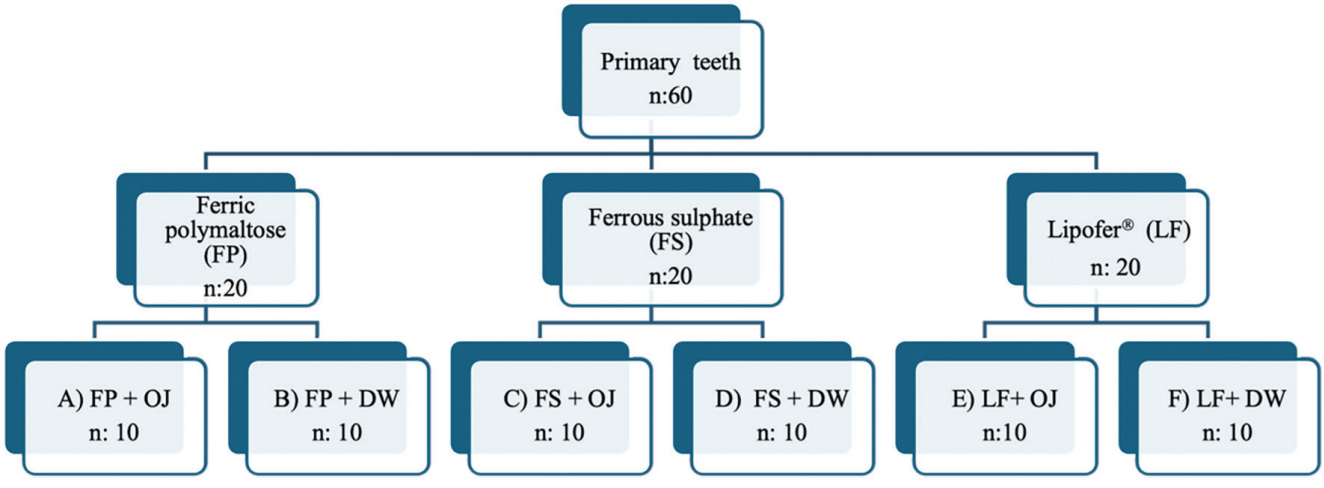

Figure 1. Flow chart. (FP: ferric polymaltose, FS: ferrous sulphate, LF: Lipofer® OJ: orange juice, DW: distilled water)

Specimen Preparation

Sixty primary canine teeth extracted within the last 3 months from patients referred to the clinic and indicated for extraction were used in this study; informed consent for using the samples in the study was obtained from the patients. The teeth were examined under a microscope (Zumax OMS2380; Suzhou, China) and those exhibiting visible caries, cracks or hypomineralised surfaces were excluded from the study. The root tissues were removed with a diamond saw under submerged and water-cooling conditions, exposing the enamel-cementum junction. Thereafter, the soft tissue residues on the crown of the tooth were removed with a periodontal curette and polishing rubber. The teeth were then fixed in acrylic resin (Integra®, Turkey) using round plastic moulds (one cm in diameter) with the buccal crown surface facing upwards.

Iron Supplements

Three distinct iron supplements, each comprising a unique active ingredient, were employed in the treatment of iron deficiency anaemia in paediatric patients (Table 1). Pure, sterile DW (Botofarma®, Turkey) and freshly squeezed OJ, prepared daily, were used to dilute the iron supplements. The samples were stored in artificial saliva between immersion cycles. The artificial saliva consisted of [NaCl, KCl, $CaCl_2$, NaH_2PO_4, urea, and distilled water; pH ≈ 6.8], and was refreshed daily. Samples were maintained at 37°C to simulate intraoral conditions.

Colour Measurement

The colour of the samples was measured at the beginning (t0) and on the 7th (t7), 14th (t14), 21st (t21) and 28th (t28) day using a spectrophotometer (Vita Easy Shade Advance 4.0, Germany). The measuring tip of the device was allowed to contact the samples at an angle of 90° and three measurements were taken from a 5-mm-diameter area and averaged.

The CIEDE2000 colour difference formula was utilised to assess the impact of iron supplements mixed with OJ or DW on the discoloration of primary teeth (12). This formula measures the colour difference by evaluating the effects of lightness, chroma and hue and the interaction between chroma and hue. The measurement was performed using the following equation:

$$\Delta E_{00} = [(\Delta L'/KLSL)^2 + (\Delta C'/KCSC)^2 (\Delta H'/KHSH)^2 + RT (\Delta C'/KC\ SC) (\Delta H'/KHSH)]^{1/2},$$

where ΔL′, ΔC′ and ΔH′ represent the differences in lightness, chroma and hue, respectively. The weighting functions (SL, SC, SH) adjust the total colour variation relative to the location in the L′, a′, b′ colour space. The parametric factors (KL, KC, KH) are the correction terms for the experimental conditions. Finally, RT corresponds to the interaction of differences between chroma and hue in the blue region (12).

Measurement of the Surface Roughness (Ra)

The Ra of the samples was measured at t0 and on t7, t14, t21 and t28 using a mechanical profilometer (Taylor Hobson The Surtronic S 128® S-128®, Leicester, UK). The arithmetic means of the data obtained by measuring three times from the same surface of each tooth sample were recorded.

Scanning Electron Microscopy

For SEM analysis, one representative sample from each group (n=6) was randomly selected after 28 days. The images presented are representative of the observed surface characteristics. The enamel surfaces were examined using

Table 1. Iron supplements used in the study

Medication Content	Trade name and batch no	Active ingredient	Auxiliary ingredients
Ferric Polymaltose (Fe^{+3}) (FP)	Ferrum Hausmann® Drops (Abdilbrahim Turkey) 23T234	Iron (III) Hydroxide Polymaltose Complex	Sugar (Sucrose) Sorbitol 70% Methyl hydroxybenzoate Propyl hydroxybenzoate cream essence, Sodium Hydroxide
Ferrous Sulphate (Fe^{+2}) (FS)	Ferro Sanol B® Syrup (ADEKA Turkey) H008	Iron (II) glycine sulphate complex	Sorbitol, saccharin sodium, sulphuric acid, orange essence (with ethanol), purified water
Lipofer® (LF)	Ocean Mikrofer® Drops (Orzax Turkey) 092310127	Ferric pyrophosphate	Deionised water, grape molasses, lipofer (corn starch, ferric pyrophosphate, hydroxypropyl, methylcellulose, lecithin) thickener: xanthan, gum, preservative: (potassium sorbate, sodium benzoate).

an SEM (LEO 1430 VP model, Germany) at 100×, 500× and 1000× magnifications.

Statistical Analysis

Data obtained from the study were analysed using the statistical software package SPSS (IBM SPSS Statistics, version 25; IBM Corp., Armonk, NY, USA). The effects of the drugs and mixing solutions on colour change and surface roughness were examined by two-way analysis of variance (ANOVA). The main effects were compared using the Bonferroni test and multiple comparisons in interactions were analysed using the Duncan test. A repeated measures two-way ANOVA test was employed to evaluate differences between the specified times. Pairwise comparisons were evaluated using the post hoc Tukey's test. The results of the analyses are presented as mean ± standard deviation. The significance level was set at $p < 0.05$.

Results

Mean Colour Change (ΔE_{00}) Values

The primary effect of iron supplements on the ΔE_{00} value was significant. The Lipofer® (LF) group demonstrated a significantly lower colour change compared to the FP and FS groups at all-time points ($p<0.05$). No statistically significant difference was observed between the FP and FS groups at any point. The primary effect of combining solutions and the interaction of iron supplements with these solutions (iron*solution) did not exhibit any statistically significant impact on the ΔE_{00} value (Table 2).

The $L^* a^* b^*$ Values

The $L^* a^* b^*$ values of the iron supplements and mixture solutions are presented in Table 3. The primary effect of iron supplements on the L^* value was found to be statistically significant ($p < 0.05$). No statistically significant differences in L^* value were observed among the drug groups on day 7. However, statistically significant differences were observed between the supplement groups on the 14th, 21st and 28th day ($p < 0.05$). The LF group demonstrated a significantly lower L^* value change than the FP and FS groups on the 14th, 21st and 28th day ($p < 0.05$).

The primary effect of iron supplements on the a^* value was also statistically significant ($p<0.05$). The FP group demonstrated significantly higher a^* values than the FS and LF groups at all-time points ($p<0.05$).

Table 2. CIEDE (ΔE00) Values of iron supplements and mixture solutions at all times

	Day	Iron Supplements	Mixing Solutions		Total
			Orange Juice	Distilled Water	
CIEDE (ΔE_{00})	7	FP	5.67 ± 0.69	6.13 ± 1.57	**5.90 ± 1.18^{A}**
		FS	4.39 ± 1.64	6.50 ± 1.63	**5.45 ± 1.91^{A}**
		LF	3.49 ± 1.39	3.47 ± 0.76	**3.48 ± 1.07^{B}**
		Total	4.51 ± 1.53	5.37 ± 1.90	**4.94± 1.75**
	14	FP	5.61 ± 0.71	7.36 ± 1.73	**6.48 ± 1.56^{A}**
		FS	6.40 ± 2.62	7.19 ± 2.40	**6.80 ± 2.43^{A}**
		LF	3.05 ± 1.75	3.47 ± 0.63	**3.26 ± 1.27^{B}**
		Total	5.02 ± 2.29	6.01 ± 2.46	**5.51 ± 2.40**
	21	FP	5.76 ± 1.71	8.14 ± 1.92	**6.95 ± 2.13^{A}**
		FS	6.93 ± 2.74	8.24 ± 2.49	**7.59 ± 2.59^{A}**
		LF	3.33 ± 1.91	3.08 ± 1.25	**3.21 ± 1.54^{B}**
		Total	5.34 ± 2.55	6.49 ± 3.08	**5.91 ± 2.85**
	28	FP	5.70 ± 2.42	8.54 ± 1.58	**7.12 ± 2.45^{A}**
		FS	8.17 ± 2.22	9.39 ± 3.027	**8.78 ± 2.61^{A}**
		LF	3.72 ± 2.22	3.94 ± 1.65	**3.83 ± 1.86^{B}**
		Total	5.86 ± 2.85	7.29 ± 3.21	**6.58 ± 3.08**

FP: Ferric polymaltose. FS: Ferrous sulphate. LF: Lipofer®
$^{A-B}$: There is no statistically significant difference between columns with the same letter ($p>0.05$).
Two-way ANOVA. Bonferroni

Table 3. $L^*a^*b^*$ values of iron supplements and mixture solutions at all times

	Day	Iron Supplements	Mixing Solutions		Total
			Orange Juice	Distilled Water	
L^* Value	**7**	**FP**	-8.38 ± 6.39	-4.35 ± 3.44	**-6.71 ± 4.10**
		FS	-2.98 ± 5.52	-6.95 ± 4.70	**-4.96 ± 5.31**
		LF	-2.48 ± 2.14	-2.83 ± 1.54	**-2.65 ± 1.79**
		Total	-4.61 ± 5.47	-4.71 ± 3.71	**-4.66 ± 4.60**
	14	**FP**	-6.71 ± 4.10	-4.95 ± 3.21	**-5.83 ± 3.63^A**
		FS	-4.03 ± 5.50	-6.20 ± 7.20	**-5.11 ± 6.21^A**
		LF	-1.83 ± 1.45	1.66 ± 3.15	**-0.08 ± 2.97^B**
		Total	-4.19 ± 4.32	-3.16 ± 5.81	**-3.67 ± 5.07**
	21	**FP**	-9.55 ± 4.76	-11.98 ±4.60	**-10.76 ± 4.64^A**
		FS	-7.91 ± 6.07	-8.81 ± 5.58	**-8.36 ± 5.58^A**
		LF	-3.66 ± 2.65	1.48 ± 2.82	**-1.09 ± 3.74^B**
		Total	-7.04 ± 5.11	-6.43 ± 7.26	**-6.74 ± 6.19**
	28	**FP**	-8.68 ± 5.40	-8.53 ± 5.16	**-8.60 ± 5.04^A**
		FS	-10.75 ± 4.47	-12.9 ± 5.75	**-11.82 ± 5.04^A**
		LF	-4.51 ± 3.67	0.45 ± 3.50	**-2.03 ± 4.29^B**
		Total	-7.98 ± 5.05	-6.99 ± 7.34	**-7.48 ± 6.23**
a^* Value	**7**	**FP**	5.13 ± 2.54	3.51 ± 2.40	**4.32 ± 2.50^A**
		FS	1.10 ± 0.95	2.18 ± 1.17	**1.64 ± 1.16^B**
		LF	2.00 ± 1.58	1.71 ± 0.56	**1.85 ± 1.14^B**
		Total	2.74 ± 2.46	2.47 ± 1.67	**2.60 ± 2.08**
	14	**FP**	3.35 ± 2.82	2.66 ± 2.22	**3.00 ± 2.45^A**
		FS	-1.61 ± 0.97	-1.30 ± 0.74	**-1.45 ± 0.83^B**
		LF	-0.46 ± 0.78	-1.41 ± 0.85	**-0.94 ± 0.92^B**
		Total	0.42 ± 2.75	-0.01 ± 2.37	**0.20 ± 2.54**
	21	**FP**	3.35 ± 2.78	4.96 ± 2.02	**4.15 ± 2.47^A**
		FS	-1.55 ± 1.94	-0.71 ± 0.73	**-1.13 ± 1.46^B**
		LF	-0.36 ± 1.02	-0.81± 0.98	**-0.59 ± 0.98^B**
		Total	0.47 ± 2.88	1.14 ± 3.06	**0.81 ± 2.95**
	28	**FP**	1.63 ± 2.09	1.93 ± 1.43	**1.78 ± 1.72^A**
		FS	-1.21 ± 1.33	0.36 ± 0.64	**-0.42 ± 1.29^B**
		LF	-0.56 ± 0.58	-1.98 ± 1.28	**-1.27 ± 1.20^B**
		Total	-0.05 ± 1.86	0.10 ± 1.99	**0.02 ± 1.90**
b^* Value	**7**	**FP**	13.41 ± 1.68^{bc}	10.33 ± 1.73^b	**11.87 ± 2.29^A**
		FS	5.56 ± 2.53^{ab}	10.13 ± 1.89^{abc}	**7.85 ± 3.19^B**
		LF	6.03 ± 2.24^{ab}	5.66 ± 2.23^a	**5.85 ± 2.14^B**
		Total	8.33 ± 4.22	8.71 ± 2.88	**8.52 ± 3.57**
	14	**FP**	3.83 ± 5.39	1.43 ± 3.56	**2.63 ± 4.53^A**
		FS	-3.91 ± 2.90	-4.11 ± 3.02	**-4.01 ± 2.83^B**
		LF	-8.76 ± 10.98	-5.85 ± 3.91	**-7.30 ± 8.01^B**
		Total	-2.95 ± 8.66	-2.84 ± 4.59	**-2.89 ± 6.83**
	21	**FP**	3.61 ± 4.57	10.2 ± 4.17	**6.90 ± 5.40^A**
		FS	-0.65 ± 5.97	-2.05 ± 4.29	**-1.35 ± 5.01^B**
		LF	-3.76 ± 4.68	-2.95 ± 5.17	**-3.35 ± 4.72^B**
		Total	-0.26 ± 5.72	1.73 ± 7.51	**0.73 ± 6.66**
	28	**FP**	1.05 ± 4.35	4.00 ± 3.40	**2.52 ± 4.02^A**
		FS	1.90 ± 6.30	2.68 ± 4.32	**2.29 ± 5.17^A**
		LF	-3.81 ± 2.79	-7.75 ± 5.69	**-5.78 ± 4.74^B**
		Total	-0.28 ± 5.12	-0.35 ± 6.90	**-0.32 ± 5.99**

FP: Ferric polymaltose, FS: Ferrous sulphate, LF: Lipofer®

$^{a-b}$There is no statistically significant difference between columns with the same letter ($p > 0.05$).

Iron supplements also demonstrated a statistically significant effect on the b^* values ($p<0.05$), with significant differences observed among the groups ($p<0.05$). The b^* value in the FP group was significantly ($p<0.05$) higher than those in the other groups on the 7th, 14th and 21st day. However, on day 28, the FP and FS groups demonstrated significantly higher b^* values than the LF group ($p<0.05$).

The primary effect of the solution and the interaction between the solution and iron exhibited no statistically significant impact on the $L^*a^*b^*$ values.

Representative images of the tooth samples at the initial time point (day 0) and after 28 days are shown in Figures 2, 3, and 4.

Surface Roughness

No statistically significant differences in surface roughness were seen among the groups at all-time points (Table 4). When the iron supplements were used, the FP group exhibited the highest surface roughness at the conclusion of the 28 days compared to the other groups (0.88±0.6).

Scanning Electron Microscopy Results

Figures 5,6 and 7 presents the SEM images of the tooth samples obtained from each group on the 28th day of the study.

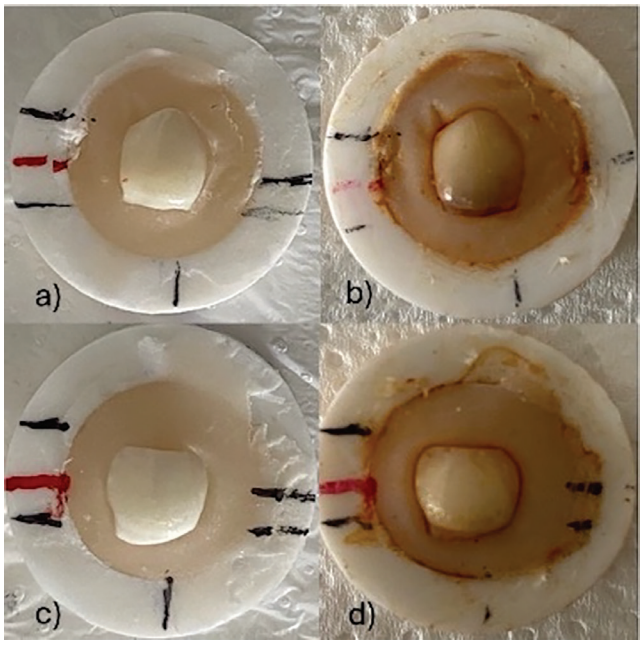

Figure 2. Representative images of tooth samples from the FP+OJ (a, b) and FP+DS (c, d) groups at baseline (a, c) and day 28 (b, d). (FP: ferric polymaltose, OJ: orange juice, DW: distilled water)

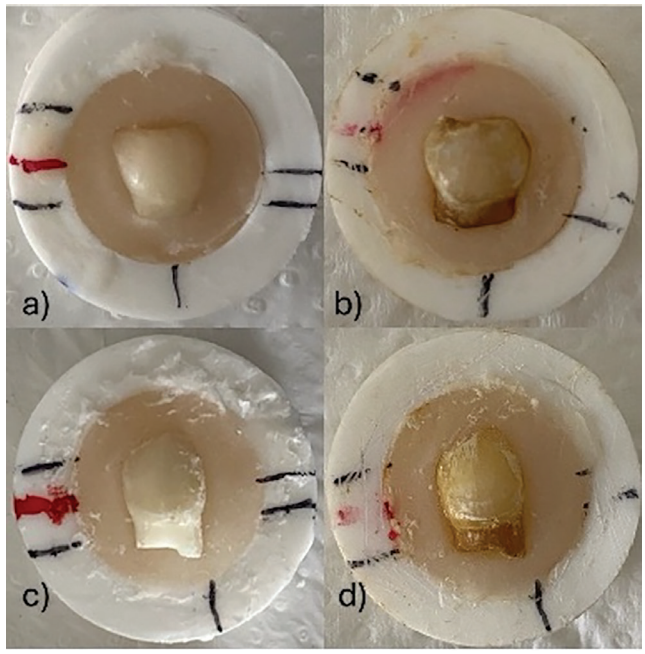

Figure 3. Representative images of tooth samples from the FS+OJ (a, b) and FS+DW (c, d) groups at baseline (a, c) and day 28 (b, d). (FS: ferrous sulphate, OJ: orange juice, DW: distilled water)

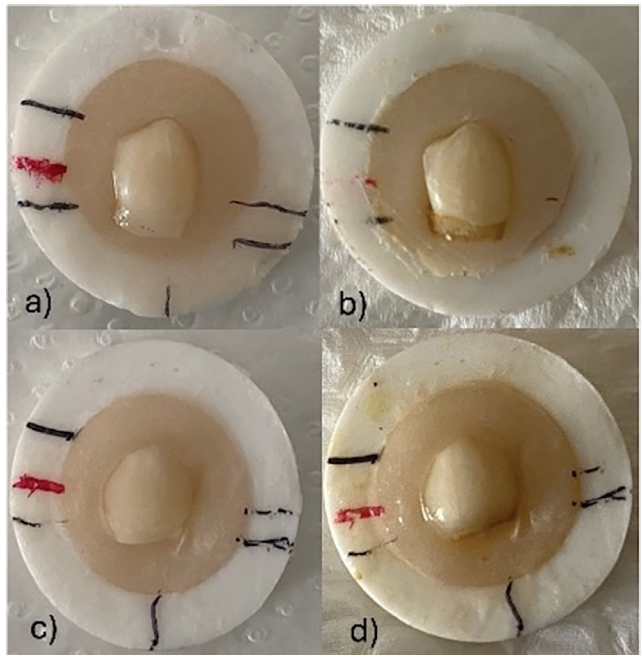

Figure 4. Representative images of tooth samples from the LF+OJ (a, b) and LF+DW (c, d) groups at baseline (a, c) and day 28 (b, d). *(LF: Lipofer®, OJ: orange juice, DW: distilled water)*

Table 4. Surface roughness results of iron supplements and mixture solutions at all times					
	Day	Iron Supplements	Mixing Solutions		Total
			Orange Juice	Distilled Water	
Surface Roughness	7	FP	0.01 ± 0.48	0.03 ± 0.19	0.02 ± 0.35
		FS	-0.33 ± 0.89	0.40 ± 0.68	0.05 ± 0.84
		LF	0.40 ± 0.26	-0.03 ± 0.42	0.18 ± 0.40
		Total	0.04 ± 0.64	0.13 ± 0.49	0.09 ± 0.56
	14	FP	-0.01 ± 0.73	0.26 ± 0.56	0.12 ± 0.63
		FS	0.10 ± 0.62	0.21 ± 0.85	0.15 ± 0.71
		LF	0.60 ± 0.58	0.30 ± 0.63	0.26 ± 0.54
		Total	0.22 ± 0.66	0.33 ± 0.61	0.30 ± 0.64
	21	FP	0.32 ± 0.50	0.48 ± 0.22	0.40 ± 0.38
		FS	-0.16 ± 0.88	0.35 ± 1.18	0.09 ± 1.03
		LF	0.62 ± 0.64	-0.2 ± 0.81	0.41 ± 0.73
		Total	0.26 ± 0.73	0.34 ± 0.79	0.30 ± 0.75
	28	FP	0.88 ± 0.88	0.88 ± 0.45	0.88 ± 0.66
		FS	-0.05 ± 1.19	1.12 ± 0.94	0.53 ± 1.19
		LF	0.68 ± 0.65	0.43 ± 1.52	0.56 ± 1.12
		Total	0.51 ± 0.97	0.81 ± 1.04	0.66 ± 1.00

Two-way ANOVA. Bonferroni
FP: Ferric polymaltose. FS: Ferrous sulphate. LF: Lipofer®

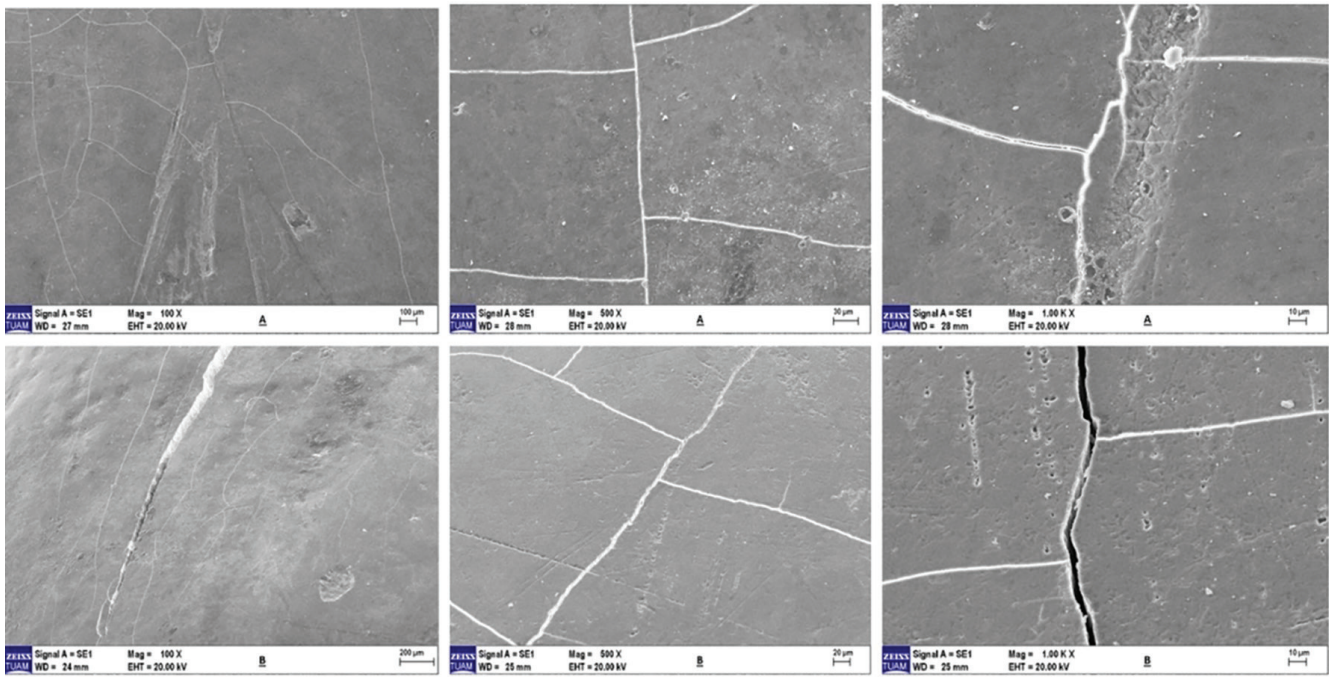

Figure 5. SEM images of tooth samples from the FP+OJ (A) and FP+DW (B) groups at 100×, 500×, and 1000× magnifications. (FP: ferric polymaltose, OJ: orange juice, DW: distilled water)

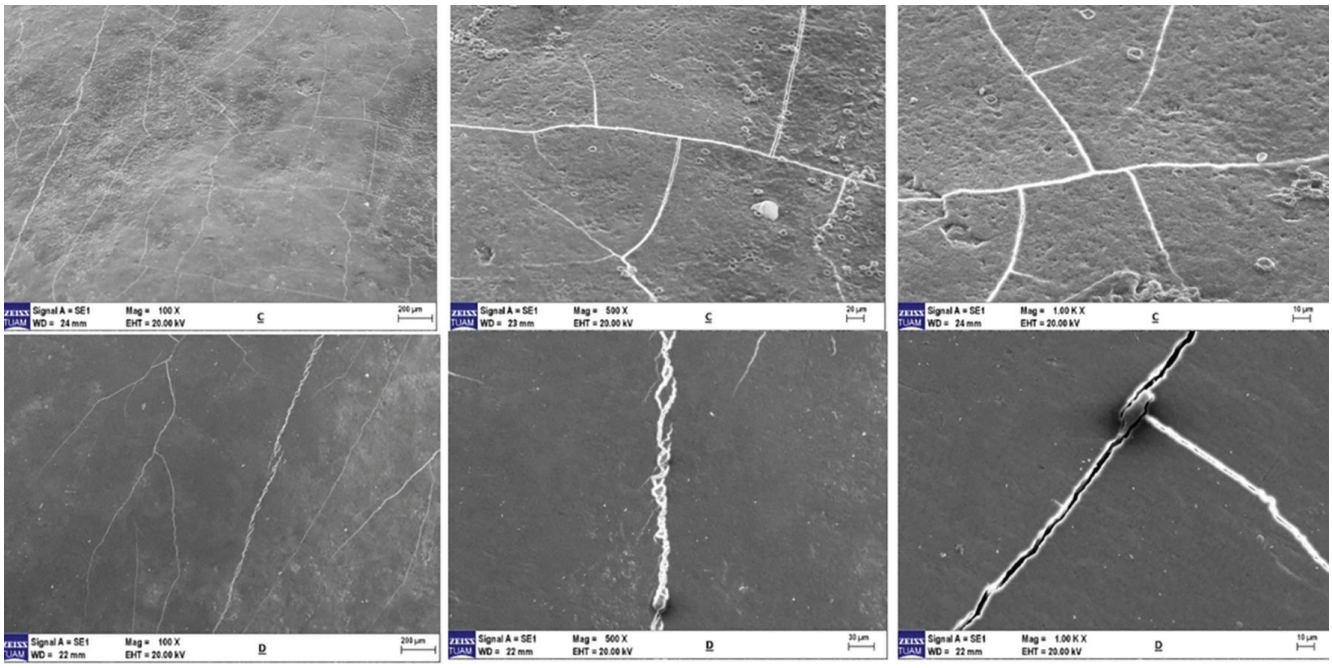

Figure 6. SEM images of tooth samples from the FS+OJ (C) and FS+DW (D) groups at 100×, 500×, and 1000× magnifications. (FS: ferrous sulphate, OJ: orange juice, DW: distilled water)

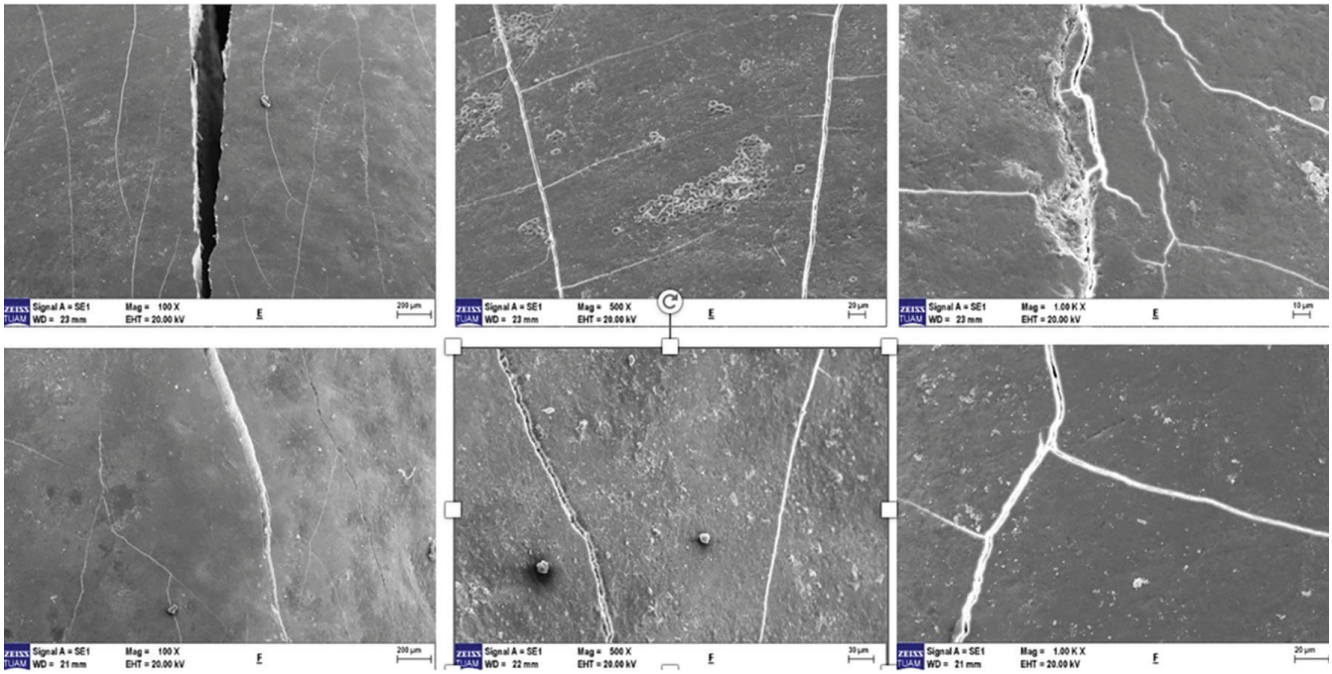

Figure 7. SEM images of tooth samples from the LF+OJ (E) and LF+DW (F) groups at 100×, 500×, and 1000× magnifications. (LF: Lipofer®, OJ: orange juice, DW: distilled water)

Discussion

This study investigated the effect of FS, FP and Lipofer® containing iron supplements mixed with OJ on the colouring and surface roughness of the primary dentition enamel in vitro.

Oral iron supplements are widely utilised for the prophylactic prevention and treatment of iron deficiency anaemia. They are available in the form of Fe^{+2} salts or Fe^{+3} complexes (2). Sucrosomial and liposomal iron preparations containing ferric pyrophosphate were recently introduced (13,14). Studies have shown that iron preparations of various forms and contents can cause tooth tissue erosion and discoloration (3-5). Tooth discoloration, a significant side effect of iron-based medications in paediatric patients, has been associated with parental anxiety and reluctance to continue treatment (15,16).

Various studies have been conducted to improve the bioavailability and absorption of iron during the treatment of iron deficiency anaemia. Various fruit acids, such as ascorbic acid (vitamin C), can augment iron absorption (6). Therefore, it is recommended that iron supplements be ingested concomitantly with OJ to facilitate both absorption and tolerance in children (7).

Oral iron supplements are commonly available in Fe^{+2} and Fe^{+3} forms. The body exhibits a high level of absorption of Fe^{+2}. FS preparations demonstrate optimal absorption and high bioavailability; however, they may be accompanied by systemic side effects such as gastrointestinal symptoms, nausea, vomiting, and abdominal pain complaints (2). The Fe^{+3} form is preferred to reduce the gastrointestinal side effects of Fe^{+2} preparations. Sucrosomial and liposomal iron preparations introduced in recent years are better tolerated systemically and have fewer undesirable side effects than traditional iron salts (2,14). A review of the extant literature revealed that FS, FP and Lipofer® (liposomal ferric pyrophosphate) supplements are the most prevalent iron preparations in contemporary use (17). Consequently, these commonly used iron supplements were selected for the current study. Given the necessity for precise dose adjustment of iron drug salts and the greater accessibility of commercially available iron supplements, these were the preferred options in the present study (16).

Iron supplements comprising three distinct active ingredients exhibited varying absorption and bioavailability rates in the present study (17). The daily doses recommended by paediatricians were used as a reference for adjusting the daily dose of iron supplements. In the event of dosage adjustment, the quantity of medicine required for each iron supplement was calculated in millilitres, with the dosage calculated based on a child with an average weight of 20 kg.

A significant challenge in the management of iron deficiency anaemia pertains to the absorption of inorganic iron once ingested by the body. Various fruit acids, such as ascorbic acid, citric acid, malic acid and tartaric acid, have been reported to be effective in increasing iron absorption in the body. Ascorbic acid is one of the main inducers in increasing iron absorption and has a dose-dependent effect on iron absorption (6). Orange, one of the fruits with the highest ascorbic acid content, has been shown to increase iron absorption because it contains various organic acids, such as citric acid, alongside ascorbic acid (8). Given the structure of ascorbic acid (a fruit acid) and its capacity to enhance iron absorption, we decided to use freshly squeezed OJ, prepared daily, in this study. This decision was made in view of the variability of the additives present in commercially available fruit juices (6).

Iron supplements cause discoloration of tooth tissue, raising concerns for parents (3,5,16). Spectrophotometers provide reliable and accurate results when measuring colour changes in teeth (18) and have been used to investigate the effect of iron supplements on tooth discoloration (3,19). In the current study, a digital spectrophotometer was utilised to evaluate the effect on colour change.

Colour systems are used to define and distinguish colours. The CIE L^* a^* b^* colour system is predicated on calculating the tristimulus values that indicate how the human visual system responds to a particular colour. In this system, the L^* coordinate corresponds to the degree of lightness/darkness, ranging from 0 (black) to 100 (white); the a^* coordinate represents the redness ($a>0$) or greenness ($a<0$); and the b^* coordinate represents yellow ($b>0$) or blue ($b<0$) variation (20). The CIEDE2000 colour system was developed to overcome the deficiencies in the CIE L^* a^* b^* colour system and to facilitate a more effective colour change analysis (12). The CIEDE2000 colour system was utilised to analyse the colour change of primary teeth in the present study.

The severity of tooth staining is contingent upon the duration of exposure of the tooth surface to the drug and the type and dosage of the supplement (3,19). In a study evaluating the erosive effect of iron supplementation and antitussive and bronchodilator drugs on dental tissue over a 28-day period, a significant decrease in microhardness was reported by day 28 (21). In the present study, the alterations observed at days 7, 14, 21 and 28 were measured to evaluate the effect of the time factor. In accordance with the extant literature the DE00 value was found to increase with time

in the present study; the highest colour change recorded was 6.58 on the 28th day (19). The immersion protocol of 5 minutes per day was designed to simulate the cumulative short-term exposure of iron supplements in the oral cavity, as previously described in similar in vitro studies (4,21).

As has been emphasised in a considerable number of studies, the type of iron supplement is one of the most important factors in tooth discoloration (3,5,15,19). Studies have shown that sucrosomial iron and specially synthesised liposomal iron supplements have a lower discoloration effect than FS preparations (5,15); similar findings were observed in the present study. Examination of the ΔE_{00} values in the FS, FP and LF supplement groups at different time intervals revealed a significantly lower colour change in the LF group than in the FS and FP groups at all-time points. In the present study, OJ did not cause an increase in the colouring potential of iron supplements. Thus, mixing supplements with OJ to enhance iron absorption and improve the taste for children did not negatively affect tooth discoloration.

In studies examining the effect of iron supplements on tooth discoloration, colour analysis was conducted using the mean discoloration value (DE) (5,19). The L^*, a^* and b^* parameters are utilised to evaluate the effect of colour change (22). Studies evaluating the effect of iron supplements on the discoloration of primary teeth in terms of $L^* a^* b^*$ parameters are lacking. Thus, the current study is the first to evaluate the effect of iron supplements on colour change in primary teeth using the $L^*a^* b^*$ colour parameters. In terms of the L^* value, teeth in the LF group showed a lighter colour appearance than those in the FS and FP groups. In terms of the a^* value, teeth in the FP group exhibited a redder colour appearance than those in the FS and LF groups; this colour difference may be attributable to the dark red colour of the iron drop containing FP. In terms of the b^* value, teeth in the FS and FP groups exhibited a more yellow colour appearance than those in the LF group.

Several factors influence the colour and appearance of teeth; for example, an increase in the roughness of the tooth surface can facilitate the attachment of chromogenic pigments and bacterial biofilm (23). Many studies have shown that the low pH of iron supplements can cause demineralisation of tooth surfaces and tooth erosion (9,24,25). In vitro studies using microhardness and surface roughness analyses have evaluated whether and to what extent dental hard tissues are affected by erosion (9,21,26). Various instruments equipped with optical or mechanical sensors are utilised to measure the surface roughness and topography. Profilometers are preferred for examining the surface properties of dental materials. In the present study, changes in enamel surface roughness were evaluated using a mechanical profilometer. Surface roughness analysis performed by quantitative methods, such as a profilometer and supported by qualitative measurements (like SEM, as utilised in the present study) contributes to the reliability of the results (27,28).

The findings of the present study revealed no significant difference in surface roughness among the groups examined. In another study employing a similar methodology, FS-containing iron drops with erosive potential were diluted with natural apple juice, reducing the adverse effects on the tooth surface (4). In the present study, the combination of iron supplements with OJ had no substantial impact on the enamel surface roughness. This may be attributed to the dilution of the supplements, which minimises the negative effects.

The present study utilised extracted primary canine teeth to evaluate the effect of different iron supplement groups on primary teeth. The study was conducted under in vitro conditions. However, in vitro studies face challenges in accurately reflecting the intraoral environmental conditions, making it impossible to mimic the oral environment completely (29,30). Therefore, the tooth samples were stored in an artificial saliva solution during the immersion cycles to simulate the oral environment for evaluating the erosive activity (30).

In the present study, the most prescribed preparations of iron supplements were preferred and their results were evaluated. However, each preparation contains varying amounts of preservative additives and by-products (31). Pure iron salts were not preferred because they are difficult to dose and supply.

Study Limitations

Despite the results being interpreted in relation to the type of iron supplements administered, the by-products contained within the supplements may have exerted some influence, which could represent a significant limitation of the study.

Iron supplements containing Lipofer® caused less tooth discoloration than those containing FP and FS. The administration of iron supplements mixed with OJ did not increase the colouring potential of iron on the teeth. Therefore, it may be recommended to mix iron supplements with OJ to increase absorption and enhance the taste of the medicine for children. When administered in conjunction with OJ or DW, the three distinct iron supplements did

not induce any surface texture alterations. Although a mechanical profilometer device was used to evaluate the surface roughness in this study, an optical profilometer or atomic force microscopy may provide more reliable results in the future.

Conclusion

The results of this study may serve as a practical guide for healthcare professionals working with children, such as pediatric dentists, pediatricians, and family physicians, as well as for parents. Moreover, this is the first study to examine the effects of ferrous sulfate, ferric polymaltose, and Lipofer®-containing iron preparations combined with orange juice on the enamel of primary teeth, specifically in terms of discoloration and surface roughness. These findings provide a scientific basis for future research evaluating the combined use of iron supplements and supportive agents such as orange juice. Within the limitations of this in vitro study, mixing iron supplements with orange juice did not increase discoloration or surface roughness. However, clinical studies are needed to confirm these findings before making definitive recommendations.

Ethics

Ethics Committee Approval: Approval for this in vitro experimental study was obtained from the Non-Interventional Clinical Research Ethics Committee of Kütahya Health Sciences University (decision no: E-41997688-050.99-130396, date: 11.03.2024).

Acknowledgements: The authors would like to thank Dr. Cemile Yılmaz and Dr. Mehmet Unal for their valuable technical assistance.

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support

Data Availability: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123:615-24.
2. Pantopoulos K. Oral iron supplementation: new formulations, old questions. Haematologica. 2024;109:1480-8.
3. Pani SC, Alenazi FM, Alotain AM, Alanazi HD, Alasmari AS. Extrinsic tooth staining potential of high-dose and sustained-release iron syrups on primary teeth. BMC Oral Health. 2015;15:90.
4. Sahebnazar N, Tavassoli-Hojjati S, Aghaei S. Effect of sucrosomial® Iron and iron drop diluted with natural fruit juice on microhardness of primary enamel. Front Dent.2022;19:5.
5. Babaei N, Molaei T, Belyad S, Hekmatfar S. Relationship of pH and viscosity of five different iron supplements with iron ion absorption and enamel discoloration in anterior primary teeth: an in vitro study. Dent Res J (Isfahan). 2021;18:1-6.
6. Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. Int J Vitam Nutr Res. 2004;74:403-19.
7. Shah M, Griffin IJ, Lifschitz CH, Abrams SA. Effect of orange and apple juices on iron absorption in children. Arch Pediatr Adolesc Med. 2003;157:1232-6.
8. Ballot D, Baynes RD, Bothwell TH, Macphail AP, Lyons G, Bezwoda WR, et al. The effects of fruit juices and fruits on the absorption of iron from a rice meal. Br J Nutr. 1987;51:331-43.
9. Pasdar N, Alaghehmand H, Mottaghi F, Tavassoli M. Experimental study of iron and multivitamin drops on enamel microhardness of primary tooth. J Int Soc Prev Community Dent. 2015;5:518-22.
10. Asgari I, Soltani S, Sadeghi MS. Effects of iron products on decay, tooth microhardness, and dental discoloration: a systematic review. Int J Pediatr. 2020;8:12647-55.
11. Kaya E. The effect of surface sealants on discoloration of primary teeth related to iron syrups. Yeditepe Dent J. 2021;17:171-6.
12. Luo MR, Cui G, Rigg B. The development of the CIE 2000 color-difference formula: CIEDE2000. Color Res Appl. 2001;26:340-50.
13. Pappalardo A, Currenti W, Ponzio R, Mellini G, Nicolosi D, Longhitano L, et al. Effects of micronized microencapsulated ferric pyrophosphate supplementation in patients with advanced cancer and iron deficiency: a single-center cohort pilot study. Blood Transfus. 2019;17:196-205.
14. Gómez-Ramírez S, Brilli E, Tarantino G, Muñoz M. Sucrosomial® Iron: a new generation iron for improving oral supplementation. Pharmaceuticals. 2018;11:97.
15. Abbasi M, Mazhari F, Jaafari MR, Afshari E, Bagheri H, Parisay I. Color change of primary teeth following exposure to an experimentally synthesized liposomal nano-encapsulated ferrous sulfate drop versus commercially available iron drops. Pediatr Dent J. 2021;31:256-67.
16. Martina S, Caruso S, Nazemisalman B, Mohseni M, Darvish S, Farsadeghi M, et al. Effects of iron salts on demineralization and discoloration of primary incisor enamel subjected to artificial cariogenic challenge versus saline immersion. Healthcare (Basel). 2023;11:569.
17. Kiliç BO, Konuksever D, Özbek NY. Comparative efficacy of ferrous, ferric and liposomal ıron preparations for prophylaxis in ınfants. Indian Pediatr. 2024;61:621-6.
18. Klotz AL, Habibi Y, Corcodel N, Rammelsberg P, Hassel AJ, Zenthöfer A. Laboratory and clinical reliability of two spectrophotometers. J Esthet Restor Dent. 2022;34:369-73.
19. Tayebi S, Esmaeilzade M, Soufi Rezai L, Fotovat F, Najafi Vosogh R, Faregh N. Color change of primary teeth following the use of four types of iron supplements available in the Iranian pharmacopeia. Avicenna J Dent Res. 2019;11:66-71.

20. Joiner A. Tooth color: a review of the literature. J Dent. 2004;32(Suppl. 1):3-12.
21. Scatena C, Galafassi D, Gomes-Silva JM, Borsatto MC, Serra MC. In vitro erosive effect of pediatric medicines on deciduous tooth enamel. Braz Dent J. 2014;25:22-7.
22. Güngör Sarıalioğlu A, Örcün ME, Dönmez N. In vitro evaluation of the effects of different whitening toothpastes on enamel color change and surface roughness. Necmettin Erbakan Univ Dent J. 2023;5:45-53.
23. Vieira-Junior WF, Vieira I, Ambrosano GMB, Aguiar FHB, Lima DANL. Correlation between alteration of enamel roughness and tooth color. J Clin Exp Dent. 2018;10:815-22.
24. Hekmatfar S, Piraneh H, Jafari K. Evaluation of the relationship between pH and titratable acidity of five different iron supplements and iron ion absorption in anterior primary teeth: an in vitro study. Dent Res J (Isfahan). 2018;15:367-71.
25. Tabari M, Alaghemand H, Rabiee M, Khefri S, Ahadi MS, Nikpour MR. Effect of silicone oil and nano-hydroxyapatite/chitosan powder on microhardness and surface structure of primary tooth enamel after iron drop consumption. J Dent Sch. 2013;31:23-9.
26. Valinoti AC, da Costa LC Jr, Farah A, Sousa VP, Fonseca-Gonçalves A, Maia LC. Are pediatric antibiotic formulations potential risk factors for dental caries and erosion? Open Dent J. 2016;10:420-4.
27. Kakaboura A, Fragouli M, Rahiotis C, Silikas N. Evaluation of surface characteristics of dental composites using profilometry, scanning electron microscopy, atomic force microscopy, and gloss-meter. J Mater Sci Mater Med. 2007;18:155-63.
28. Ertuğrul CÇ. Demineralization effects of breast milk, formula milk and cow's milk on the primary teeth. A study of SEM-EDX analysis. Pam Med J. 2024;17:510-9.
29. White DJ. The application of in vitro models to research on demineralization and remineralization of the teeth. Adv Dent Res. 1995;9:175-93.
30. Fu Y, Ekambaram M, Li KC, Zhang Y, Cooper PR, Mei ML. In vitro models used in cariology mineralisation research: a review of the literature. Dent J (Basel). 2024;12:323.
31. Puścion-Jakubik A, Zimnoch KM, Socha K. Food supplements containing iron: comparison of actual content with declared content and health consequences. Molecules. 2024;29:4796.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Positive Discipline and Socioeconomic Factors in Vietnam's Child Development

Olumlu Disiplin ve Sosyoekonomik Faktörlerin Vietnam'da Çocuk Gelişimine Etkisi

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Cite this article as: Nguyen-Huu CD, Pham N-H, Nguyen-Ho MT, Dang TT, Nguyen V-t. Positive discipline and socioeconomic factors in Vietnam's child development. J Curr Pediatr. 2026;24(2):89-96

Abstract

Introduction: Early childhood development is critical for lifelong health and well-being, influenced by parenting practices and socioeconomic conditions, particularly in low- and middle-income countries like Vietnam. This study examines how positive discipline and socioeconomic factors shape developmental outcomes in young children.

Materials and Methods: Data from 2,705 children aged 24–59 months were analyzed from a national survey conducted in Vietnam from 2020 to 2021. A 20-item index assessed health, learning, and psychosocial outcomes. Multivariable logistic regression, adjusted for maternal education, residence, ethnicity, and wealth, evaluated associations with discipline practices.

Results: Positive discipline, such as explaining behavior or offering alternatives, was associated with better developmental outcomes (odds ratio= 2.37 and 2.10, respectively). Higher maternal education (odds ratio= 1.84, $p<0.001$), urban residence (odds ratio= 1.48, $p=0.013$), pre-primary education attendance (odds ratio= 1.74, $p<0.001$), and majority ethnicity (odds ratio= 2.37, $p<0.001$) also associated with improved outcomes. Violent discipline showed no significant effect ($p=0.82$). Rural and ethnic minority children faced developmental disparities.

Conclusion: Positive discipline and favorable socioeconomic conditions enhance early childhood development in Vietnam. Interventions like parenting training and expanded early education access can reduce disparities, particularly for rural and ethnic minority families, improving pediatric outcomes.

Öz

Giriş: Erken çocukluk gelişimi, özellikle Vietnam gibi düşük ve orta gelirli ülkelerde, ebeveynlik uygulamaları ve sosyoekonomik koşullardan etkilenerek yaşam boyu sağlık ve esenlik için kritik öneme sahiptir. Bu çalışma, olumlu disiplin ve sosyoekonomik faktörlerin küçük çocuklarda gelişimsel sonuçları nasıl şekillendirdiğini incelemektedir.

Gereç ve Yöntem: 2020-2021 yılları arasında Vietnam'da gerçekleştirilen ulusal bir anketten, 24-59 aylık 2.705 çocuğa ait veriler analiz edildi. 20 maddelik bir endeks, sağlık, öğrenme ve psikososyal sonuçları değerlendirdi. Anne eğitimi, ikamet yeri, etnik köken ve refah düzeyine göre ayarlanmış çok değişkenli lojistik regresyon, disiplin uygulamalarıyla ilişkileri değerlendirdi.

Keywords
Early childhood development, positive discipline, socioeconomic status, Vietnam, child well-being

Anahtar kelimeler
Erken çocukluk gelişimi, olumlu disiplin, sosyoekonomik durum, Vietnam, çocuk refahı

Received/Geliş Tarihi : 16.07.2025
Accepted/Kabul Tarihi : 04.06.2026
Epub : 11.06.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.60320

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Bulgular: Davranışı açıklama veya alternatifler sunma gibi olumlu disiplin, daha iyi gelişimsel sonuçlarla ilişkilendirilmiştir (sırasıyla olasılık oranı= 2,37 ve 2,10). Daha yüksek anne eğitimi (olasılık oranı= 1,84, p<0,001), kentsel ikamet (olasılık oranı= 1,48, p=0,013), okul öncesi eğitime katılım (olasılık oranı = 1,74, p<0,001) ve çoğunluk etnik kökeni (olasılık oranı = 2,37, p<0,001) da iyileştirilmiş sonuçlarla ilişkilendirilmiştir. Şiddet içeren disiplinin anlamlı bir etkisi olmadığı görüldü (p=0,82). Kırsal kesimdeki ve etnik azınlık çocuklarında gelişimsel farklılıklar gözlendi.
Sonuç: Olumlu disiplin ve elverişli sosyoekonomik koşullar, Vietnam'da erken çocukluk gelişimini destekler. Ebeveynlik eğitimi ve erken eğitime erişimin genişletilmesi gibi müdahaleler, özellikle kırsal ve etnik azınlık aileleri için eşitsizlikleri azaltarak pediatrik sonuçları iyileştirebilir.

Introduction

The international community, supported by decades of research, recognizes early childhood as a critical period in human development. During these formative years, children acquire essential skills and capacities that serve as the foundation for future learning and growth. Early childhood development (ECD), typically defined as the developmental period from birth to approximately eight years of age, encompasses a broad range of domains, including motor, cognitive, language, socio-emotional, and self-regulatory competencies (1,2). Globally, more than 200 million children in low- and middle-income countries (LMICs) are estimated to fail to reach their full developmental potential within the first five years of life due to factors such as poverty, inadequate nutrition, and limited access to early learning opportunities (3). The caregiving environment is a key determinant of ECD, with socioeconomic status, parental education, and parenting practices playing significant roles (4,5). Research consistently shows that higher maternal education and household wealth are associated with better developmental outcomes, as they enable enriched caregiving environments and access to resources (4-6). Similarly, access to early childhood education, such as pre-primary programs, is linked to improved cognitive and social skills, particularly in disadvantaged populations (2,7). Parenting styles, particularly positive discipline strategies like explaining behavioral expectations or redirecting misbehavior, are associated with enhanced emotional regulation and problem-solving abilities, while harsh disciplinary measures, such as physical punishment, are linked to increased risks of behavioral and emotional difficulties (8-10).

In Vietnam, ECD has gained increasing attention as policymakers recognize its role in supporting long-term educational and socioeconomic outcomes. Studies have identified key developmental risk factors, including socioeconomic disparities, limited access to quality early education, and prevalent use of punitive discipline practices (8,9). For instance, research in Vietnam has shown that children in rural areas and from ethnic minority groups face greater developmental challenges due to systemic inequities in income, education, and service access (8,11,12). While progress has been made in expanding pre-primary education, disparities persist, with urban children and those from the Kinh/Hoa majority benefiting more than their rural and ethnic minority counterparts (12). Additionally, traditional disciplinary approaches, including spanking and shouting, remain common, potentially affecting children's socio-emotional well-being (9). These findings align with global evidence from LMICs, where socioeconomic and cultural factors shape ECD outcomes, yet the specific interplay of these determinants remains underexplored (4,6,13).

Despite this knowledge, significant gaps remain in understanding how multiple determinants interact to shape ECD, particularly in the context of the Early Childhood Development Index 2030 (ECDI2030), a standardized measure designed to track developmental progress across health, learning, and psychosocial well-being (1). Previous studies using MICS data have provided valuable insights into ECD determinants. For example, Frongillo et al. (14) analyzed Multiple Indicator Cluster Survey (MICS) data from 29 LMICs and found that positive family care behaviors, such as providing books and engaging in stimulating activities, were associated with better ECD outcomes, while harsh discipline was linked to poorer developmental progress. In Vietnam, while studies have explored socioeconomic disparities and parenting practices separately (10,12), there is limited evidence on how these factors collectively relate to ECDI2030 outcomes, especially among children aged 24-59 months, a critical period for school readiness. Internationally, this gap is particularly relevant for LMICs, where diverse socioeconomic and cultural contexts, like Vietnam's urban-rural divide and ethnic diversity, mirror challenges faced by millions of children at risk of developmental delays (3,6). Furthermore, the recent adoption of the ECDI2030 provides a unique opportunity to assess these associations using a globally comparable metric, yet few studies have applied

this measure to explore discipline and socioeconomic factors together in LMIC settings.

This study aims to address these gaps by investigating the associations of residence, ethnicity, maternal education, pre-primary attendance, and positive discipline practices with ECDI2030 outcomes among Vietnamese children aged 24-59 months, using data from the Vietnam MICS 2020–2021 (15). By analyzing a nationally representative dataset, the study seeks to generate evidence on how these determinants interact in Vietnam's diverse socioeconomic and cultural context, offering insights for targeted interventions to reduce developmental disparities. For an international audience, this study contributes to the global literature by providing a case study of how positive discipline and socioeconomic factors relate to ECD in an LMIC, informing scalable strategies for other countries with similar challenges, such as rural-urban disparities, ethnic inequities, and prevalent use of harsh discipline (3,13). Ultimately, the findings aim to support evidence-based policies to promote equitable ECD outcomes in Vietnam and beyond.

Materials and Methods

Sources of Data and Sampling

This secondary analysis utilized the Vietnam Multiple Indicator Cluster Survey (MICS6) 2020–2021, a nationally representative cross-sectional survey conducted by the General Statistics Office with UNICEF and UNFPA support. The MICS6 employed a stratified, multi-stage cluster sampling design to ensure representativeness across urban/rural areas, socioeconomic strata, and ethnic groups (15).

Ethics committee approval was waived by the Institutional Review Board of Hue University of Medicine and Pharmacy, as this study was a secondary analysis of de-identified data from the Vietnam Multiple Indicator Cluster Survey (MICS) 2020–2021. All procedures adhered to the ethical standards of the 1964 Helsinki Declaration and its later amendments.

Participants

A total of 2,705 children aged 24–59 months were included. Eligibility was determined by the MICS survey design, and all children with complete data on ECDI2030 and discipline were analyzed.

Measurement

ECDI2030: The ECDI2030 comprises 20 items across three domains (learning, psychosocial well-being, and health). A child was considered "on track" if performance standards were met for age-appropriate tasks (1).

$$\text{ECDI2030} = \frac{\text{Number of children aged } 24-59 \text{ months who have achieved the minimun number of milestones expected for their age groud}}{\text{Total number of children aged } 24-59 \text{ months}}$$

Discipline practices: Caregivers reported discipline behaviors in the past month. Following UNICEF methodology, we distinguished:

- Positive discipline: Explaining why behavior was wrong, offering an alternative activity, or removing privileges.
- Violent discipline: Including both psychological aggression and physical punishment. Psychological aggression comprised behaviors such as shouting, yelling, or calling the child offensive names, while physical punishment included spanking with a bare hand, slapping, hitting with an object (e.g., a belt or stick), or other forms of physical force (14).

Covariates: Maternal education (low < secondary vs. high ≥ secondary), residence (urban vs. rural), ethnicity (majority Kinh/Hoa vs. minority), and pre-primary attendance were included as covariates.

Statistical Analysis

Multivariable logistic regression was used to estimate odds of being on track in ECDI2030 (15). To control for confounding, models were adjusted for key variables identified as potential confounders based on prior literature and their association with both exposures and ECDI2030 outcomes (4,5,11,12). Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Interaction terms for ethnicity x residence and ethnicity x discipline were tested but found nonsignificant. Analyses were performed in R 4.3.1 and SPSS 20.0.

Results

Descriptive Statistics and Child Discipline

The study analyzed 2,705 children aged 24–59 months from the Vietnam MICS 2020–2021 dataset, reflecting Vietnam's diverse population. As shown in Table 1, the sample was balanced by sex (52.6% male, 47.4% female) and age (30.5% aged 24–35 months, 33.7% aged 36–47 months, 35.9% aged 48–59 months). Most children lived in rural areas (75.5% vs. 24.5% urban), and 78.9% attended pre-primary education, indicating broad but uneven access

Table 1. Characteristics of children aged 24–59 months, Vietnam, 2021 (n=2705)			
Characteristics		**n**	**%**
Sex	Male	1423	52.6
	Female	1282	47.4
Age	24 to 35 months	824	30.5
	36 to 47 months	911	33.7
	48 to 59 months	970	35.9
Area	Urban	663	24.5
	Rural	2042	75.5
Attendance to pre-primary	Attending	1485	78.9
	Not attending	396	21.1
Maternal education	No education	5	0.2
	Primary	301	14.4
	Secondary	704	33.7
	Higher	1081	51.7
Ethnicity of household head	Majority	1444	53.4
	Minority	1261	46.6
Data from Vietnam MICS 2020-2021. Percentages may not sum to 100% due to rounding			

to early learning. Maternal education varied widely - 51.7% had higher education, 33.7% secondary, 14.4% primary, and 0.2% none - highlighting disparities in caregiver resources. Ethnicity was nearly evenly split (53.4% Kinh/Hoa majority, 46.6% minority), underscoring the need to address ethnic inequities.

Table 2 outlines child discipline practices, revealing a mix of approaches. Positive discipline was common, with 80.1% of caregivers explaining why behavior was wrong, 31.9% taking away privileges, and 13.5% suggesting alternative activities. These practices foster emotional and cognitive growth by encouraging understanding and self-regulation. However, harsh methods were also prevalent: 60.6% shouted or yelled, 47.4% spanked with a bare hand, and 10.3% used objects like belts or sticks, potentially undermining socio-emotional well-being. Severe practices, such as slapping the face (1.7%) or beating (0.4%), were rare but concerning. Notably, only 7.1% of mothers endorsed physical punishment, suggesting an opportunity to shift norms toward positive discipline through education.

ECDI Domains

Figure 1 illustrates ECDI2030 performance, with 71% of children developmentally on track. Gross motor skills, such as walking on uneven surfaces, were consistently strong across ages, reflecting early physical development. Language and cognitive skills, like forming five-word sentences or recognizing five letters, improved significantly from 24 - 29 to 48 - 59 months, indicating that older children are better equipped for school readiness. This developmental progression highlights the importance of early interventions to support language and literacy, especially for children at risk of falling behind.

Socioeconomic Status and Education Impact

Table 3 examines socioeconomic factors associated with ECDI2030 outcomes. Multivariable logistic regression showed that urban children had 48% higher odds of meeting developmental benchmarks (OR=1.48, p=0.013) than rural

Table 2. Child discipline for children aged 24–59 months in Vietnam, 2021 (n=2705)		
Child discipline	**n**	**%**
Took away privileges	862	31.9
Explained wrong behavior	2167	80.1
Shook him/her	93	3.4
Shouted, yelled, screamed	1638	60.6
Gave something else to do	364	13.5
Spanked, hit, slapped on bottom with bare hand	1283	47.4
Hit with belt, hairbrush, stick or other hard object	278	10.3
Called dumb, lazy or another name	154	5.7
Hit/slapped on face, head or ears	47	1.7
Hit/slapped on hand, arm or leg	385	14.2
Beat up, hit over and over as hard as one could	10	0.4
Mother believes that in order to bring up, raise, or educate a child properly, the child needs to be physically punished	192	7.1
Data from Vietnam MICS 2020–2021. Percentages reflect proportion experiencing each method		

Figure 1. ECDI for children aged 24–59 months in Vietnam, 2021 (n=2705)

The figure illustrates the proportion of children developmentally on track across gross motor, language, and cognitive skills, stratified by age groups (24–29, 30–35, 36–47, and 48–59 months), based on the Early Childhood Development Index 2030 (ECDI2030). Data were sourced from the Vietnam Multiple Indicator Cluster Survey (MICS) 2020–2021 (n=2705). Motor skills include tasks like walking on uneven surfaces; language skills include forming sentences of five or more words; cognitive skills include recognizing five letters of the alphabet

peers, likely due to better access to resources and education. Pre-primary attendance was associated with 74% higher odds (OR=1.74, p<0.001), underscoring the role of structured early learning in boosting cognitive and social skills. Children of mothers with higher education had 84% higher odds (OR=1.84, p<0.001), reflecting enriched caregiving environments. Majority ethnic (Kinh/Hoa) children had over twice the odds of achieving ECDI2030 benchmarks (OR=2.37, p<0.001) compared to minority groups, signaling systemic inequities that require targeted interventions. These disparities emphasize the need for policies to expand equitable access to education and resources, particularly for rural and ethnic minority communities.

Discipline Impact

Table 4 highlights the associations of discipline on ECDI2030. Positive discipline practices were associated with better outcomes: explaining wrong behavior increased odds by 137% (OR=2.37, p=0.42) and offering alternative activities by 110% (OR=2.10, p<0.001). These approaches promote emotional regulation and problem-solving, critical for long-term development. A binary dummy variable for positive discipline (1= positive, e.g., explaining, alternatives; 0= non-positive, e.g., shouting, spanking) showed a significant positive association (OR=1.89, p=0.02), reinforcing the benefits of positive practices. In contrast, violent discipline showed no significant impact in multivariable models, suggesting they neither enhance nor consistently harm ECDI2030 outcomes in this context, possibly due to cultural norms. These findings advocate for promoting positive discipline to support developmental outcomes, offering a practical pathway for parenting interventions.

A visual overview of associations is provided in Figure 2 (Infographic Summary of Key Findings).

Discussion

Our findings indicate significant associations between positive discipline, socioeconomic determinants, and ECD outcomes in Vietnam based on the MICS 2020–2021 survey. Positive discipline was associated with higher ECDI2030 achievement (OR 1.45, p<0.001), consistent with global evidence demonstrating the beneficial effects of supportive parenting practices on child development (2,8,16). Recent evidence further supports this relationship. A study from Turkey reported that positive parenting behaviors were associated with improved social-emotional competence and reduced behavioral difficulties among young children, highlighting the importance of nurturing caregiving environments for optimal developmental outcomes (17). Similarly, a recent international study emphasized that responsive caregiving and positive parent-child interactions are key contributors to healthy early childhood development across diverse socioeconomic settings (18).

Higher maternal education and household wealth were also associated with better developmental outcomes in our study, aligning with findings from Bangladesh, where Alam et al. (19) reported comparable effects of socioeconomic factors on ECD using MICS data as well as studies from other low- and middle-income countries (4,6,13). These

Table 3. The role of socioeconomic status, and education on ECDI among children aged 24–59 months in Vietnam, 2021 (n=2705)

Characteristics		ECDI2030 OR (95% CI)	Univariable logistic regression		Multivariable logistic regression	
			p	OR (95% CI)	p	
Sex	Male	69.6	0.87 (0.72–1.02)	0.089		
	Female	72.5	-			
Area	Urban	82.8	2.36 (1.88–2.35)	<0.001	1.48 (1.09–2.03)	0.013
	Rural	67.1	-			
Attendance to pre-primary	Attending	70.4	1.66 (1.32–2.08)	<0.001	1.74 (1.30–2.33)	<0.001
	Not attending	59.1	-			
Mother's education	Low education	60.1	-			
	High education	78.0	2.35 (1.82–3.03)	<0.001	1.84 (1.33–2.53)	<0.001
Ethnicity of household head	Majority	82.0	3.25 (2.73–3.87)	<0.001	2.37 (1.82–3.08)	<0.001
	Minority	58.4				

Data from Vietnam MICS 2020–2021. ECDI2030 = proportion developmentally on track. OR=Odds ratio; 95% CI= 95% confidence interval. Adjusted for maternal education, residence, ethnicity, and household wealth. Survey weights and cluster design applied

Table 4. The role of child discipline on ECDI among children aged 24–59 months in Vietnam, 2021 (n=2705)

Child discipline	ECDI2030 (Yes/No)	Univariable logistic regression		Multivariable logistic regression	
		OR (95% CI)	p	OR (95% CI)	p
Positive discipline*	75.1/54.1	2.56 (2.10–3.12)	<0.001	1.89 (1.13–2.66)	0.020
Explained wrong behavior	75.2/54.2	2.56 (2.11–3.11)	<0.001	2.37 (1.05–3.67)	0.042
Gave something else to do	84.6/68.8	2.13 (1.61–2.83)	<0.001	2.10 (1.34–2.91)	<0.001
Discipline (non-violent vs. Violent)	66.6/72.2	0.77 (0.63–0.93)	0.008	0.98 (0.79–1.20)	0.82

Data from Vietnam MICS 2020–2021. *Positive discipline: 1= explaining behavior or offering alternatives, 0= non-positive. OR=Odds ratio; 95% CI= 95% confidence interval. Adjusted for maternal education, residence, ethnicity, and household wealth. Survey weights and cluster design applied

findings suggest that socioeconomic resources may enhance children's developmental opportunities through improved access to education, health services, and stimulating home environments. Although the cross-sectional design limits causal inference, the observed associations indicate that interventions promoting positive discipline alongside policies addressing socioeconomic disparities may contribute to improved early childhood development outcomes.

The MICS6 data indicates a high prevalence of violent discipline (78.2% of children experienced psychological aggression or physical punishment in the past month), but also 80.4% of children experienced positive discipline (e.g., explaining wrong behavior, 80.1%; giving something else to do, 13.5%). In multivariable logistic regression, positive discipline was associated with higher ECDI2030 achievement (OR=1.89, p<0.001, Table 4), affirming the benefits of supportive parenting practices. These practices, rooted in reasoning and redirection, foster emotional regulation and cognitive growth, consistent with findings from meta-analyses and MICS-based studies (2,8,16,20).

This diverges from evidence linking corporal punishment to increased aggression, anxiety, and developmental delays (3,9,21,22). The lack of effect may stem from cultural acceptance of physical discipline in Vietnam (10), the ECDI2030's broad focus (1), or a desensitization to moderate punishment in high-prevalence settings (23). Notably, only 7.1% of mothers endorsed physical punishment, a trend echoing shifts in parenting norms observed elsewhere (5,24), suggesting potential for behavior change with education (10).

Socioeconomic factors were critical predictors of ECD (Table 3). Urban residence (OR=1.484, p=0.013) conferred advantages over rural areas, reflecting disparities in resources and early learning access, a pattern noted in Vietnam (12) and across developing nations (4,6), Pre-primary attendance (OR=1.737, p<0.001) strongly associated with better outcomes, supporting evidence that structured

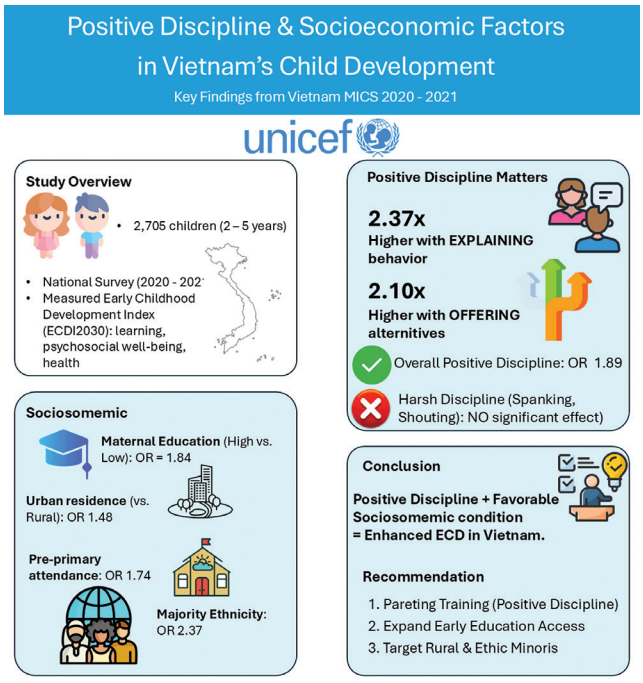

Figure 2. Infographic summary of key findings

early education is linked to improved cognitive and social skills (2,7). Maternal education's impact (OR=1.835, p<0.001) aligns with research linking caregiver education to enriched environments and health practices (4,5,25). Ethnic disparities were pronounced, with majority ethnic children outperforming minorities (OR=2.365, p<0.001), a gap tied to systemic inequities in income, education, and services (11), mirroring global patterns of disadvantage.

Developmental trends in Figure 1 - strong motor skills across ages, with language and literacy advancing later - reflect typical ECD sequences (1,2). This suggests foundational skills are widely attained, but gaps in higher-order competencies may grow without intervention, particularly for rural and minority groups (12,26).

This study has several limitations that should be acknowledged. First, the cross-sectional design restricts causal inference, as associations between discipline practices, socioeconomic factors, and developmental outcomes cannot establish directionality. Second, all measures relied on caregiver reports, which may be subject to recall bias and social desirability effects. Third, the composite ECDI2030 index may obscure domain-specific differences in health, learning, and psychosocial development. Fourth, important family-context variables - including father's involvement, mother's social support, the presence of siblings or peers, and reasons for preschool enrollment - were not collected in the MICS dataset; their absence may limit interpretation, as these factors are known to shape early development. Finally, no study-specific power calculation was conducted, although the MICS survey was nationally designed to ensure adequate statistical power for key indicators. Future studies should consider longitudinal approaches, conduct power analyses tailored to specific research questions, and incorporate qualitative insights into discipline norms to further elucidate these relationships (10,27).

Conclusion

Positive discipline practices, higher maternal education, urban residence, majority ethnicity, and pre-primary attendance are associated with improved ECD outcomes in Vietnam. Policymakers should prioritize interventions that (1) promote positive discipline through parenting education, (2) expand access to early education in rural and minority communities, and (3) address structural inequities in education and resources.

Ethics

Ethical Approval: Ethics committee approval was waived by the Institutional Review Board of Hue University of Medicine and Pharmacy, as this study was a secondary analysis of de-identified data from the Vietnam Multiple Indicator Cluster Survey (MICS) 2020–2021. All procedures adhered to the ethical standards of the 1964 Helsinki Declaration and its later amendments.

Acknowledgements: We thank the United Nations Children's Fund (UNICEF) and the General Statistics Office of Vietnam for providing access to the Multiple Indicator Cluster Survey (MICS) 2020–2021 dataset, which made this study possible.

Data Availability Statement: The data analyzed in this study are publicly available from the UNICEF Multiple Indicator Cluster Survey (MICS) 2020–2021 dataset, accessible at https://mics.unicef.org/surveys. No additional data are available due to the secondary analysis nature of the study.

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. United Nations Children's Fund. The Early Childhood Development Index 2030: a new measure of early childhood development. New York: UNICEF; 2023.
2. Black MM, Walker SP, Fernald LCH, Andersen CT, DiGirolamo AM, Lu C, et al. Early childhood development coming of age: science through the life course. Lancet. 2017;389:77-90.
3. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. Lancet. 2007;369:60-70.
4. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet. 2011;378:1325-38.
5. Mudiyanselage SB, Wanni Arachchige Dona S, Angeles MR, Majmudar I, Marembo M, Tan EJ, et al. The impact of maternal health on child's health outcomes during the first five years of child's life in countries with health systems similar to Australia: a systematic review. PLoS One. 2024;19:e0295295.
6. Bradley R, Corwyn R. Socioeconomic status and child development. Annu Rev Psychol. 2002;53:371-99.
7. Engle PL, Fernald LC, Alderman H, Behrman J, O'Gara C, Yousafzai A, et al. Strategies for reducing inequalities and improving developmental outcomes for young children in low-income and middle-income countries. Lancet. 2011;378:1339-53.
8. Gershoff ET, Grogan-Kaylor A. Spanking and child outcomes: old controversies and new meta-analyses. J Fam Psychol. 2016;30:453-69.
9. Gershoff ET. Spanking and child development: we know enough now to stop hitting our children. Child Dev Perspect. 2013;7:133-7.
10. Cappa C, Dam H. Prevalence of and risk factors for violent disciplinary practices at home in Viet Nam. J Interpers Violence. 2014;29:497-516.
11. Dang H-A. Vietnam: a widening poverty gap for ethnic minorities. in: indigenous peoples, poverty and development: Cambridge University Press; 2012.
12. Duc NH. Developmental risk factors in Vietnamese preschool-age children: cross-sectional survey. Pediatr Int. 2016;58:14-21.
13. Rao N, Cohrssen C, Sun J, Su Y, Perlman M. Early child development in low- and middle-income countries: is it what mothers have or what they do that makes a difference to child outcomes? Adv Child Dev Behav. 2021;61:255-77.
14. Frongillo EA, Kulkarni S, Basnet S, de Castro F. Family care behaviors and early childhood development in low- and middle-income countries. J Child Fam Stud. 2017;26:3036-44.
15. General Statistics Office, UNICEF. Survey measuring Viet Nam Sustainable Development Goal indicators on Children and Women 2020-2021, Survey Findings Report. Ha Noi, Viet Nam: General Statistics Office; 2021.
16. Durrant J, Ensom R. Physical punishment of children: lessons from 20 years of research. CMAJ. 2012;184:1373-7.
17. Karaoğlan D, Dayioğlu M, Saraçoğlu DŞ, Sağir S. Unlevel playing field: socioeconomic determinants of early childhood development in Turkiye. Child Indicators Research. 2024;17:1741-70.
18. Gezgen Kesen G, Yalçın SS. Association between family planning and early childhood development: Secondary Analysis of the 2018 Turkey Demographic and Health Surveys. Children (Basel). 2025;12.
19. Alam MI, Mohaimen M, and Barman P. Early childhood development in Bangladesh and its socio-demographic determinants of importance. Early Child Dev Care. 2022;192:1901-20.
20. Baumrind D. Effects of authoritative parental control on child behavior. Child Dev. 1966;37:887-907.
21. Straus M, Paschall M. Corporal punishment by mothers and development of children's cognitive ability: a longitudinal study of two nationally representative age cohorts. J Aggress Maltreat Trauma. 2009;18:459-83.
22. Taylor CA, Lee SJ, Guterman NB, Rice JC. Use of spanking for 3-year-old children and associated intimate partner aggression or violence. Pediatrics. 2010;126:415-24.
23. Lansford JE, Chang L, Dodge KA, Malone PS, Oburu P, Palmérus K, et al. Physical discipline and children's adjustment: cultural normativeness as a moderator. Child Dev. 2005;76:1234-46.
24. Grogan-Kaylor A, Castillo B, Pace GT, Ward KP, Ma J, Lee SJ, et al. Global perspectives on physical and nonphysical discipline: a Bayesian multilevel analysis. Int J Behav Dev. 2021;45:216-25.
25. Bornstein MH, Putnick DL. Cognitive and socioemotional caregiving in developing countries. Child Dev. 2012;83:46-61.
26. Heckman JJ. Skill formation and the economics of investing in disadvantaged children. Science. 2006;312:1900-2.
27. Richter LM, Daelmans B, Lombardi J, Heymann J, Boo FL, Behrman JR, et al. Investing in the foundation of sustainable development: pathways to scale up for early childhood development. Lancet. 2017;389:103-18.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Association of Delayed Vitamin D Supplementation and Low Thyroxine Levels with Bronchopulmonary Dysplasia Severity in Preterm Infants

Prematüre Bebeklerde D Vitamini Takviyesinin Gecikmesi ve Düşük Tiroid Hormon Seviyelerinin Bronkopulmoner Displazi Şiddetiyle İlişkisi

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Cite this article as: Candan Gök S, Çakır U. Association of delayed vitamin D supplementation and low thyroxine levels with bronchopulmonary dysplasia severity in preterm infants. J Curr Pediatr. 2026;24(2):97-104

Abstract

Introduction: The development of bronchopulmonary dysplasia (BPD) is multifactorial, and the extent to which individual risk factors influence its development may vary. The aim of this study is to analyse the risk factors for BPD and to determine preventive future approaches for them.

Materials and Methods: This study was conducted on newborns with a gestational age ≤32 weeks. admitted to the neonatal intensive care unit, Antenatal, natal, and postnatal risk factors for premature infants were evaluated by collecting data from patient files using a retrospective cross-sectional descriptive study method.

Results: According to the inclusion criteria, 539 patients were included in the study. BPD was detected in 172 patients (31.9%) at any stage (mild-moderate-severe). Low gestational age, low birth weight, delayed transition to enteral feeding, low free thyroxine levels, delayed initiation of vitamin D supplementation, erythrocyte transfusion and counts, and prolonged respiratory support durationwere found to be risk factors for BPD development ($p<0.05$). According to the results of the multivariate logistic regression analysis, the day of oxygen restriction [odds ratio (OR), 1.332; 95% confidence interval (CI) 1.064–1.667, $p=0.012$] and red blood cell transfusion (OR 41.865, 95% CI 1.337–1310.596, $p=0.034$) were found to be independent risk factors for BPD.

Conclusion: In our study, oxygen support period and erythrocyte transfusion may independent risk factors for BPD development. Additionally, as a significant new finding, we determined that low free thyroxine levels and delayed initiation of vitamin D supplementation may be related to the severity of BPD.

Öz

Giriş: Bronkopulmoner displazinin (BPD) gelişimi çok faktörlüdür ve bireysel risk faktörlerinin gelişimini etkileme derecesi değişebilir. Bu çalışmanın amacı, BPD için risk faktörlerini analiz etmek ve bunlar için gelecekteki önleyici yaklaşımları belirlemektir.

Gereç ve Yöntem: Bu çalışma, gebelik yaşı ≤32 hafta olan ve yenidoğan yoğun bakım ünitesine yatırılan yenidoğanlar üzerinde gerçekleştirilmiş olup, prematüre bebekler için doğum öncesi, doğum sırası ve doğum sonrası risk faktörleri, retrospektif kesitsel tanımlayıcı çalışma yöntemi kullanılarak hasta dosyalarından veri toplanarak değerlendirilmiştir.

Keywords
Bronchopulmonary dysplasia, prematurity, risk factors, vitamin D, free thyroxine

Anahtar kelimeler
Bronkopulmoner displazi, prematürite, risk faktörleri, D vitamini, serbest tiroksin

Received/Geliş Tarihi : 07.04.2026
Accepted/Kabul Tarihi : 05.06.2026
Epub: : 12.06.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.90094

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Bulgular: Dahil edilme kriterlerine göre, çalışmaya 539 hasta dahil edildi. BPD, herhangi bir evrede (hafif, orta, şiddetli) 172 hastada (%31,9) tespit edildi. Düşük gebelik yaşı, düşük doğum ağırlığı, enteral beslenmeye geçişin gecikmesi, düşük serbest tiroksin seviyeleri, D vitamini takviyesinin gecikmeli başlatılması, eritrosit transfüzyonu ve sayımları ve uzun süreli solunum desteği süresi, BPD gelişimi için risk faktörleri olarak bulundu (p<0,05). Çok değişkenli lojistik regresyon analizinin sonuçlarına göre, oksijen kısıtlamasının uygulandığı gün [olasılık oranı (OR), 1,332; %95 güven aralığı (CI) 1,064–1,667, p=0,012] ve kırmızı kan hücresi transfüzyonu (OR 41,865, %95 CI 1,337–1310,596, p=0,034) BPD için bağımsız risk faktörleri olarak bulundu.
Sonuç: Çalışmamızda, oksijen desteği süresi ve eritrosit transfüzyonu, bronkopulmoner displazi (BPD) gelişimi için bağımsız risk faktörleri olabileceği belirlenmiştir. Ayrıca, önemli yeni bir bulgu olarak, düşük serbest tiroksin seviyelerinin ve D vitamini takviyesine geç başlanmasının BPD'nin şiddetiyle ilişkili olabileceğini tespit ettik.

Introduction

Northway and colleagues were the first to observe bronchopulmonary dysplasia (BPD) approximately half a century ago. BPD has been defined as a chronic lung disease resulting in pulmonary fibrosis following mechanical ventilation treatment due to respiratory distress in a relatively larger number of premature infants (1). In time, with the development of treatment strategies aimed at reducing respiratory distress and premature morbidity, smaller premature babies are able to survive. A new clinical presentation is emerging in the alveolar and pulmonary vascular structures of smaller preterm infants due to impaired extrauterine development. Chronic respiratory failure in small preterm infants is currently defined as "New BPD." According to current guidelines, premature infants born before 32 weeks of gestation who require respiratory support by the time they reach the postmenstrual corrected 36th week are diagnosed with BPD at different stages (2).

The maturation of the pulmonary system in premature infants continues even after birth (2). The pathogenesis of BPD in preterm infants involves an inflammatory cascade that leads to impaired alveolarization and abnormal angiogenesis during lung development (3). During the extrauterine pulmonary development period oxygen, invasive respiratory support and numerous prenatal and postnatal factors may increase the risk of BPD development. Nevertheless, the most important known risk factors for BPD development are low gestational age and weight at birth (1). The presence of genetic and environmental factors in the development of BPD in preterm infants can further complicate the pathophysiology. The degree of severity of the effects of all other additional risk factors on BPD development may vary between neonatal intensive care units and over time (3).

BPD is the most significant respiratory morbidity in premature infants and methods developed to reduce BPD are primarily based on identifying risk factors, followed by reducing these risk factors and implementing preventive approaches (3,4). Therefore, identifying BPD risk factors is crucial to help prevent BPD (5). There is still a need for current research on the pathophysiology, risk factors and treatment of BPD. As the influence of BPD risk factors differs across neonatal units, ongoing evaluation of changes in these risk patterns over time is necessary (2,6,7).

According to our study hypothesis, identifying BPD risk factors in premature infants in our unit may enable us to develop preventive and therapeutic approaches for potential BPD risk factors in the future. This can lead to improved quality of care for premature infants and a reduction in the severity or frequency of BPD and improved quality of life. Our study aimed to facilitate clinical decision-making by identifying prenatal, natal, and postnatal BPD risk factors in preterm infants born at ≤32 weeks of gestation, enabling early prediction and prevention of BPD.

Materials and Methods

Design and Participants

This study was conducted on premature newborns with a gestational age ≤32 weeks who were admitted to the Neonatal Intensive Care Unit at Ankara Bilkent City Hospital Children's Hospital and Women's Hospital of Health Sciences University between September 1, 2019, and December 31, 2020. The data from our study population were evaluated using a retrospective cross-sectional descriptive study method to identify antenatal, natal, and postnatal risk factors for BPD. Newborns with a gestational age >32 weeks and those with major congenital anomalies were excluded from the study. The criterion of oxygen support requirement on postnatal 28th day was used for staging the severity of BPD in the neonatal period. Therefore, patients born at ≤32 weeks gestation and lost within the first 28 days were excluded from the study.

Ethical approval was obtained before the study commenced from the Clinical Research Ethics Committee of University of Health Sciences Türkiye, Ankara Bilkent City Hospital, Hospital (decision no. E2-21-364, date: 07.04.2021).

The study process was performed by the researchers in accordance with the Helsinki principles.

Demographic and Clinical Characteristics

Patient data were obtained from patient files and the hospital-based electronic data system. The patients' prenatal, natal, and postnatal history, demographic data laboratory results, and treatments were recorded for the study. Patients' gestational age at birth, birth weight, sex, maternal age, preeclampsia, gestational diabetes mellitus, multiple pregnancy, antenatal steroids, chorioamnionitis, mode of delivery, 1. and 5. minute Apgar scores, clinical risk ındex for babies (CRIB) II score, score for neonatal acute physiology perinatal extension (SNAP-PE) II score, delivery room resuscitation (positive pressure ventilation or intubation or cardiac compression), time to start vitamin D supplementation, free thyroxine (fT4) levels, thyroid-stimulating hormone (TSH) levels, time to transition to full enteral feeding, early neonatal sepsis (within the first 3 days of birth) late-onset neonatal sepsis (after the first 3 days), respiratory distress syndrome (RDS), hemodynamically significant patent ductus arteriosus (PDA) requiring medical treatment, (stage ≥2) necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), severe (≥stage 3) intraventricular hemorrhage (IVH), need for erythrocyte transfusion, number of erythrocyte transfusions, total noninvasive ventilation time, mechanical ventilation time, oxygen support time, length of stay, and mortality data were recorded. Vitamin D was administered orally at a dose of 1200 IU/day for each infant. In all our study patients, fT4 and TSH levels were assessed on the 10th postnatal day as a standard procedure. Both early and late neonatal sepsis were defined as sepsis in patients with culture-positive and clinical sepsis. RDS was defined for patients with surfactant deficiency who received surfactant. According to our unit transfusion policy, all erythrocyte transfusions are administered at a dose of 10 ml/kg. Patients were grouped as having no BPD, mild, moderate, and severe BPD and were compared in terms of demographic and clinical characteristics.

Bronchopulmonary Dysplasia Classification

BPD classification is performed for preterm infants born before 32 weeks of gestation at 36 weeks postmenstrual (PM) or at the time of hospital discharge. Premature infants must have received at minimum 21% oxygen support therapy for the first 28 days to be discharged or, if not receiving oxygen support at 36 weeks gestational age, have mild BPD, if the patient requires <30% oxygen support, it is classified as moderate BPD and if the patient requires ≥30% oxygen support or positive pressure ventilation support, it is classified as severe BPD (2).

Statistical Analysis

The number (n) and percentage (%) values were used to show the distribution of the individuals in the demographic information. The normality of the continuous variables included in the study was assessed graphically and using the Shapiro-Wilk test. Median (minimum-maximum) values were used in the presentation of descriptive statistics. According to the BPD status, cross-tables were created for the comparison of categorical variables, and the number (n), percentage (%), and chi-square (χ^2) test statistic were given. Kruskal-Wallis was used to compare continuous variables according to BPD status. Analysis results were presented with Bonferroni correction for paired comparisons. Potential risk factors may be associated with BPD were examined using multivariate logistic regression analyses. Results are presented as odds ratios (Exp (B)] and 95% confidence intervals. IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS-Excel 2007 software was used for statistical analyses and calculations. Statistical significance was defined as $p<0.05$.

Results

A total of 687 preterm infants born at ≤32 weeks gestation during the study period were reviewed. Since patients must survive for at least 28 days to receive a BPD diagnosis, 148 patients who died before the first 28 days were excluded from the study, and statistical analysis was performed on 539 patients.

BPD was not detected in 68.1% (n=367) of the total 539 patients, while it was detected in 31.9% (n=172) at any stage. Of the 172 patients with BPD, 12.6% (n=68) had mild BPD, 9.3% (n=50) had moderate BPD, and 10.0% (n=54) had severe BPD. The prevalence of BPD at any stage was found to be 31.9% (n=172). Of the patients 42.7% (n=220) were female and 57.3% (n=319) male gender. The mean gestational age was determined to be 29.7±2.4 weeks.

There was no significant difference between genders according to BPD stages. BPD severity increased significantly as birth weight and gestational age decreased among groups with birth week ≤28 weeks and >28-32 weeks, and birth weight ≤750 g, 750-1000 g, 1000-1500 g, and >1500 g (Table 1).

Table 1. Comparison of gender, gestational age, and birth weight according to bronchopulmonary dysplasia classification

Variables	Bronchopulmonary dysplasia				p
	None (n=367)	Mild (n=68)	Moderate (n=50)	Severe (n=54)	
	n (%)	n (%)	n (%)	n (%)	
Gender					
Female	166 (45.2)	24 (35.3)	20 (40.0)	23 (43.4)	0.481
Male	201 (54.8)	44 (64.7)	30 (60.0)	31 (56.6)	
Gestational age					
≤28 weeks	51 (13.7)	30 (44.1)	33 (66.0)	36 (66.7)	<0.001*
>28-32 weeks	316 (86.3)	39 (55.9)	17 (34.0)	18 (33.3)	
Birth weight					
≤750 g	9 (2.5)	9 (13.2)	7 (14.0)	14 (25.9)	<0.001*
750-1000 g	28 (7.7)	4 (5.9)	10 (20.0)	14 (25.9)	
>1000-1500 g	117 (32.0)	35 (51.5)	22 (44.0)	21 (38.9)	
>1500 g	213 (57.8)	21 (29.4)	11 (22.0)	5 (9.3	

*Statistically significant p values are highlighted

There were no significant differences between groups in terms of maternal age, preeclampsia, gestational diabetes mellitus, multiple pregnancy, antenatal steroids, chorioamnionitis, cesarean delivery, and TSH levels according to BPD stages (p>0.05). The CRIB II score, SNAP-PE II score, delivery room resuscitation rates, day of starting vitamin D, and transition to full enteral feeding day were found to increase in direct proportion to BPD severity, while the 1. and 5. minute Apgar scores and fT4 levels decreased significantly as BPD severity increased (p<0.05) (Table 2).

Early and late neonatal sepsis, RDS, PDA, NEC, ROP, erythrocyte transfusion frequency, number of erythrocyte transfusions, noninvasive ventilation duration, mechanical ventilation duration, oxygen support duration, and length of stay were found to be significantly increased with BPD severity (p<0.05). Mortality rates were significantly lower in the mild and moderate BPD group compared to the severe and non-BPD group (p=0.001). No significant difference was found between the groups in the frequency of intraventricular hemorrhage (p>0.05) (Table 3).

Logistic regression analysis was performed by controlling for gestational age and birth weight risk factors independently may be associated with an increase in BPD rate. Multivariate logistic regression analysis revealed that the risk of BPD increased by 1.332 times as oxygen support duration increased and by 41.865 times with erythrocyte transfusion (p=0.012 and p=0.034, respectively) (Table 4).

Discussion

In our study analyzing premature infants born at ≤32 weeks gestation, we found that the incidence and severity of BPD increased with gestational age. We observed that increasing BPD severity may be associated with lower Apgar scores and significantly higher CRIB II and SNAP-PE II scores. Increased BPD severity may be associated with increased frequency of other preterm morbidities, excluding IVH. Our findings suggest that low fT4 levels and delayed starting of vitamin D supplementation may be associated with the development of severe BPD. In addition, based on our results following regression analysis, we may state that the primary risk factors for BPD development are the duration of oxygen support and erythrocyte transfusion.

BPD is a common complication of preterm birth and is associated with serious short- and long-term complications (8). BPD is one of the morbidities of prematurity that can cause long-term, destructive consequences in premature infants, affecting multiple organ systems, including adverse effects on lung function and neurodevelopmental outcomes (9).

Table 2. Relationship between bronchopulmonary dysplasia classification and demographic characteristics

Characteristics	Bronchopulmonary dysplasia				p
	None (n=367)	Mild (n=68)	Moderate (n=50)	Severe (n=54)	
Maternal age, years[a]	29.0 (15-44)	27.5 (18-42)	28.0 (16-41)	28.5 (18-41	0.376
Preeclampsia[b]	69 (20.4)	7 (11.7)	9 (21.4)	14 (31.8)	0.095
Gestasyonel diabetes mellitus[b]	30 (9.0)	2 (3.6)	3 (7.0)	2 (4.7)	0.387
Multiple pregnancy[b]	110 (29.9)	25 (36.7)	15 (30)	10 (18.5)	0.491
Antenatal steroid[b]	234 (84.5)	43 (82.7)	26 (72.2)	32 (86.5)	0.291
Chorioamnionitis[b]	12 (21.8)	2 (10.5)	3 (25.0)	4 (33.3)	0.462
Cesarean delivery[b]	327 (89.2)	64 (92.4)	44 (93.6)	45 (84.3)	0.399
1. min Apgar score[a]	6.0 (1-9)	6.0 (0-7)	5.0 (1-7)	4.0 (0-7)	<0.001*
5. min Apgar score[a]	8.0 (0-10)	7.0 (2-9)	7.0 (3-8)	7.0 (2-9)	<0.001*
Resusitation in delivery room[b]	120 (32.6)	33 (48.5)	26 (52)	39 (72.2)	<0.001*
CRIB II score[a]	3.0 (0-17)	6.0 (2-15)	7.0 (0-13)	10.0 (2-14)	<0.001*
SNAP-PE II score[a]	0.0 (0-35)	0.0 (0-35)	0.0 (0-35)	18.0 (0-47)	<0.001*
Day of starting vitamin D, days[a]	11.0 (4-50)	13.0 (7-66)	12.0 (7-59)	15.0 (7-88)	<0.001*
f T4, ng/dL[a]	1.4 (0.2-10.0)	1.2 (0.2-3.1)	1.1 (0.2-8.3)	1.1 (0.6-3.6)	<0.001*
TSH, uIU/L[a]	3.9 (0.3-112.0)	3.8 (0.3-65.3)	3.9 (0.5-5.80)	3.9 (0.6-100.0)	0.692
Full enteral feeding day, days[a]	8.0 (1-53)	14.0 (5-53)	13.0 (7-56)	20.0 (8-121)	<0.001*

*Statistically significant p values are highlighted, [a]median (minimum-maximum), [b]n (%), CRIB: Clinical Risk Index For Babies, SNAP-PE II: Score for Neonatal Acute Physiology Perinatal Extension II, fT4: Free thyroxine, TSH: Thyroid-stimulating hormone

Table 3. Premature morbidity and mortality outcomes according to bronchopulmonary dysplasia stage

Characteristics	Bronchopulmonary dysplasia				p
	None (n=367)	Mild (n=68)	Moderate (n=50)	Severe (n=54)	
Early neonatal sepsis[a]	198 (54.1)	46 (63.2)	39 (80.4)	36 (65.4)	0.004*
Late neonatal sepsis[a]	163 (46.7)	52 (77.6)	44 (91.7)	53 (100.0)	<0.001*
Respiratory distress syndrome[a]	103 (28.2)	42 (63.6)	38 (74.0)	47 (84.6)	<0.001*
Patent ductus arteriosus[a]	44 (12.9)	28 (41.8)	31 (63.3)	32 (61.5)	<0.001*
Necrotizing enterocolitis[a]	13 (3.6)	7 (10.3)	5 (10.0)	9 (16.7)	0.002*
Retinopathy of prematurity[a]	47 (16.4)	30 (45.5)	29 (58.0)	40 (74.1)	<0.001*
Intraventricular hemorrhage[a]	2 (0.5)	1 (1.4)	1 (2)	2 (3.7)	0.315
Erythrocyte transfusion[a]	93 (25.9)	44 (64.7)	47 (95.9)	51 (96.2)	<0.001*
Number of erythrocyte transfusion[b]	2.0 (1-5)	2.0 (1-7)	2.0 (1-9)	5.0 (1-14)	<0.001*
Total non invasive ventilation time, days[b]	2.0 (0-41)	12.0 (1-51)	17.5 (2-51)	17.0 (0-63)	<0.001*
Total mechanical ventilation time, days[b]	1.0 (0-61)	11.5 (0-96)	28.0 (0-95)	73.0 (15-261)	<0.001*
Oxygen support time, days[b]	6.0 (0-61)	37.0 (8-112)	60.0 (4-123)	103.5 (50-185)	<0.001*
Hospital stay, days[b]	31.0 (6-128)	54.0 (32-137)	78.0 (37-169)	134.0 (66-378)	<0.001*
Mortality[a]	34 (9.5)	1 (1.5)	0 (0.0)	7 (11.3)	0.001*

*Statistically significant p values are highlighted, [a]n (%), [b]median (minimum-maximum)

Table 4. Potential risk factors associated with bronchopulmonary dysplasia in the multivariate logistic regression model

Variables	β	Standart error	Wald	p	Exp(B)	95% confidence interval for Exp(B)	
						Low	High
1. min Apgar score	0.657	1.347	0.238	0.626	1.930	0.138	27.035
5.min Apgar score	-3.334	2.013	2.742	0.098	0.036	0.001	1.844
Full enteral feeding day	0.179	0.116	2.369	0.124	1.196	0.952	1.502
CRIB score	0.372	0.543	0.471	0.493	1.451	0.501	4.203
SNAP-PE score	-0.212	0.175	1.464	0.226	0.809	0.574	1.140
Respiratory distress syndrome	3.024	2.110	2.053	0.152	20.566	0.329	1287.048
Total mechanical ventilation time	-0.063	0.120	0.281	0.596	0.939	0.743	1.186
Total non invasive ventilation time	-0.283	0.165	2.939	0.086	0.754	0.546	1.041
Oxygen support time	0.287	0.114	6.274	0.012*	1.332	1.064	1.667
Late neonatal sepsis	0.062	1.994	0.001	0.975	1.063	0.021	52.988
Retinopathy of prematurity	2.721	1.900	2.052	0.152	15.202	0.367	629.367
Erythrocyte transfusion	3.734	1.757	4.517	0.034*	41.865	1.337	1310.596

*Statistically significant p values are highlighted, CRIB: Clinical Risk Index For Babies, SNAP-PE II: Score for Neonatal Acute Physiology Perinatal Extension II

BPD development is associated with many risk factors that appear during the prenatal, natal, and postnatal periods. Identifying the main risk factors and indicators in premature babies who will develope significant respiratory problems after birth and be diagnosed with BPD at 36 weeks is one of the most challenging research topics today. The aim of studies is often to identify the target group of BPD patients who will benefit most from specific treatment alternatives in the early postnatal (2,8). In this context, units strive to identify risk factors for BPD development and, based on the results obtained, are able to develop BPD prevention strategies (1,2,8). In our study, we aimed to reduce the risk factors for BPD development and identify preventive methods for BPD by determining our unit conditions and risk factors for BPD.

Low gestational age and birth weight are the main risk factors for BPD due to extrauterine immature lung development (8,9). Compared to full-term infants, the prevalence of BPD in infants born at ≤32 weeks of gestation ranges from 21% to 47% (9). The incidence of BPD in preterm infants with a gestational age of less than 32 weeks is 29.2%, and in those born before 28 weeks, it can increase to 47.8% (10). This frequency may varies across countries and between units. It is thought that variability in clinical care standards and genetic factors are primarily responsible for the changing prevalence of BPD (9). Our results appear to be consistent with these informations. Maternal illnesses, infections, prenatal and natal characteristics may negatively affect BPD development (5,11). In our results, maternal diseases, mode of delivery, multiple pregnancy, chorioamnionitis, and frequency of antenatal steroid administration were not significant risk factors affecting the BPD incidence. The reason for the varying effects of antenatal and natal factors on BPD may stem from the variability in BPD risks or risk-reducing procedures in the databases of different studies. Furthermore, the genetic, epigenetic, and immunological characteristics of the study groups may be the key factors in the development of BPD (8,9,12). The increased severity of BPD in our results appears to be associated with increased CRIB II, SNAP-PE II, and low Apgar scores, a high need for resuscitation, a longer time to transition to full enteral feeding, and the fact that patients with severe BPD were born at a lower gestational age (5,8,9,12).

A premature baby born with immature lungs, due to a lower birth week and weight, faces significant respiratory support treatment and impaired lung development. Increased incidence of RDS associated with immature lungs, increased

infections due to immature immune systems, prolonged hospital stays, high mortality, and other morbidities of prematurity such as PDA and NEC are associated with low gestational age and increased BPD severity, as reported in our study (2,8,9,11).

All newborn babies are given vitamin D supplementation unless there is a gastrointestinal contraindication, in according with the national nutrition protocol. The timing of initiation of vitamin D supplementation due to lack of sunlight, low cord blood vitamin D levels, and low maternal milk vitamin D levels, and its effect on BPD are unknown (13). An important and novel finding of our study is that delayed initiation of vitamin D supplementation increases the severity of BPD. Vitamin D, with its anti-inflammatory properties, affects the inflammatory process in BPD development and also regulates alveolar signaling pathways that support perinatal lung maturation (14). These effects of vitamin D may explain the result in our findings that early vitamin D supplementation reduces the severity of BPD. Animal studies on vitamin D have found that vitamin D has a protective effect against neonatal lung injury caused by hyperoxia, a major factor in the development of BPD (15). Based on experimental data and our findings, there is a need for new studies to test the role of vitamin D in preventing BPD in premature infants. Ge et al. (16) administered 800 IU of vitamin D supplementation to small premature infants at 32 weeks of gestation within the first 48 hours after birth. They showed a significant reduction in the incidence of BPD in the vitamin D supplemented group compared to the control group. Vitamin D may bind to vitamin D receptors to regulate inflammatory response, immune response, and hormone secretion. During lung development and maturation, vitamin D may increase the expression of alveolar epithelial-mesenchymal differentiation agents, improve the proliferation of alveolar and vascular endothelial cells, and promote the synthesis of alveolar surfactants. Ge et al. (16) demonstrated that the positive effect of vitamin D on BPD development was due to the reduction of inflammatory cytokines.

Premature babies often require long-term supplemental oxygen to ensure adequate oxygenation due to their immature lungs. In this situation, exposure to hyperoxia leads to oxidative stress, impaired lung development, and the development of BPD as a result of pulmonary fibrosis (5,17). In our patients, longer oxygen support duration was strongly associated with BPD severity; however, this finding should be interpreted cautiously because oxygen requirement is part of the diagnostic definition of BPD. Despite improvements in the survival rates of more premature infants and advances in medical care, BPD remains a significant cause of morbidity in premature infants. Therefore, there is still a need to study new mechanisms that mediate oxidative stress and lung development in newborns (17,18).

We found that fT4 levels were significantly reduced in patients with severe BPD. Regarding the effect of thyroid hormones on lung development, it has been reported that thyroid hormones, including T4 and triiodothyronine play a role in regulating fetal lung development and that serum T4 levels decrease in hyperoxia-exposed mice (19,20). Reducing oxidative stress-induced mitochondrial dysfunction through thyroid hormones deficiency and thyroid hormone supplementation may be a useful strategy for reducing neonatal lung injury and BPD (17). However, based on limited evidence, systemic thyroid hormone supplementation has been shown to provide minimal respiratory beneficial effects on BPD (21). In this context, based on our results and limited literature data, it remains unknown whether thyroid hormones can improve hyperoxic lung injury and reduce the risk of BPD in preterm infants. Therefore, the effect of thyroid hormones on BPD appears to be a pathophysiological issue that has not been sufficiently elucidated and needs to be clarified through further studies.

Erythrocyte transfusion has been shown to be an independent risk factor for BPD severity in our patient population. The transfusion of erythrocyte may increase the risk of oxidative damage, infection, and other complications (22). Increased oxidative damage with erythrocyte transfusion, increased transferrin-unbound iron, and inflammatory mediators present in transfused blood products are implicated as possible mechanisms of transfusion's effect on the development or severity of BPD (9,23). Before now, the relationship between blood transfusions and BPD has not been clearly distinguished in terms of causality (5). Our study brings to mind the need for a more detailed examination of the relationship between erythrocyte transfusion and BPD.

Study Limitations

The main limitations of our study can be considered to be its retrospective design and the limited data available from a single unit. We were unable to provide more detailed data on thyroid hormones monitoring, red blood cell transfusion data, maternal and umbilical cord vitamin D levels, and neurodevelopmental outcomes.

Conclusion

Our study reiterates the negative effect of hyperoxia on the development of BPD. Limited and guideline-compliant applications, instead of liberal oxygen and red blood cell transfusion practices, may have a positive effect on BPD development. In addition, our study found that starting vitamin D supplementation later and having low fT4 levels may increase the severity of BPD. Furthermore, our study reported a potential association between late initiation of vitamin D supplementation, low fT4 levels, and increased BPD severity. Our current findings may offer an additional perspective on BPD development and a new perspective for further studies.

Ethics

Ethical Approval: Ethical approval was obtained before the study commenced from the Clinical Research Ethics Committee of Health Sciences University Ankara Bilkent City Hospital, Hospital (decision no. E2-21-364, date: 07.04.2021). The study process was performed by the researchers in accordance with the Helsinki principles.

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Northway WH Jr, Rosan RC, Porter DY. Pulmonary disease following respirator therapy of hyaline-membrane disease. Bronchopulmonary dysplasia. N Engl J Med. 1967;276:357-68.
2. Arsan S, Korkmaz A, Oğuz S. Turkish Neonatal Society guideline on prevention and management of bronchopulmonary dysplasia. Turk Pediatri Ars. 2018;53:S138-50.
3. Cakir U, Tayman C, Tugcu AU, Yildiz D. Role of systemic inflammatory indices in the prediction of moderate to severe bronchopulmonary dysplasia in preterm infants. Arch Bronconeumol. 2023;59:216-22.
4. Yıldız D, Çakır U, Tugcu AU, Tayman C. Prematürelerde kan gruplarının bronkopulmoner displaziye etkisi. Acta Medica Nicomedia. 2022;5:199-203.
5. Xiong P, Li L, Yu Z, Pu Y, Tang H. Risk factors for bronchopulmonary dysplasia in preterm infants: a systematic review and meta-analysis. PeerJ. 2025;13:e20202.
6. Thébaud B, Goss KN, Laughon M, Whitsett JA, Abman SH, Steinhorn RH, et al. Bronchopulmonary dysplasia. Nat Rev Dis Primers. 2019;5:78.
7. Dankhara N, Holla I, Ramarao S, Kalikkot Thekkeveedu R. Bronchopulmonary dysplasia: pathogenesis and pathophysiology. J Clin Med. 2023;12:4207.
8. Schmidt AR, Ramamoorthy C. Bronchopulmonary dysplasia. Paediatr Anaesth. 2022;32:174-80.
9. Hwang JS, Rehan VK. Recent advances in bronchopulmonary dysplasia: pathophysiology, prevention, and treatment. Lung. 2018;196:129-38.
10. Cao Y, Jiang S, Sun J, Hei M, Wang L, Zhang H, et al. Assessment of neonatal intensive care unit practices, morbidity, and mortality among very preterm infants in China. JAMA Netw Open. 2021;4:e2118904.
11. Abushahin A, Hamad SG, Sabouni A, Alomar S, Sudarsanan A, Kammouh H, et al. Incidence and predictors of bronchopulmonary dysplasia development and severity among preterm infants born at 32 weeks of gestation or less. Cureus. 2024;16:e59425.
12. Shukla VV, Ambalavanan N. Recent advances in bronchopulmonary dysplasia. Indian J Pediatr. 2021;88:690-5.
13. Kültürsay N, Bilgen H, Türkyılmaz C. Turkish Neonatal Society guideline on enteral feeding of the preterm infant. Turk Pediatri Ars. 2018;53:S109-S118.
14. Sakurai R, Shin E, Fonseca S, Sakurai T, Litonjua AA, Weiss ST, et al. 1alpha,25(OH)2D3 and its 3-epimer promote rat lung alveolar epithelial-mesenchymal interactions and inhibit lipofibroblast apoptosis. Am J Physiol Lung Cell Mol Physiol. 2009;297:L496-505.
15. Yurt M, Liu J, Sakurai R, Gong M, Husain SM, Siddiqui MA, et al. Vitamin D supplementation blocks pulmonary structural and functional changes in a rat model of perinatal vitamin D deficiency. Am J Physiol Lung Cell Mol Physiol. 2014;307:859-67.
16. Ge H, Qiao Y, Ge J, Li J, Hu K, Chen X, et al. Effects of early vitamin D supplementation on the prevention of bronchopulmonary dysplasia in preterm infants. Pediatr Pulmonol. 2022;57:1015-21.
17. Vamesu BM, Nicola T, Li R, Hazra S, Matalon S, Kaminski N, et al. Thyroid hormone modulates hyperoxic neonatal lung injury and mitochondrial function. JCI Insight. 2023;8:e160697.
18. Benali M, Ben Hamida N, Jaouhari S, Ayadi I, Ben Hamida E. Prevalence and risk factors of bronchopulmonary dysplasia among very premature infants in a Tunisian neonatal intensive care unit. Tunis Med. 2024;102:551-7.
19. Hume R, Richard K, Kaptein E, Stanley EL, Visser TJ, Coughtrie MW. Thyroid hormone metabolism and the developing human lung. Biol Neonate. 2001;80:18-21.
20. Kowallick M, Serdar M, Markova B, Salveridou E, Felderhoff-Müser U, Führer-Sakel D, et al. Hyperoxia leads to transient endocrine alterations in the neonatal rat during postnatal development. Front Pediatr. 2021;9:723928.
21. Biswas S, Buffery J, Enoch H, Bland M, Markiewicz M, Walters D. Pulmonary effects of triiodothyronine (T3) and hydrocortisone (HC) supplementation in preterm infants less than 30 weeks gestation: results of the THORN trial--thyroid hormone replacement in neonates. Pediatr Res. 2003;53:48-56.
22. Collard KJ. Is there a causal relationship between the receipt of blood transfusions and the development of chronic lung disease of prematurity? Med Hypotheses. 2006;66:355-64.
23. Bolat F, Dursun M, Sarıaydın M. Packed red blood cell transfusion as a predictor of moderate-severe bronchopulmonary dysplasia: a comparative cohort study of very preterm infants. Am J Perinatol. 2024;41:e1499-507.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Depressive Symptoms in Primary Caregivers of Children with Beta-thalassemia

Beta-talasemili Çocukların Birincil Bakım Verenlerinde Depresif Belirtiler

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Cite this article as: Turmus GH, Akpınar F, Koca Yozgat A, Karakütük A, Yeşil AM, Öztürk Emiral G, et al. Depressive symptoms in primary caregivers of children with beta-thalassemia. J Curr Pediatr. 2026;24(2):105-10

Abstract

Introduction: Beta-thalassemia major is a chronic hematologic condition that requires lifelong medical care and imposes substantial psychosocial demands on families. Primary caregivers, particularly parents, face ongoing emotional, financial, and practical stressors that may place them at increased risk for depressive symptoms. Despite this burden, routine screening for caregiver mental health remains limited in many pediatric settings. This study aimed to assess depressive symptoms among primary caregivers of children with beta-thalassemia major using the Patient Health Questionnaire-2 (PHQ-2) and to explore potential associations with sociodemographic and clinical characteristics.

Materials and Methods: This cross-sectional descriptive study included 49 primary caregivers of children with beta-thalassemia major followed at a tertiary pediatric hematology center in Türkiye. Data were collected using a structured sociodemographic questionnaire and the PHQ-2. Relationships between depressive symptoms and caregiver- and child-related variables were examined.

Results: Sixteen percent of caregivers scored above the PHQ-2 cutoff, indicating increased risk for depression. PHQ-2 scores did not differ significantly according to the child's gender, transfusion frequency, medication use, or presence of medical complications. Similarly, no significant associations were found with parental age, education level, chronic illness, household income, household size, or immigration status. Although not statistically significant, higher depressive symptom scores were observed among caregivers with first-degree relatives affected by chronic illness and among those whose children did not receive formal social support services.

Conclusion: A meaningful proportion of caregivers of children with beta-thalassemia major exhibited elevated depressive symptoms, even in the absence of clear sociodemographic or clinical predictors. These findings highlight the importance of incorporating brief mental health screening tools into routine pediatric hematology follow-up and emphasize the need for multidisciplinary approaches that address both medical and psychosocial aspects of chronic childhood illness. Further studies with larger samples are warranted to better identify risk factors and to inform targeted support strategies for caregivers.

Keywords
Beta-thalassemia, caregiver, depressive signs

Anahtar kelimeler
Beta talasemi, bakım veren, depresyon bulguları

Received/Geliş Tarihi : 14.01.2026
Accepted/Kabul Tarihi : 09.06.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.23245

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Öz

Giriş: Beta-talasemi majör, yaşam boyu süren tedavi gereksinimi olan kronik bir hastalık olup yalnızca çocukları değil, bakım veren aile üyelerini de önemli ölçüde etkilemektedir. Süregelen hastane ziyaretleri, tedaviye bağlı yük ve geleceğe yönelik belirsizlikler, birincil bakım verenlerde ruhsal zorlanmaya yol açabilmektedir. Bu çalışmanın amacı, beta-talasemili çocukların birincil bakım verenlerinde depresif belirtilerin sıklığını Patient Health Questionnaire-2 (PHQ-2) ile değerlendirmek ve bu belirtilerin sosyodemografik ve klinik değişkenlerle ilişkisini incelemektir.

Gereç ve Yöntem: Bu kesitsel tanımlayıcı çalışmaya, üçüncü basamak bir çocuk hematoloji merkezinde izlenen beta-talasemi majör tanılı çocukların 49 birincil bakım vereni dahil edilmiştir. Veriler, sosyodemografik özellikleri içeren yapılandırılmış anket formu ve PHQ-2 ölçeği kullanılarak toplanmıştır. Depresif belirtiler ile bakım verene ve çocuğa ait değişkenler arasındaki ilişkiler değerlendirilmiştir.

Bulgular: Bakım verenlerin %16'sının PHQ-2 eşik puanının üzerinde skor aldığı ve depresyon açısından risk altında olduğu saptanmıştır. PHQ-2 skorları; çocuğun cinsiyeti, transfüzyon sıklığı, medikal komplikasyon varlığı ve ilaç kullanımı gibi klinik değişkenlere göre anlamlı farklılık göstermemiştir. Benzer şekilde, ebeveyn yaşı, eğitim düzeyi, kronik hastalık öyküsü, hane geliri ve göçmenlik durumu ile depresif belirtiler arasında anlamlı bir ilişki bulunmamıştır. Bununla birlikte, birinci derece akrabasında kronik hastalık bulunan bakım verenlerde ve sosyal destek hizmetlerinden yararlanmayan çocukların bakım verenlerinde depresif belirti puanlarının daha yüksek olduğu gözlenmiştir; ancak bu fark istatistiksel olarak anlamlı değildir.

Sonuç: Beta-talasemili çocukların bakım verenlerinin kayda değer bir bölümünde depresif belirtiler bulunmasına karşın, bu durumun belirgin sosyodemografik ya da klinik yordayıcıları saptanamamıştır. Bulgular, pediatrik hematoloji izleminde bakım verenlerin ruh sağlığının kısa tarama araçlarıyla rutin olarak değerlendirilmesinin önemini vurgulamaktadır. Ayrıca, kronik hastalık yönetiminde yalnızca tıbbi değil, psikososyal boyutları da kapsayan bütüncül yaklaşımlara gereksinim olduğunu göstermektedir.

Introduction

β-thalassemia major (β-TM) is an autosomsbal recessive hemoglobinopathy characterized by impaired production of the beta-globin chain. This condition is particularly prevalent in the Mediterranean region and is typically diagnosed in early childhood, requiring lifelong medical management. Children diagnosed with β-TM depend on regular red blood cell transfusions and iron chelation therapy to sustain life (1). These medical requirements not only affect the physical health of the child but also significantly impact the family system and the psychological well-being of the primary caregivers. The presence of chronic illnesses during childhood represents a substantial source of stress, particularly for primary caregivers. Continuous hospital visits, financial burdens of treatment, uncertainties regarding the child's quality of life, and social isolation are among the factors that may negatively influence the mental health of parents (2). Depression is one of the most commonly reported psychological problems among this group. Studies have shown that parents of children with chronic illnesses exhibit higher levels of depressive symptoms compared to the general parent population (3).

Studies from different sociocultural contexts have reported inconsistent findings regarding depressive symptoms among families of children with β-TM. Research from Sri Lanka and Pakistan highlights an increased psychosocial burden among parents, with coping being influenced by caregiver burden and spiritual beliefs (4,5). In Türkiye, depression was reported in 13.15% of parents of children with β-TM (6). Overall, low socioeconomic status, limited education, insufficient social support, and gender have consistently been identified as key factors associated with parental depression (7). Depressive symptoms not only diminish the quality of life of parents but may also adversely affect the child's treatment adherence, developmental outcomes, and overall psychosocial functioning. Therefore, early identification and provision of psychological support services are as crucial as the medical follow-up of the child.

In Türkiye, studies focusing on depression screening among parents of children with chronic pediatric conditions such as β-TM remain limited. This study aims to assess the prevalence of depressive symptoms using the Patient Health Questionnaire-2 (PHQ-2) among parents of children with β-TM followed at Ankara Bilkent City Hospital, and to explore potential associations between depressive symptoms and parental sociodemographic characteristics. The findings of this study are expected to highlight the need for psychosocial support and contribute to the development of follow-up policies.

Materials and Methods

This cross-sectional descriptive study was conducted to evaluate the depression levels of mothers of children diagnosed with β-TM followed in the Pediatric Hematology Department of City Hospital. The study included mothers of 49 children with β-TM aged between 7 and 18 years.

Children whose mothers declined participation or could not be reached were excluded from the study. Data were collected using a sociodemographic information form and the Patient Health Questionnaire-2 (PHQ-2). The PHQ-2 is a brief screening tool that assesses depressive symptoms experienced in the past two weeks, with total scores ranging from 0 to 6 (8,9).

The relationships between PHQ-2 scores and various factors, such as the child's gender, age group, parental education, presence of chronic illness, medication use, transfusion frequency, and household income level, were statistically analyzed. In addition to medical and sociodemographic data, the study assessed whether families had obtained the "Report for Children with Special Needs" (ÇÖZGER), which is a formal document issued in Türkiye to facilitate children's access to educational and social support services (10). Ethical approval was obtained from the Scientific and Ethical Evaluation Board for Medical Research (TABED; approval no.: 2-25-1051, date: 19.03.2025). Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). The normality of distribution for continuous variables was assessed using the Shapiro-Wilk test. For comparisons between two groups with normally distributed data, the independent samples Student's t-test was used, while one-way analysis of variance (One-Way ANOVA) was applied for comparisons involving more than two groups. For non-normally distributed data, non-parametric tests such as the Mann-Whitney U test and the Kruskal-Wallis test were employed. A p-value of <0.05 was considered statistically significant for all analyses.

Results

A total of 49 primary caregivers of children with β-TM were included in the study. The relationships between caregiver depressive symptoms (measured via PHQ-2) and various sociodemographic and clinical variables were examined.

Depressive symptom scores (PHQ-2) did not significantly differ according to the child's gender (female: M = 2.03, SD = 0.94; male: M = 2.30, SD = 0.98; p = 0.345). Similarly, medication use (yes: M = 2.16, SD = 0.91; no: M = 2.00, SD = 1.41; p = 0.729) and transfusion frequency (3 weeks: M = 2.16; 4 weeks: M = 2.08; p = 0.692) were not associated with statistically significant differences in PHQ-2 scores.

Although not statistically significant, caregivers of children with medical complications reported higher mean PHQ-2 scores (M = 2.27, SD = 1.03) compared to those without complications (M = 2.09, SD = 0.93; p = 0.553). Similarly, caregivers of children without a ÇÖZGER (Report for Children with Special Needs) had higher PHQ-2 scores than those with the report (2.27 vs. 2.04; p = 0.397). Receiving a social support payment through ÇÖZGER was also associated with slightly higher mean scores (2.29 vs. 2.09; p = 0.515), though this was not statistically significant.

No significant differences were observed in PHQ-2 scores in relation to mother's age (<35: M = 2.13; ≥35: M = 2.15; p = 0.909), mother's education level (<8 years: M = 1.94; ≥8 years: M = 2.26; p = 0.370), or mother's chronic illness (yes: M = 2.00; no: M = 2.17; p = 0.303).

For fathers, neither age (<35: M = 2.00; ≥35: M = 2.24; p = 0.338) nor education (<8 years: M = 2.33; ≥8 years: M = 2.03; p = 0.328) was significantly associated with PHQ-2 scores. Caregivers whose fathers were unemployed had higher PHQ-2 scores than those whose fathers were employed; however, this difference was not statistically significant (p = 0.102).

A trend toward higher depressive symptoms was also noted among caregivers with first-degree relatives with chronic illness (M = 2.47, SD = 0.87) compared to those without (M = 1.97, SD = 0.97), though the difference was not statistically significant (p = 0.074).

Household income (≤ minimum wage: M = 2.22; > minimum wage: M = 1.92; p = 0.371) and household size (≤4 persons: M = 2.07; ≥5 persons: M = 2.17; p = 0.745) were also not significantly associated with PHQ-2 scores.

Across all analyses, none of the sociodemographic or clinical variables demonstrated statistically significant associations with caregiver depressive symptoms ($p > 0.05$) (Table 1).

Discussion

In this study, 16% of parents of children with β-TM scored above the PHQ-2 cutoff, indicating increased risk for depression. No significant associations were found between parental PHQ-2 scores and children's sociodemographic or clinical characteristics. These findings suggest that parental psychological well-being in β-TM may not be directly determined by the child's clinical profile or socioeconomic factors.

Compared to previous literature, the proportion of parents scoring above the PHQ-2 cutoff in this sample was lower. While research from Malaysia, Sri Lanka, and Pakistan has documented relatively high rates of depressive symptoms among caregivers of children with β-thalassemia major (β-TM), ranging from 29% to over 60%, a study from Türkiye reported prevalence rates comparable to our findings (4,6,11-15). These cross-national differences may reflect variations in sociocultural contexts and the presence of protective factors.

Table 1. Variables that may influence Patient Health Questionnaire-2 (PHQ) scores

Variables	n (%)	Mean PHQ score (SD)	Statistical test (F/t; p)
Gender			
Female	29 (59.2)	2.03 (0.94)	0.953; 0.345
Male	20 (40.8)	2.30 (0.98)	
Medication use			
Yes	44 (89.8)	2.16 (0.91)	0.349; 0.729
No	5 (10.2)	2.00 (1.41)	
Transfusion frequency			
3 weeks	37 (75.5)	2.16 (0.16)	0.574; 0.692
4 weeks	12 (24.5)	2.08 (0.26)	
Complication status			
Yes	15 (30.6)	2.27 (1.03)	0.597; 0.553
No	34 (69.4)	2.09 (0.93)	
Report for Children with Special Needs (ÇÖZGER)			
Yes	27 (55.2)	2.04 (1.13)	0.855; 0.397
No	22 (44.9)	2.27 (1.03)	
Immigrant status			
Turkish	18 (36.7)	2.00 (0.94)	244.0; 0.335
Immigrant	31 (63.3)	2.23 (0.98)	
Social support payment granted through the Child Special Needs Report (ÇÖZGER)			
Yes	14 (28.6)	2.29 (1.07)	0.657; 0.515
No	35 (71.4)	2.09 (0.92)	
Mother's age			
<35 years	16 (32.7)	2.13 (0.50)	0.114; 0.909
≥35 years	33 (67.3)	2.15 (1.12)	
Mother's education			
<8 years	18 (36.7)	1.94 (1.11)	0.896; 0.370
≥8 years	31 (63.3)	2.26 (0.85)	
Mother's chronic illness			
Yes	9 (18.4)	2.00 (0.00)	1.045; 0.303
No	40 (81.6)	2.17 (1.06)	
Father's age			
<35 years	5 (10.2)	2.00 (0.00)	1.110; 0.338
≥35 years	40 (81.6)	2.24 (0.66)	
Father deceased	4 (8.2)	1.79 (1.00)	
Father's education			
<8 years	18 (36.7)	2.33 (1.02)	0.978; 0.328
≥8 years	31 (63.3)	2.03 (0.91)	
Father's chronic illness			
Yes	11 (22.4)	2.55 (1.29)	1.260; 0.231
No	38 (77.6)	2.03 (0.82)	
Working status of father			
Working	38 (77.6)	1.97 (0.75)	1.775; 0.102
Not working	11 (22.4)	2.73 (1.35)	
Paternal consanguinity			
Yes	38 (77.6)	2.05 (0.87)	1.025; 0.324
No	11 (22.4)	2.45 (1.21)	
Chronic illness in 1st degree relatives			
Yes	17 (34.7)	2.47 (0.87)	1.842; 0.074
No	32 (65.3)	1.97 (0.97)	
Household income			
≤ Minimum wage	36 (73.5)	2.22 (0.93)	0.915; 0.371
> Minimum wage	13 (26.5)	1.92 (1.04)	
Household size			
≤ 4	14 (28.6)	2.07 (1.14)	0.125; 0.745
≥ 5	35 (71.4)	2.17 (0.89)	

Although no statistically significant difference was found in our study, PHQ-2 scores were observed to be higher among parents who reported a history of chronic illness in first-degree relatives. This finding suggests that the presence of similar health conditions among family members, may contribute to increased psychological burden for caregivers. Supporting this, a study conducted in Bangladesh by Islam et al. (11) investigated depression levels among parents of children diagnosed with β-TM and reported that a family history of mortality due to β-TM was associated with higher depression scores among caregivers. This similarity highlights that the disease burden in relatives may have not only medical but also psychosocial consequences, underscoring the need for comprehensive support for these families.

Similarly, PHQ-2 scores were relatively higher among parents of children with β-TM living in households with income at or below the minimum wage, although this difference was not statistically significant. This finding suggests that β-TM, which is already more prevalent in low-income populations, may impose not only a medical but also an economic burden, thereby negatively affecting the mental well-being of families (16). Similarly, a study conducted in

Bangladesh demonstrated that parental depression scores were associated not only with household income levels but also with monthly treatment-related expenses (11). In our study, we did not specifically investigate treatment-related expenses, as all medical costs are covered by the government. However, factors such as frequent hospital visits may still impact the economic stability of families and adversely affect the mental health of caregivers.

Another notable finding of our study may be related to the presence of social support mechanisms. Parents who had obtained the ÇÖZGER (Report for Children with Special Needs) showed lower PHQ-2 scores, suggesting that the financial and social support provided by the state may contribute to greater psychological resilience. In Türkiye, the ÇÖZGER report allows families to access various social services and economic benefits based on the child's special needs. This finding indicates that social support systems contribute not only to financial stability but also to the mental well-being of caregivers. Therefore, expanding and tailoring social support programs based on individual needs may serve as an important strategy for promoting caregiver mental health.

With regard to clinical factors, no statistically significant association was observed between transfusion frequency and parental depression levels, although parents of children with medical complications showed relatively higher PHQ-2 scores. In contrast, previous studies have reported significant associations between transfusion-related factors and caregiver depression, suggesting that more intensive treatment and medical complications may increase psychological burden (4,11). The absence of a significant relationship in our study may be explained by the limited sample size and the higher mean age of the children, which may have given parents more time to adapt psychologically to chronic illness and the demands of long-term treatment.

Finally, no significant association was observed between immigrant status and parental PHQ-2 scores. Although migration has frequently been associated with increased psychological vulnerability among caregivers of children with chronic illnesses (16), this finding may reflect the influence of contextual protective factors such as access to healthcare services, social support networks, and adaptive coping mechanisms within our study population (17). This underscores the importance of considering sociocultural context when interpreting psychosocial risk among families of children with β-thalassemia major.

Study Limitations

One of the strengths of this study is that it was conducted in a major thalassemia center in Türkiye, providing access to a representative clinical population. Another strength is the use of a screening tool with established validity and reliability. However, the study has several limitations. Its cross-sectional design does not allow for causal inferences between variables. In addition, the relatively small sample size and the absence of a comparative control group limit the contextual interpretation of the observed depression levels.

Conclusion

In conclusion, although depressive symptoms were found to be higher among certain risk groups of caregivers of children diagnosed with β-TM, no statistically significant associations were identified in our study. These findings highlight the importance of integrating mental health assessments into routine follow-up protocols and indicate the need for further research with larger sample sizes to better understand the psychosocial needs of this population.

During the preparation of this work, the author(s) utilized ChatGPT (OpenAI) to assist with language editing. The tool was used to refine sentence structure, ensure coherence, and check grammar throughout the article. The validity and appropriateness of all AI-generated outputs were carefully reviewed, edited, and approved by the author(s). After thoroughly evaluating and modifying the content as needed, full responsibility for the publication's content is taken by the author(s). This incorporation of AI tool usage primarily impacted the language editing and phrasing aspects of the manuscript.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Scientific and Ethical Evaluation Board for Medical Research (TABED; approval no.: 2-25-1051, date: 19.03.2025).

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Cappellini MD, Cohen A, Eleftheriou A, Piga A, Porter J, Taher A. Guidelines for the clinical management of thalassaemia. 2nd revised ed. Nicosia: Thalassaemia International Federation; 2008.
2. Zhou T, Luo Y, Xiong W, Meng Z, Zhang H, Zhang J. Problem-solving skills training for parents of children with chronic health conditions: a systematic review and meta-analysis. JAMA Pediatr. 2024;178:226-36.
3. Streisand R, Braniecki S, Tercyak KP, Kazak AE. Childhood illness-related parenting stress: the pediatric inventory for parents. J Pediatr Psychol. 2001;26:155-62.
4. Mettananda S, Peiris R, Pathiraja H, Chandradasa M, Bandara D, de Silva U, et al. Psychological morbidity among children with transfusion dependent β-thalassaemia and their parents in Sri Lanka. PLoS One. 2020;15:e0228733.
5. Anum J, Dasti R. Caregiver burden, spirituality, and psychological well-being of parents having children with thalassemia. J Relig Health. 2016;55:941-55.
6. Aydinok Y, Erermis S, Bukusoglu N, Yilmaz D, Solak U. Psychosocial implications of thalassemia major. Pediatr Int. 2005;47:84-9.
7. Li L, Sun W, Luo J, Huang H. Associations between education levels and prevalence of depressive symptoms: NHANES (2005-2018). J Affect Disord. 2022;301:360-7.
8. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. Med Care. 2003;41:1284-92.
9. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression: two questions are as good as many. J Gen Intern Med. 1997;12:439-45.
10. e-Rapor. Çocuklar için özel gereksinim raporu (ÇÖZGER). Available from: https://erapor.saglik.gov.tr/portal/detay/cocuklar-Icin-ozel-gereksinim-raporu-cozger-13
11. Islam F, Seemanta S, Rezina S, Mehrab A, Raheem E, Hossain MS. Depression, anxiety, and stress among mothers of children with thalassemia in Bangladesh: a cross-sectional study. BMC Womens Health. 2025;25:221.
12. Chong LT, Chong MC, Tang LY, Ramoo V, Chui PL, Hmwe NTT. The relationship between psychological distress and religious practices and coping in Malaysian parents of children with thalassemia. J Pediatr Nurs. 2019;48:e15-20.
13. Hafeez N, Iftikhar I, Humayun T, Shehnaz A, Sannan A, Najeeb N, et al. Blood and sorrow: depression in care providers of thalassemic children. IAPS J Pract Ment Health. 2023;1:43.
14. Aziz K, Sadaf B, Kanwal S. Psychosocial problems of Pakistani parents of thalassemic children: a cross-sectional study done in Bahawalpur, Pakistan. Biopsychosoc Med. 2012;6:15.
15. Sharghi A, Karbakhsh M, Nabaei B, Meysamie A, Farrokhi A. Depression in mothers of children with thalassemia or blood malignancies: a study from Iran. Clin Pract Epidemiol Ment Health. 2006;2:27.
16. Thalassaemia International Federation. Global thalassaemia review. Available from: https://thalassaemia.org.cy/what-we-do/global-thalassaemia-review/
17. Fazel M, Reed RV, Panter-Brick C, Stein A. Mental health of displaced and refugee children resettled in high-income countries: risk and protective factors. Lancet. 2012;379:266-82.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Menstrual Knowledge Among Adolescents and Young Adults Across Developmental Stages

Ergenler ve Genç Yetişkinlerde Gelişimsel Dönemlere Göre Menstrüel Bilgi Düzeyi

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Cite this article as: Kalkan EŞ, Bilgin ZE, Kharbatia SN, Pehlivantürk Kızılkan M, Akgül S. Menstrual knowledge among adolescents and young adults across developmental stages. J Curr Pediatr. 2026;24(2):111-8

Abstract

Introduction: As the menstrual cycle is considered a vital sign of adolescent health, understanding normal menstrual characteristics is crucial. This study aimed to evaluate menstrual knowledge among adolescent and young adult females across different developmental stages and to examine the association between receiving menstrual information and menstrual knowledge.

Materials and Methods: A total of 257 adolescent and young adult females aged 10-24 years were included in the study and completed an online, self-administered questionnaire. Participants were categorized into early (10-14 years), middle (15-18 years), and late adolescence/young adulthood (19-24 years). Sociodemographic characteristics, menstrual information sources, and menstrual knowledge were assessed using multiple-choice questions. Each correct response to menstrual knowledge questions in accordance with the American College of Obstetricians and Gynecologists 2015 Committee opinion, was scored as 1 point (total score: 0-4), with higher scores indicating greater menstrual knowledge. Participants who correctly answered all items were classified as having complete menstrual knowledge.

Results: Overall, 91.4% of participants reported receiving menstrual information, most commonly from parents (70.8%), followed by the internet/media (58.8%) and school/teachers (58.4%). Complete menstrual knowledge rates (64.3% vs 31.8%, p=0.003) and menstrual knowledge scores (3.66±0.59 vs. 3.00±1.12, p=0.002) were significantly higher among those who had received menstrual information compared with those who had not. Both complete menstrual knowledge rates and knowledge scores increased across developmental stages (p=0.029 and p=0.003, respectively), with the highest levels observed in late adolescence/young adulthood.

Conclusion: Although most adolescents and young adults reported having received menstrual information, correct menstrual knowledge remained suboptimal, particularly during early and middle adolescence. These findings underscore the importance of structured, developmentally adapted menstrual health education programs that extend beyond simple information dissemination. Integrating age-appropriate menstrual education into school curricula and routine adolescent healthcare may facilitate earlier recognition of abnormal menstrual patterns and support informed health-seeking behaviors.

Keywords
Menstrual knowledge, adolescents, young adults, menstrual health education, developmental stages

Anahtar kelimeler
Menstrüel bilgi; ergen, genç yetişkin, menstrüel sağlık eğitimi, gelişimsel evreler

Received/Geliş Tarihi : 06.05.2026
Accepted/Kabul Tarihi : 12.06.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.34032

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Öz

Giriş: Menstrüel döngü, ergen sağlığında hayati bir belirteç olarak kabul edilmektedir ve normal menstrüel özelliklerin bilinmesi büyük önem taşımaktadır. Bu çalışmada, ergen ve genç yetişkin kadınlarda farklı ergenlik evrelerinde menstrüel bilgi düzeyinin değerlendirilmesi ve menstrüasyon hakkında bilgi alma durumu ile menstrüel bilgi arasındaki ilişkinin incelenmesi amaçlanmıştır.
Gereç ve Yöntem: Çalışmaya, çevrimiçi olarak uygulanan öz-bildirim temelli anketi tamamlayan 10-24 yaş aralığındaki toplam 257 ergen ve genç yetişkin kadın dahil edildi. Katılımcılar erken (10-14 yaş), orta (15-18 yaş) ve geç ergenlik/genç yetişkinlik (19-24 yaş) olmak üzere üç gruba ayrıldı. Sosyodemografik özellikler, menstrüasyon hakkında bilgi kaynakları ve menstrüel bilgi düzeyi çoktan seçmeli sorular kullanılarak değerlendirildi. Menstrüel bilgiyle ilgili sorulara verilen her doğru yanıt 1 puan kabul edildi (toplam puan: 0-4), daha yüksek puanlar daha fazla menstrüel bilgi olarak değerlendirildi. Tüm soruları doğru yanıtlayan katılımcılar American College of Obstetricians and Gynecologists 2015 Komite görüşüne göre tam doğru menstrüel bilgiye sahip olarak sınıflandırıldı.
Bulgular: Katılımcıların %91,4'ü menstrüasyon hakkında bilgi aldığını bildirdi. En sık bildirilen bilgi kaynağı ebeveynler (%70,8) olup bunu internet/medya (%58,8) ve okul/öğretmenler (%58,4) izledi. Tam doğru menstrüel bilgi oranları (%64,3 ve %31,8; p=0,003) ve menstrüel bilgi puanları (3,66±0,59 ve 3,00±1,12; p=0,002) bilgi aldığını bildirenlerde almayanlara göre anlamlı derecede daha yüksek bulundu. Hem tam doğru bilgi oranları hem de menstrüel bilgi puanları ergenlik evreleri arasında yaşla birlikte artış göstererek en yüksek bilgi düzeyleri geç ergenlik/genç yetişkinlik grubunda gözlemlendi (sırasıyla p=0,029 ve p=0,003).
Sonuç: Katılımcıların çoğu menstrüasyon hakkında bilgi aldığını bildirmiş olsa da doğru menstrüel bilgi özellikle erken ve orta ergenlik dönemlerinde yetersiz kalmıştır. Bulgularımız, basit bilgi aktarımının ötesine geçen, gelişimsel olarak uyarlanmış ve yapılandırılmış menstrüel sağlık eğitimi programlarının gerekliliğini ortaya koymaktadır. Yaşa uygun menstrüel sağlık eğitiminin okul müfredatına ve rutin ergen sağlık hizmetlerine entegre edilmesi, anormal menstrüel paternlerin erken tanınmasına ve bilinçli sağlık başvurularının desteklenmesine katkı sağlayabilir.

Introduction

The menstrual cycle is a normal physiological process in females and is considered a vital sign of overall health during adolescence and young adulthood. Menarche typically occurs between 12 and 13 years, within 2-3 years after thelarche (1). Menstrual cycles generally range from 21 to 45 days, with an average bleeding duration of 2-7 days (1). In adolescents, deviations from this normal pattern in terms of frequency, duration, volume or regularity are considered as abnormal uterine bleeding and may range from amenorrhea to heavy menstrual bleeding. Menstrual periods that do not begin within 3 years of thelarche or by 15 years of age, occur more frequently than every 21 days or less frequently than every 45 days, last longer than 7 days, occur 90 days apart even after a one spontaneous cycle, bleeding that soaks through one pad or tampon within two hours or less, or bleeding between periods should be considered abnormal (1,2). Although anovulatory cycles are common during adolescence, due to immaturity of the hypothalamic-pituitary-ovarian axis, these deviations can also be indicators of underlying health problems and may negatively impact quality of life, academic performance, and social participation in adolescents.

Despite being a normal physiological process, menstruation remains surrounded by misconceptions, taboos, and varying levels of knowledge among adolescents. Data from low- and middle-income countries indicate that many adolescent girls enter menarche with limited information, demonstrating insufficient understanding of menstrual hygiene, cycle regularity, and underlying physiological processes, and often experiencing anxiety or fear due to inadequate preparation (3). In a large study of Turkish schoolgirls aged 10-17 years, approximately half of the participants were unaware of the interval between pubertal onset and menarche, and most reported their mothers as their primary source of information, underscoring the need for structured education on puberty and menstruation (4). Furthermore, beyond gaps in knowledge, many menstrual challenges and symptoms are perceived as normal by young people, which may delay recognition and appropriate management of menstrual health concerns (5).

Although several studies have explored menstrual knowledge and related practices among adolescents, important gaps remain in the existing literature. Most research has focused on narrow age ranges or school-based populations, limiting understanding of how menstrual knowledge differs across developmental stages. Moreover, few studies have examined menstrual knowledge across early, middle, and late adolescence while also incorporating young adulthood as a distinct developmental stage. As a result, age-related differences in menstrual knowledge and the potential influence of prior menstrual information across this broader age spectrum remain insufficiently characterized.

To address these gaps in the literature, this study aimed to evaluate menstrual knowledge among adolescent and young adult females by examining different developmental stages separately and to investigate the association between prior

exposure to menstrual information and correct menstrual knowledge. Covering a wide age range and focusing on self-reported menstrual knowledge components, this study aims to raise awareness of differences in understanding normal menstrual characteristics among adolescents and young adults and to identify priority areas for targeted health education interventions.

Materials and Methods

Study Design and Participants

This cross-sectional study was conducted among adolescent and young adult females aged 10-24 years. All participants who provided informed consent, and additionally parental consent for those under 18 years of age, were invited to complete an online questionnaire. Participants were categorized into early (10-14 years), middle (15-18 years), and late adolescence/young adulthood (19-24 years) based on chronological age.

Eligibility was assessed through screening questions prior to answering the questionnaire, and adolescents and young adults who had not yet experienced menarche, had known endocrine disorders affecting menstruation, or were under clinical follow-up for menstrual problems were excluded. The study was approved by the Health Sciences Research Ethics Committee of Hacettepe University (decision no: 2025/06-35, date: 04.03.2025).

Data Collection

Data were collected between June and December 2025 through an online, self-administered questionnaire. The study was conducted and coordinated by the Adolescent Medicine Division at Hacettepe University. Participants were recruited through two approaches: 1) adolescents and young adults presenting to the Adolescent Medicine outpatient clinic for a routine well child visit were invited to participate and provided with a questionnaire link/QR code, and 2) the same link/QR code was distributed via social media platforms to reach a broader population.

Sociodemographic characteristics (age, parental education level, and family income level) and menstruation-related information were collected using a structured, self-administered questionnaire consisting of multiple-choice questions. Participants were asked whether they had previously received information about menstruation and to indicate their primary sources of information (family, school/teachers, friends, internet/media, or other).

Menstrual Knowledge

Menstrual knowledge was assessed using a researcher-developed questionnaire consisting of multiple-choice items covering key domains of menstrual physiology in adolescents, including expected age range at menarche, normal menstrual cycle interval, average duration of menstrual bleeding, and daily number of menstrual pads/tampons used. Each item had one correct response, and correct answers were scored as 1 point, yielding a total knowledge score ranging from 0 to 4, with higher scores indicating greater menstrual knowledge. Participants who correctly answered all menstrual knowledge questions were classified as having complete menstrual knowledge. The correct responses to menstrual knowledge items were determined according to American College of Obstetricians and Gynecologists 2015 Committee opinion (1). According to these criteria, regular menstruation was defined as age at menarche between 10.5-15 years, menstrual cycle interval between 21-45 days during adolescence and 21-35 days in individuals more than 5 years post-menarche, menstrual bleeding duration between 2-7 days, and the use of 3-6 pads or tampons per day during menstruation. Accordingly, the questionnaire was adapted such that the normal menstrual cycle interval was presented as 21-45 days for early and middle adolescents, and 21-35 days for late adolescents/young adults.

Study Sample

The sample size was calculated based on previously reported knowledge gaps regarding normal puberty and menstrual patterns among Turkish schoolgirls by İşgüven et al. (4). Using G*Power software, with a significance level of 0.05, a statistical power of 80%, and 3 age groups, the minimum required total sample size was estimated as 241 participants. The final sample of 257 participants exceeded this threshold and was considered sufficient for the planned analyses.

Statistical Analysis

Descriptive statistics were presented as mean ± standard deviation for numerical variables and as number and percentage for categorical variables. The normality of distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Non-normally distributed age data were compared between groups using the Mann-Whitney U test. Comparisons between two groups were conducted using Pearson's chi-square test or Fisher's exact test, as appropriate. Differences in menstrual knowledge across age groups were evaluated using Pearson's chi-square test. Effect sizes were

calculated using Cramér's V for chi-square and Fisher's exact tests, and rank-biserial correlation for Mann–Whitney U tests. A p value<0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 257 adolescents and young adults were included (77 early adolescents, 76 middle adolescents, and 104 late adolescents/young adults). The mean age was 17.48±3.96 years, and the mean time since menarche was 6.68±3.46 years. Age and time since menarche increased across developmental stages (Table 1).

Regarding parental education, university graduation was the most frequently reported education level for both mothers (n=105, 40.9%) and fathers (n=95, 37.0%). In terms of family income, the most reported level was average income (n=126, 49.0%). The sociodemographic characteristics of the participants are presented in Table 1.

Overall, 235 participants (91.4%) reported having received prior information about menstruation. The most common sources of information were parents (n=182, 70.8%), followed by internet/media (n=151, 58.8%) and school/teachers (n=150, 58.4%) (Table 1).

Participants who had received menstrual information showed significantly higher rates of complete menstrual knowledge compared to those who had not (n=151, 64.3% vs n=7, 31.8%; p=0.003). Similarly, menstrual knowledge score was significantly higher among those who had received information (3.66±0.59 vs 3.00±1.12; p=0.002). Age did not differ between two groups (p=0.610). Regarding specific knowledge components, adolescents who had received menstrual information demonstrated significantly higher correct knowledge of the age at menarche (n=218, 92.8% vs n=15, 68.2%; p=0.045) and the average duration of menstrual bleeding (n=226, 96.2% vs n=19, 86.4%; p=0.024). There was no significant difference between adolescents who had received menstrual information and those who had not in knowledge of the normal interval between menstrual periods (p=0.455) and daily number of menstrual pads/tampons used (p=0.102) (Table 2).

The proportion of participants who had received menstrual information did not differ significantly across age groups (p=0.402). In contrast, the frequency of correct menstrual knowledge increased across age groups. Complete menstrual knowledge was observed in 53.2% (n=41) of early adolescents, 56.6% (n=43) of middle adolescents, and 71.2% (n=74) of late adolescents and young adults. Post-hoc analyses indicated that the late adolescence/young adulthood group demonstrated significantly higher complete menstrual knowledge compared with both early and middle adolescence (p=0.029). Similarly, menstrual knowledge scores were higher in the late adolescence/young adulthood group compared to early adolescence and middle adolescence groups (p=0.003) (Table 3).

Discussion

One of the two key findings of our study is that although a large proportion of adolescents and young adults (91.4%)

Table 1. Sociodemographic characteristics and menstruation-related information

Characteristic	mean ± SD / n (%)
Age, years	17.48±3.96
Early adolescent	12.98±0.94
Middle adolescent	16.63±1.13
Late adolescent/young adult	21.42±2.46
Time since menarche, years	6.68±3.46
Early adolescent	1.28±0.68
Middle adolescent	4.76±1.56
Late adolescent/young adult	9.11±2.62
Mother's education level	
Illiterate	3 (1.2)
Primary school	44 (17.1)
Middle school	19 (7.4)
High school	49 (19.1)
University	105 (40.9)
Postgraduate	37 (14.4)
Father's education level	
Illiterate	0 (0.0)
Primary school	31 (12.1)
Middle school	22 (8.6)
High school	42 (16.3)
University	95 (37.0)
Postgraduate	67 (26.0)
Family income level	
Very poor	1 (0.4)
Poor	9 (3.5)
Average	126 (49.0)
Good	108 (42.0)
Very good	13 (5.1)
Received any information about menstruation	235 (91.4)
Source(s) of menstrual information*	
Mother/father	182 (70.8)
Friends	103 (40.1)
School/teachers	150 (58.4)
Internet/media	151 (58.8)
Other	6 (2.3)

*Multiple responses allowed

Table 2. Comparison of menstrual knowledge between adolescents who received menstrual information and those who did not

Characteristic	Received menstrual information (n=235)	Did not receive menstrual information (n=22)	Total (n=257)	p*	Cramér's V
Age, years, mean ± SD	17.42±3.12	18.02±6.12	17.48±3.96	0.610[a]	0.040[c]
Adolescents with complete menstrual knowledge, n (%)	151 (64.3)	7 (31.8)	158 (61.5)	**0.003[b]**	0.212
Age at menarche, n (%) <10.5 years 10.5-15 years >15 years Do not know	3 (1.3) 218 (92.8) 6 (2.5) 8 (3.4)	2 (9.1) 15 (68.2) 1 (4.5) 4 (18.2)	5 (1.9) 233 (90.7) 7 (2.7) 12 (4.7)	**0.045**	0.249
Normal interval between two menstrual periods, n (%) <21 days 21-45 days >45 days Do not know	14 (6.0) 211 (89.8) 1 (0.4) 9 (3.8)	3 (13.6) 18 (81.8) 0 (0.0) 1 (4.6)	17 (6.6) 229 (89.1) 1 (0.4) 10 (3.9)	0.455	0.100
Average duration of menstrual bleeding, n (%) <2 days 2-7 days >7 days Do not know	2 (0.9) 226 (96.2) 5 (2.1) 2 (0.9)	1 (4.5) 19 (86.4) 1 (4.5) 1 (4.5)	3 (1.2) 245 (95.3) 6 (2.3) 3 (1.2)	**0.024**	0.277
Daily number of pads/tampons used, n (%) <3 pads/tampons 3-6 pads/tampons >6 pads/tampons Do not know	18 (7.7) 191 (81.3) 6 (2.5) 20 (8.5)	5 (22.7) 13 (59.1) 0 (0.0) 4 (18.2)	23 (8.9) 204 (79.4) 6 (2.3) 24 (9.3)	0.102	0.191
Menstrual knowledge score, mean ± SD	3.66 ± 0.59	3.00 ± 1.12	3.61 ± 0.67	**0.002[a]**	0.215[c]

[a]Mann-Whitney U test, [b]Pearson Chi-square test, [c]Rank-biserial (effect size for Mann-Whitney U test)
*Fisher's Exact test

Table 3. Comparison of menstrual information status and menstrual knowledge by age group

	EA (n=77)	MA (n=76)	LAYA (n=104)	p	Effect size
Received menstrual information, n (%)	73 (94.8)	67 (88.2)	97 (93.3)	0.402[a]	0.096[c]
Complete menstrual knowledge, n (%)	41 (53.2)	43 (56.6)	74 (71.2)	**0.029[a]***	0.166[c]
Menstrual knowledge score, mean ± SD	3.38±0.87	3.47±0.76	3.72±0.58	**0.003[b]†**	0.037[d]

*EA-MA: 0.679, **EA-LAYA: 0.013, MA-LAYA: 0.043**
†EA-MA: 0.620, **EA-LAYA: 0.002, MA-LAYA: 0.007**

[a]Pearson Chi-square test, [b]Kruskal-Wallis test, [c]Cramér's V (effect size for Pearson Chi-square test), [d]Eta-squared (effect size for Kruskal-Wallis test)
EA: Early adolescent, MA: Middle adolescent, LAYA: Late adolescent/young adult, SD: Standard deviation

had received information about menstruation, less than two-thirds had complete menstrual knowledge. The other finding is that complete menstrual knowledge rates and menstrual knowledge scores varied significantly depending on the adolescence developmental stage. Considering that the menstrual cycle is a vital sign of women's health from menarche onwards, the insufficient knowledge may delay recognition of abnormal bleeding patterns and timely help-seeking.

In our study, the majority of participants reported having received menstrual information from at least one source. Parents were identified as the most frequently

reported source of information, followed by internet/media and school/teachers. The fact that parents are the primary information source may be related to their accessibility and reliability for adolescents, a finding consistent with previous literature (4,6). However, reliance on parents may also have limitations, as the accuracy and comprehensiveness of the information provided can vary depending on parental knowledge, beliefs, and potential sociocultural taboos surrounding menstruation. The second most common source was the internet and media which indicates that adolescents also seek information outside of face-to-face educational settings; which may introduce variability in the accuracy and consistency of information received. In addition, online sources may expose adolescents to misinformation, unverified content, and non-evidence-based recommendations, potentially leading to misconceptions and inappropriate health practices (7).

Notably, healthcare providers were not reported as a source of menstrual information in our study. This finding may reflect limited engagement of adolescents with healthcare services for preventive or educational purposes, as well as missed opportunities within clinical encounters to address menstrual health proactively. In many settings, menstrual health is not routinely discussed unless a specific complaint is raised, which may further limit adolescents' exposure to accurate, evidence-based information. In addition, the lack of adolescent medicine as a formally recognized subspecialty in Türkiye may further contribute to this gap, as structured, youth-focused preventive counseling is not systematically integrated into routine care (8). The absence of healthcare professionals as a reported source is particularly important, given their potential role in delivering standardized and reliable education. This highlights the need to integrate menstrual health counseling into routine adolescent healthcare visits and to adopt more proactive, developmentally appropriate communication strategies.

Although a large proportion of participants reported having received menstrual information, complete menstrual knowledge was identified in only 61.5% of the participants. While those who reported prior exposure to menstrual information demonstrated significantly higher knowledge levels than those who had not, nearly one-third of the informed group still exhibited incorrect or incomplete knowledge. This finding suggests that exposure to information alone does not always mean having accurate information. Consistent with this observation, the literature emphasizes that menstrual health knowledge is related not only to access to information but also to the understanding and application of that information in daily life. Studies show that interactive, structured interventions delivered through reliable sources are more effective and engaging than purely didactic or written approaches (9). A study conducted among grade 8-12 students in Canada demonstrated that menstrual health education not only improved knowledge but also increased confidence in menstrual health understanding, prioritization of menstrual health, and comfort in discussing menstruation (10). In another intervention study, a nurse-managed education program was observed to improve menstrual knowledge in adolescent girls and promote a more positive attitude and increase confidence (11). Importantly, several school-based intervention studies have demonstrated that structured menstrual health education delivered within the school setting significantly improves adolescents' knowledge, beliefs, and practices. For example, a school-based educational intervention conducted among adolescent girls reported a marked increase in menstrual knowledge scores after a 6-month programme (12). Similarly, some studies have shown that health education interventions implemented in schools lead to substantial improvements in both knowledge and menstrual hygiene practices compared with non-intervention groups (13). In this context, the Health Promoting Schools framework provides a comprehensive and effective approach for integrating menstrual health education into the school environment through coordinated curricula, supportive school policies, and engagement with families and communities (14). Integrating menstrual health education into this framework may help provide consistent, age-appropriate and stigma-sensitive learning and improve knowledge, attitudes, confidence, and health-seeking behaviors.

In our study, the significant increase in both complete menstrual knowledge rates and menstrual knowledge scores from early adolescence to late adolescence/young adulthood suggests that knowledge may develop over time through accumulated experience and repeated exposure to information. However, despite this increase, knowledge remained suboptimal even in late adolescence/young adulthood, where approximately one-third of participants still lacked complete menstrual knowledge. Existing literature indicates that many girls enter menarche insufficiently prepared, highlighting a critical gap in premenarcheal education (15). Cultural factors may further influence this process, as negative feelings such as embarrassment, fear, or anxiety about talking about menstruation, particularly during premenarche and early adolescence, can create substantial barriers to information acquisition (16,17). In this context, the relatively lower knowledge levels observed in

early and middle adolescence in our study, together with the persistent knowledge gaps observed even in late adolescence/young adulthood, underscore the importance of the premenarcheal and early postmenarcheal periods as critical windows for intervention, as well as the need for continued education across all developmental stages. By examining early, middle, and late adolescence and young adulthood as distinct developmental stages, our study provides insight into age-related differences in menstrual knowledge across a broader developmental spectrum. These findings support the need for developmentally adapted menstrual health education programs that target early adolescence before misconceptions become established and extend into later stages to address persistent knowledge gaps.

Study Limitations

This study has some limitations. First, due to its cross-sectional design, a causal relationship between prior exposure to menstrual information and menstrual knowledge levels could not be evaluated. Second, the fact that data were collected via an online, self-administered, multiple-choice questionnaire may have led to selection bias, including potential participation of individuals only who have digital access or a greater interest in the subject.

Conclusion

In conclusion, although most adolescents and young adults reported having received information about menstruation, complete menstrual knowledge was suboptimal. Knowledge levels increased with age but remained suboptimal, particularly during early and middle adolescence. Notably, healthcare providers were not identified as a source of menstrual information, highlighting a critical missed opportunity for delivering accurate and evidence-based education. These findings highlight the need for structured, developmentally adapted menstrual health education programs that provide accurate information and extend beyond simple information dissemination. Integrating age-appropriate menstrual health education into school curricula and routine adolescent healthcare checkups may facilitate earlier recognition of abnormal menstrual patterns, support informed health-seeking behaviors, and promote acceptance of menstruation as a physiological process, potentially reducing fear and anxiety. In this context, the formal recognition and expansion of adolescent medicine as a subspecialty may play a key role in strengthening youth-focused preventive care and ensuring the systematic delivery of developmentally appropriate health education.

Ethics

Ethics Committee Approval: The study was approved by the Health Sciences Research Ethics Committee of Hacettepe University (decision no: 2025/06-35, date: 04.03.2025).

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. ACOG Committee Opinion No. 651: Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Obstet Gynecol. 2015;126:e143-e6.
2. Bennett AR, Gray SH. What to do when she's bleeding through: the recognition, evaluation, and management of abnormal uterine bleeding in adolescents. Curr Opin Pediatr. 2014;26:413-9.
3. Coast E, Lattof SR, Strong J. Puberty and menstruation knowledge among young adolescents in low- and middle-income countries: a scoping review. Int J Public Health. 2019;64:293-304.
4. İşgüven P, Yörük G, Çizmecioğlu FM. Educational needs of adolescents regarding normal puberty and menstrual patterns. J Clin Res Pediatr Endocrinol. 2015;7:312.
5. Abreu-Sánchez A, Parra-Fernández ML, Onieva-Zafra MD, Fernández-Martínez E. Perception of menstrual normality and abnormality in Spanish female nursing students. Int J Environ Res Public Health. 2020;17:6432.
6. Mittermeier T, Hawkey A, Bush D, Marriott J, Tewhaiti-Smith J, Burgess W, et al. Menstrual health symptoms and literacy among young women in aotearoa New Zealand: a nationwide cross-sectional survey. J Pediatr Adolesc Gynecol. 2025;38:328-35.
7. John JN, Gorman S, Scales D, Gorman J. Online misleading information about women's reproductive health: a narrative review. J Gen Intern Med. 2025;40:1123-31.
8. Kalkan E, Pehlivantürk Kızılkan M, Akgül S. Adolescent medicine in the first 100 years of the Republic of Türkiye. Turk J Pediatr. 2025;67:129-32.
9. Evans RL, Harris B, Onuegbu C, Griffiths F. Systematic review of educational interventions to improve the menstrual health of young adolescent girls. BMJ Open. 2022;12:e057204.
10. Wahl K, Albert A, Larente M, Lopez de Arbina E, Kennedy L, Sutherland JL, et al. Does menstrual health and endometriosis education affect knowledge among middle and secondary school students? A cluster-randomised controlled trial. J Obstet Gynaecol Can. 2024;46:102583.
11. Su JJ, Lindell D. Promoting the menstrual health of adolescent girls in China. Nurs Health Sci. 2016;18:481-7.
12. Haque SE, Rahman M, Itsuko K, Mutahara M, Sakisaka K. The effect of a school-based educational intervention on menstrual health: an intervention study among adolescent girls in Bangladesh. BMJ Open. 2014;4:e004607.
13. Ghimire S, Gahatraj NR, Shrestha N, Manandhar S, Dhital SR. Effects of health education intervention on menstrual hygiene

knowledge and practices among the adolescent girls of Pokhara Metropolitan, Nepal. PLoS One. 2024;19:e0291884.

14. World Health Organization, United Nations Educational Scientific and Cultural Organization. Making every school a health-promoting school: global standards and indicators. Geneva; 2021 22 June 2021.
15. Msovela J, Shija AE, Ntuyeko H, Imeda C, Mugula A, Mgina E, et al. puberty and menstruation knowledge, information sources and needs among secondary school adolescent girls and boys in Kibaha, Tanzania. PLOS Glob Public Health. 2025;5:e0004176.
16. Marván ML, Molina-Abolnik M. Mexican adolescents' experience of menarche and attitudes toward menstruation: role of communication between mothers and daughters. J Pediatr Adolesc Gynecol. 2012;25:358-63.
17. Holmes K, Curry C, Sherry, Ferfolja T, Parry K, Smith C, et al. Adolescent menstrual health literacy in low, middle and high-income countries: a narrative review. Int J Environ Res Public Health. 2021;18.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Serum 25-Hydroxyvitamin D Levels in Infants with Urolithiasis: A Retrospective Study

Ürolitiyazisi Olan İnfantlarda Serum 25-Hidroksivitamin D Düzeyleri: Retrospektif Bir Çalışma

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Cite this article as: Köksoy AY, Önal HG. Serum 25-hydroxyvitamin d levels in ınfants with urolithiasis: a retrospective study. J Curr Pediatr. 2026;24(2):119-25

Abstract

Introduction: The relationship between vitamin D supplementation and urinary stone formation in infancy remains controversial, leading to variability in clinical practice regarding continuation or discontinuation of vitamin D in infants diagnosed with urolithiasis. This study aimed to evaluate whether serum 25-hydroxyvitamin D levels are associated with the presence of urolithiasis in infants.

Materials and Methods: This retrospective study included 77 infants who underwent renal ultrasonography for suspected urinary stone disease. Patients were classified according to the presence or absence of ultrasonographically detected urolithiasis. Clinical and laboratory parameters, including serum 25-hydroxyvitamin D levels and urinary calcium-to-creatinine ratios, were recorded. Hypercalciuria was defined using age-specific reference values. Factors associated with urolithiasis were evaluated using univariate and multivariate logistic regression analyses.

Results: Of the 77 infants, 54 had ultrasonographically detected urolithiasis. Mean serum 25-hydroxyvitamin D levels were similar between infants with and without urolithiasis (34.44±13.63 vs 34.81±15.68 ng/mL, p=0.917). None of the infants exhibited vitamin D excess or intoxication. Infants with stones had higher median urinary calcium-to-creatinine ratios compared with those without urolithiasis median (min-max) [0.58 (0.02–1.98) ve 0.34 (0.08–1.8) mg/mg; p=0.031], and hypercalciuria was more frequent in this group (37% vs 13%, p=0.030). Although younger age and hypercalciuria were associated with urolithiasis in univariate analyses, these associations did not remain statistically significant in multivariable models. Serum vitamin D levels were not associated with stone presence in either univariate or multivariate analyses.

Conclusion: In this study, serum 25-hydroxyvitamin D levels were not found to be associated with urolithiasis in infants. These findings suggest that vitamin D status alone may not fully explain stone formation during early infancy. Decisions regarding continuation or discontinuation of vitamin D supplementation should therefore consider the overall metabolic and clinical context, including urinary calcium excretion, rather than relying solely on serum vitamin D levels.

Keywords
Infant, urolithiasis, vitamin D, hypercalciuria, ultrasonography

Anahtar kelimeler
İnfant, ürolitiyazis, vitamin D, hiperkalsiüri, ultrasonografi

Öz

Giriş: İnfantlarda vitamin D desteği ile üriner taş oluşumu arasındaki ilişki tartışmalı olup, bu durum ürolitiyazis tanısı alan bebeklerde vitamin D desteğinin sürdürülmesi veya kesilmesi konusunda klinik uygulamalarda değişkenliğe yol açmaktadır. Bu çalışmanın amacı, infantlarda serum 25-hidroksivitamin D düzeyleri ile ürolitiyazis varlığı arasında bir ilişki olup olmadığını değerlendirmektir.

Received/Geliş Tarihi : 07.01.2026
Accepted/Kabul Tarihi : 03.07.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.85069

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Gereç ve Yöntem: Bu retrospektif çalışmaya, üriner taş hastalığı şüphesiyle renal ultrasonografi yapılan 77 infant dâhil edildi. Hastalar, ultrasonografide ürolitiyazis saptananlar ve saptanmayanlar olmak üzere iki gruba ayrıldı. Serum 25-hidroksivitamin D düzeyleri ve idrar kalsiyum/kreatinin oranı dâhil olmak üzere klinik ve laboratuvar verileri kaydedildi. Hiperkalsiüri, yaşa özgü referans değerler kullanılarak tanımlandı. Ürolitiyazis ile ilişkili faktörler tek değişkenli ve çok değişkenli lojistik regresyon analizleri ile değerlendirildi.
Bulgular: Toplam 77 infantın 54'ünde ultrasonografik olarak renal taş veya mikrolitiyazis saptandı. Taş saptanan ve saptanmayan gruplar arasında serum 25-hidroksivitamin D düzeyleri açısından anlamlı fark yoktu (34.44±13.63 ve 34.81±15.68 ng/mL; p=0.917). Hiçbir infantta vitamin D fazlalığı veya intoksikasyonu saptanmadı. Taş saptanan grupta idrar kalsiyum/kreatinin oranı daha yüksek bulundu median (min-max) [0.58 (0.02–1.98) ve 0.34 (0.08–1.8) mg/mg; p=0.031] ve hiperkalsiüri sıklığı daha fazlaydı (%37 ve %13; p = 0.030). Ancak yaş ve hiperkalsiüri, çok değişkenli analizlerde taş varlığı ile bağımsız olarak ilişkili bulunmadı. Serum vitamin D düzeyleri ise hem tek değişkenli hem de çok değişkenli analizlerde taş varlığı ile ilişkili değildi.
Sonuç: Bu çalışmada, infantlarda serum 25-hidroksivitamin D düzeyleri ile ürolitiyazis varlığı arasında bir ilişki saptanmamıştır. Bulgularımız, erken infant döneminde taş oluşumunun yalnızca vitamin D durumu ile açıklanamayacağını düşündürmektedir. Bu nedenle, ürolitiyazisi olan infantlarda vitamin D desteğinin sürdürülmesi veya kesilmesine ilişkin kararlar, yalnızca serum vitamin D düzeylerine değil; idrar kalsiyum atılımı başta olmak üzere genel metabolik ve klinik bağlam göz önünde bulundurularak verilmelidir.

Introduction

Urinary stone disease has been increasingly recognized in adults; however, stone formation during infancy represents a distinct clinical entity with important differences from adult disease in terms of epidemiology, etiology, clinical presentation, and management (1-3). Pediatric urolithiasis is of particular clinical relevance because it is frequently associated with underlying metabolic abnormalities and carries a potential risk for recurrence, underscoring the importance of early diagnosis and appropriate follow-up (4,5). Among the various factors implicated in pediatric urolithiasis, the relationship between vitamin D status and stone formation during infancy remains incompletely understood and, at times, controversial (6-9). Vitamin D plays a central role in calcium homeostasis and bone mineralization. While deficiency may impair skeletal health, excessive vitamin D exposure can increase intestinal calcium absorption and urinary calcium excretion, potentially contributing to stone formation in susceptible individuals (10-13). Genetic factors, including variations in the vitamin D receptor (VDR), may also modulate individual susceptibility to stone formation (14,15). Despite these observations, evidence specifically addressing infants remains scarce and often inconsistent, and the threshold at which vitamin D becomes potentially lithogenic in early life is uncertain.

Given the widespread use of vitamin D supplementation in infancy and the ongoing uncertainty surrounding its potential lithogenic effects, further research is needed to clarify whether elevated serum 25-hydroxyvitamin D levels are associated with biochemical or ultrasonographic markers of stone risk in this age group. Although key metabolic stone-forming parameters such as urinary oxalate, citrate, and cystine were not available in our cohort, the present study focuses on vitamin D status in relation to ultrasonographically detected urolithiasis. By characterizing this association independently of metabolic evaluations, our findings provide clinically relevant descriptive data that may help guide decision-making regarding continuation or discontinuation of vitamin D supplementation in infants with urolithiasis.

In the context of widespread vitamin D supplementation during infancy and ongoing uncertainty regarding its potential lithogenic effects, the objective of this retrospective study is to evaluate whether serum 25-hydroxyvitamin D levels are associated with the presence of urolithiasis in infants. By analyzing clinical, laboratory, and ultrasonographic data, we aimed to compare vitamin D status between infants with and without ultrasonographic evidence of urolithiasis, without inferring causality. This study also seeks to provide descriptive evidence to support clinical decision-making regarding whether vitamin D supplementation should be continued or discontinued in infants diagnosed with urolithiasis.

Materials and Methods

This retrospective study included infants younger than 12 months who were evaluated in the pediatric nephrology clinic with ultrasonography for suspected urolithiasis between June 2023 and November 2025. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Samsun University Non-Interventional Clinical Research Ethics Committee (approval number: 2025/23/13, date: 03.12.2025).

Medical records of 121 patients were reviewed. One infant with Zellweger syndrome, eleven preterm infants, one infant with an ectopic kidney, and one infant receiving calcium

folinate therapy, six infants with inconclusive laboratory data, nine infants with unknown vitamin D use at admission and fifteen infants without calcium-to-creatinine ratio were excluded due to the potential confounding effects of these conditions or treatments on mineral metabolism. Ultimately, 77 patients were enrolled in the final analysis.

All infants in our cohort had been started on routine vitamin D prophylaxis as part of standard national practice. Serum 25-hydroxyvitamin D concentrations were measured using the chemiluminescent microparticle immunoassay (CMIA), in accordance with the manufacturer's instructions.

For each patient, serum creatinine, albumin, calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH), and 25-hydroxyvitamin D levels were extracted from the hospital laboratory system. Spot urine calcium and creatinine measurements were also recorded. Hypercalciuria was defined according to age-specific cutoffs: a urinary calcium-to-creatinine ratio above 0.8 mg/mg for infants aged 0–6 months and above 0.6 mg/mg for those aged 7–12 months (16). Because of the retrospective nature of the study, comprehensive metabolic stone risk profiles (such as urinary oxalate, citrate, and cystine) were not consistently available across the cohort and were therefore not included in the analysis.

All ultrasonographic evaluations were conducted by radiologists with different levels of pediatric imaging expertise using the same ultrasound platform (Resona R9, Mindray Medical International, Shenzhen, China). In radiology reports, stone size was inconsistently recorded. When a numeric size in millimeters was available, findings were categorized as microlithiasis (≤3 mm) or calculus (>3 mm), consistent with prior pediatric literature. When size was not reported and findings were described qualitatively (e.g.'millimetric echogenic/crystalloid foci'), cases were retained as ultrasound-positive but were not included in size-based analyses.

Urinary tract calculi were defined by punctate echogenic foci, typically with posterior acoustic shadowing and/or color Doppler twinkling artifacts, acknowledging the inherent difficulty of distinguishing true calculi from transient microlithiasis in infancy. Due to the retrospective design, the interval between ultrasonography and serum 25(OH)D measurement varied among patients (median 9 days, min–max 0–108).

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp, Armonk, NY). Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), while non-normally distributed variables are reported as median (min-max). Categorical variables are expressed as numbers and percentages (n, %).

Comparisons between infants with and without urolithiasis were performed using the independent samples t-test for normally distributed continuous variables, and the Mann–Whitney U test for non-normally distributed variables. Chi-square or Fisher's exact tests were used for categorical variables, as appropriate.

Correlations were assessed using Spearman's rank correlation coefficient (ρ).

Univariate logistic regression analyses were first conducted to identify potential associations between clinical and laboratory variables and the presence of urolithiasis. Variables with univariate p-values <0.10 were considered for inclusion in multivariate logistic regression models to adjust for potential confounding. Two multivariate models were constructed: Model 1 included age and other relevant variables meeting the univariate inclusion criteria, while Model 2 additionally included hydronephrosis to adjust for its potential confounding effect. Odds ratios (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) were reported. A two-tailed p-value <0.05 was considered statistically significant for all analyses.

Results

A total of 77 infants were included in the study, of whom 54 (70.1%) had ultrasonographic evidence of urolithiasis. The clinical and laboratory features of the groups are summarized in Table 1. Among the 54 infants with ultrasonographically detected urolithiasis, stone size was not quantitatively reported in 10 cases and was described qualitatively as millimetric crystalloid echogenic foci. In the remaining 44 infants with documented stone measurements, the median (min–max) stone size was 2.8 mm (1.3–8.0). Among the 54 infants with ultrasonographically detected urolithiasis, stone location was reported as the upper pole in 2 (3.7%), middle pole in 12 (22.2%), lower pole in 27 (50.0%), and renal pelvis in 2 (3.7%) cases. In 11 infants (20.4%), stones were described as renal without further specification of intrarenal location.

Infants with urolithiasis were significantly younger than those without urolithiasis (median 3.06 vs. 4.56 months, p=0.009). Gender distribution and serum biochemical markers including total calcium, phosphate, parathyroid hormone, and 25-hydroxyvitamin D levels were comparable between the two groups (p>0.05 for all). The distribution of

Table 1. Clinical and laboratory features of patients

			Urolithiasis absent N:23	Urolithiasis present N:54	P
Age			4.56 (1.08–11.16)	3.06 (0.12–10.08)	**0.009**
Sex, n (%)		Female	11 (47.8)	17 (31.5)	0.202
		Male	12 (52.2)	37 (68.5)	
Stone size (mm) [median (min-max)]			-	2.8 (1.3–8.0)	
Stone size reported, n (%)		Yes	-	44 (81.5)	
		No	-	10 (18.5)	
Creatinine (mg/dL) [median (min-max)]			0.25 (0.13–0.47)	0.23 (0.13–0.42)	0.101
Ca (mg/dL) [median (min-max)]			10.42 (9.08–11.74)	10.47 (9.42–12.14)	0.501
P (mg/dL) [median (min-max)]			6.00 (4.7–6.8)	6.10 (3.6–7.6)	0.448
ALP (U/L) [median (min-max)]			211.00 (135–388)	270.00 (149–450)	**0.004**
25-OH VitD (ng/mL) (mean ± SD)			34.81 ± 15.68	34.44 ± 13.63	0.917
25-OH Vit D (ng/mL) categories, n (%) [median (min-max)]		<20	4 (17.4)	10 (18.5)	
30–50		20–29.9	6 (26.1)	9 (16.7)	
		10 (43.5)	30 (55.6)		
		>50	3 (13)	5 (9.3)	
PTH (pg/mL) [median (min-max)]			21.70 (5.1–52.2)	18.55 (1.2–52.6)	0.644
Uca/cre (mg/mg) [median (min-max)]			0.34 (0.08–1.8)	0.58 (0.02–1.98)	**0.031**
Hypercalciuria n (%)	(-)		20 (87.0)	34 (63.0)	**0.030***
	(+)		3 (13.0)	20 (37.0)	
Hydronephrosis n (%)	(-)		20 (87.0)	49 (90.7)	0.689
	(+)		3 (13.0)	5 (9.3)	

Continuous variables are presented as mean ± standard deviation or median (min-max), as appropriate. Ca: Calcium, P: Phosphorus, ALP: Alkaline phosphatase, PTH: Parathormone, $U_{ca/cre}$ (urine calcium-to-creatinine ratio) *Fisher's exact test was used for hypercalciuria

serum 25-hydroxyvitamin D categories did not differ between infants with and without urolithiasis (χ^2=1.42, p=0.701). The urinary calcium-to-creatinine ratio was higher in infants with urolithiasis (median 0.58 vs. 0.34 mg/mg, p=0.031), and hypercalciuria was more frequent in infants with urolithiasis (37% vs. 13%, p=0.030). The prevalence of hydronephrosis did not differ between the groups. Median serum creatinine levels were slightly lower in the urolithiasis group (0.23 vs 0.25 mg/dL, p=0.101). Median serum ALP levels were higher in patients with urolithiasis (270 vs 211, p=0.004). This difference is likely attributable to age-related variations in bone turnover rather than stone-related pathology.

Spearman correlation analyses showed no significant association between serum 25-hydroxyvitamin D levels and the urinary calcium-to-creatinine ratio (ρ = -0,111, p=0.336) or serum calcium levels (ρ = -0.169, p=0.142). A moderate positive correlation was observed between serum calcium and urinary calcium excretion (ρ = 0.294, p=0.010), while age was inversely correlated with the urinary calcium-to-creatinine ratio (ρ = -0.494, p<0.001) consistent with the expected physiological decrease in urinary calcium excretion with increasing age in infancy.The findings of the univariate and multivariate logistic regression analyses are summarized in Table 2. In the univariate models, younger age (OR: 0.78 95% CI: 0.63–0.96, p=0.021) and the presence of hypercalciuria (OR: 3.92 95% CI: 1.03–14.87, p=0.045) were significantly associated with urolithiasis. However, these associations were no longer statistically significant after adjustment for potential confounders. In the multivariate models, the effect of age attenuated (aOR: 0.82, 95% CI: 0.66–1.03, p=0.097), and the association between hypercalciuria and stone presence also weakened (aOR: 3.92–2.68, p=0.045–0.174). This attenuation likely reflects the strong age dependence of urinary calcium excretion and the limited number of infants

Table 2. Logistic regression analysis of confounding factors among patients with urolithiasis regarding vitamin D status and hypercalciuria Model 1 and 2

Variable	Univariate (Model) OR	Multivariate (Model 1) aOR	Multivariate (Model 2) aOR
	(95% CI), p	(95% CI), p	(95% CI), p
Age (months)	0.78 (0.63–0.96), p=**0.021**	0.82 (0.66–1.03), p=0.097	0.83 (0.66–1.05), p=0.124
25-OH Vitamin D	0.99 (0.96–1.03), p=0.916	0.99 (0.96–1.03), p=0.903	0.99 (0.96–1.03), p=0.909
Hypercalciuria	3.92 (1.03–14.87), **p=0.045**	2.68 (0.64–11.13), p=0.174	2.89 (0.67–12.50), p=0.154
Hydronephrosis	0.68 (0.14–3.11), p=0.620	-	0.559 (0.10–3.37), p=0.584

presenting with hypercalciuria in the cohort.

Serum 25-hydroxyvitamin D concentrations showed no association with urolithiasis in either univariate or multivariate analyses (unadjusted OR: 0.99, 95% CI: 0.96–1.03, p=0.916; adjusted OR: 0.99, 95% CI: 0.96–1.03, p=0.903), suggesting that vitamin D status did not influence the likelihood of detecting stones or microlithiasis on ultrasonography. Hydronephrosis was similarly not associated with stone presence in the adjusted models (unadjusted OR: 0.68, p=0.620; adjusted OR: 0.55, p=0.584).

Discussion

Previous studies investigating the association between vitamin D use and kidney stone risk have yielded inconsistent results. While some reports suggest that vitamin D supplementation may increase stone risk depending on dose and duration, others have found no increased risk outside specific high-risk populations, such as individuals with underlying genetic or metabolic conditions predisposing to stone formation (17,18). Several studies focusing on infantile urolithiasis have reported higher serum 25-hydroxyvitamin D levels in affected infants compared with controls, frequently accompanied by hypercalcemia and increased urinary calcium excretion, suggesting a contributory role of vitamin D primarily through calcium dysregulation rather than a direct lithogenic effect (7-9). In a well-designed prospective study of exclusively breastfed infants, Yilmaz et al. (9) reported that higher serum vitamin D levels were associated with stone formation, along with suppressed parathyroid hormone levels and increased urinary calcium excretion. In the present study, serum 25-hydroxyvitamin D levels did not differ between infants with and without ultrasonographically detected urolithiasis and were not independently associated with stone presence. This finding is biologically plausible, as none of the infants in our cohort exhibited vitamin D excess or overt intoxication (19). Although upper reference limits for serum 25-hydroxyvitamin D have been proposed in clinical guidelines, the specific level at which vitamin D may contribute to lithogenic risk remains poorly defined, particularly in infancy. Moreover, emerging evidence suggests that serum 25-hydroxyvitamin D concentrations may not accurately reflect tissue-level vitamin D activity or downstream effects on calcium and phosphate metabolism (12). Razzaque has emphasized that adverse effects of vitamin D supplementation, including hypercalciuria and ectopic calcification, may occur even in the absence of markedly elevated serum vitamin D levels due to complex regulatory mechanisms and local vitamin D metabolism, while normal serum levels do not necessarily exclude biological effects (12). Accordingly, serum vitamin D status alone may be insufficient to explain stone formation in early infancy and should be interpreted within a broader metabolic and developmental context. In addition, previous studies have suggested that interindividual differences in susceptibility to stone formation may be influenced by vitamin D receptor polymorphisms and potential defects in 24-hydroxylation of vitamin D, which may partly explain why some children develop stones despite receiving similar prophylactic or therapeutic vitamin D doses (15,20,21).

Although no significant association was observed between serum 25-hydroxyvitamin D levels and presence of urolithiasis in our cohort, infants with ultrasonographically detected urolithiasis exhibited higher urinary calcium-to-creatinine ratios, and hypercalciuria was more frequently observed in this group. Hypercalciuria was defined using age-specific reference values, supporting its pathological significance rather than reflecting physiological age-related variation. While hypercalciuria did not retain statistical significance in multivariable analyses, this finding likely

reflects limited sample size and reduced statistical power rather than a lack of clinical relevance. Large pediatric series have demonstrated that infantile urolithiasis differs from stone disease in older children with respect to metabolic risk factors, clinical presentation, and natural history, with hypercalciuria being the most common abnormality in infancy, whereas hypocitraturia becomes more prominent later in childhood (4,5,22-24). Importantly, most stones detected during infancy—particularly microlithiasis—tend to resolve spontaneously, underscoring the generally favorable prognosis in this age group (9). These observations highlight the variability in clinical interpretation and management strategies, particularly regarding decisions about vitamin D supplementation in infants with ultrasonographic stone findings.

Clinical practice varies widely: primary care physicians and clinicians in pediatric stone clinics differ in their decisions about whether vitamin D supplementation should be discontinued in infants diagnosed with urolithiasis. Observations from our center suggest that vitamin D supplementation is frequently withheld in such infants, although these decisions often reflect individual clinical preference rather than evidence-based recommendations.

Recent data also indicate that discontinuation of routine vitamin D prophylaxis in infants with urolithiasis does not significantly affect stone recurrence or progression, arguing against a causal relationship between standard prophylactic vitamin D dosing and stone growth (6). These observations support the concept that metabolic factors, rather than vitamin D exposure alone, may play a more prominent role in stone formation during early life.

From a pathophysiological perspective, calcium and phosphorus homeostasis is regulated through the coordinated interaction of vitamin D, the kidneys, intestines, parathyroid glands, and bone tissue (25). Although excessive vitamin D exposure may increase intestinal calcium absorption and promote hypercalciuria, establishing a direct and linear relationship between vitamin D supplementation and kidney stone formation remains challenging. Current evidence suggests that elevated serum vitamin D levels do not uniformly translate into clinically evident stone disease, particularly in the absence of sustained hypercalcemia or marked hypercalciuria. This may partly explain why routine vitamin D supplementation does not consistently result in stone formation in otherwise healthy infants.

Clinically, these findings support an individualized approach to the management of vitamin D supplementation in infants with urolithiasis. Routine discontinuation of prophylactic vitamin D supplementation based solely on the presence of ultrasonographic stone findings or serum vitamin D levels may not be justified. Decisions regarding vitamin D supplementation should therefore be guided by the overall clinical context, including urinary calcium excretion and other relevant clinical factors, rather than serum vitamin D concentrations alone. These observations should be interpreted within the limitations of a retrospective design and are intended to inform clinical judgment rather than establish definitive treatment recommendations.

Study Limitations

This study has several limitations inherent to its retrospective design. The timing of ultrasonographic evaluation and serum 25-hydroxyvitamin D measurement was not standardized, potentially introducing temporal variability. Comprehensive metabolic stone risk profiles, including urinary oxalate, citrate, and cystine levels, were unavailable, limiting assessment of additional lithogenic or protective factors. Stone detection relied on ultrasonography, which may not always reliably distinguish true calculi from transient microlithiasis in infancy. Finally, the relatively small sample size may have limited statistical power, particularly in multivariable analyses. The retrospective design and modest sample size limited detailed biochemical characterization of stone composition and comprehensive anatomical assessment; however, the study provides descriptive data reflecting real-world clinical practice in infants undergoing routine ultrasonography. These limitations should be considered when interpreting the findings, and prospective studies with standardized imaging and metabolic evaluation are warranted to further clarify the relationship between vitamin D status and stone formation in infancy.

Conclusion

Clinically, our findings support an individualized approach to decisions regarding continuation or discontinuation of vitamin D supplementation in infants with urolithiasis. Routine discontinuation of prophylactic vitamin D supplementation based solely on ultrasonographic stone findings or serum vitamin D levels may not be appropriate. Instead, clinical decision-making should be guided by the overall metabolic and clinical context, including urinary calcium excretion and other relevant factors, rather than serum vitamin D concentrations alone.

These findings should be interpreted as descriptive and hypothesis-generating rather than causal. Well-designed

prospective studies are needed to clarify the potential role of vitamin D supplementation in kidney stone formation and to define serum vitamin D levels that can be considered safe or potentially unsafe with respect to stone development, both in terms of incident stone formation and disease progression in individuals with existing stones.

Ethics

Ethics Committee Approval: The study was approved by the Samsun University Non-Interventional Clinical Research Ethics Committee (approval number: 2025/23/13, date: 03.12.2025).

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Fallahzadeh MA, Hassanzadeh J, Fallahzadeh MH. What do we know about pediatric renal microlithiasis? J Renal Inj Prev. 2017;6:70-5.
2. Lang J, Narendrula A, El-Zawahry A, Sindhwani P, Ekwenna O. Global trends in incidence and burden of urolithiasis from 1990 to 2019: an analysis of global burden of disease study data. Eur Urol Open Sci. 2022;35:37-46.
3. Zhu X, Zhou Y, Yang X, Zhou K, Zhou M. Global, regional and national burden of paediatric urinary stone disease from 1990 to 2021: a systematic analysis for the global burden of disease study 2021. BMJ Open. 2025;15:e098722.
4. Alpay H, Ozen A, Gokce I, Biyikli N. Clinical and metabolic features of urolithiasis and microlithiasis in children. Pediatr Nephrol. 2009;24:2203-9.
5. Demirtas F, Çakar N, Özçakar ZB, Akıncı A, Burgu B, Yalçınkaya F. Risk factors for recurrence in pediatric urinary stone disease. Pediatr Nephrol. 2024;39:2105-13.
6. Akinci A, Karaburun MC, Kubilay E, Solak VT, Sanci A, Soygur T, et al. Urinary stone in infants; should vitamin D prophylaxis be stopped? J Pediatr Urol. 2024;20:604.e1-e6.
7. Eskandarifar A, Roshani D, Tabarkhun A, Ataee E. Assessment of serum level of vitamin D in infants with nephrolithiasis. Iran J Kidney Dis. 2021;15:116-20.
8. Fallahzadeh MH, Zare J, Al-Hashemi GH, Derakhshan A, Basiratnia M, Arasteh MM, et al. Elevated serum levels of vitamin D in infants with urolithiasis. Iran J Kidney Dis. 2012;6:186-91.
9. Yılmaz N, Yüksel S, Altıntaş F, Koçyiğit A. Nephrolithiasis during the first 6 months of life in exclusively breastfed infants. Pediatr Nephrol. 2021;36:1227-31.
10. Banerjee S, Sengupta J, Basu S. The clinical relevance of native vitamin D in pediatric kidney disease. Pediatr Nephrol. 2023;38:945-55.
11. Ozkan B, Hatun S, Bereket A. Vitamin D intoxication. Turk J Pediatr. 2012;54:93-8.
12. Razzaque MS. Can adverse effects of excessive vitamin D supplementation occur without developing hypervitaminosis D? J Steroid Biochem Mol Biol. 2018;180:81-6.
13. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008;122:1142-52.
14. Ergon EY, Akil İO, Taneli F, Oran A, Ozyurt BC. Etiologic risk factors and vitamin D receptor gene polymorphisms in under one-year-old infants with urolithiasis. Urolithiasis. 2018;46:349-56.
15. Goknar N, Öktem F, Torun E, Gok O, Demir AD, Kucukkoc M, et al. The role of vitamin D receptor gene polymorphisms in Turkish infants with urolithiasis. Ren Fail. 2016;38:545-51.
16. Baştuğ F, Düşünsel R. Pediatric urolithiasis: causative factors, diagnosis and medical management. Nat Rev Urol. 2012;9:138-46.
17. Zhang F, Li W. The complex relationship between vitamin D and kidney stones: balance, risks, and prevention strategies. Front Nutr. 2024;11:1435403.
18. Gallo S, Comeau K, Vanstone C, Agellon S, Sharma A, Jones G, et al. Effect of different dosages of oral vitamin D supplementation on vitamin D status in healthy, breastfed infants: a randomized trial. JAMA. 2013;309:1785-92.
19. Levita J, Wilar G, Wahyuni I, Bawono LC, Ramadaini T, Rohani R, et al. Clinical toxicology of vitamin D in pediatrics: a review and case reports. Toxics. 2023;11:642.
20. Lin Y, Mao Q, Zheng X, Chen H, Yang K, Xie L. Vitamin D receptor genetic polymorphisms and the risk of urolithiasis: a meta-analysis. Urol Int. 2011;86:249-55.
21. Vogiatzi MG, Jacobson-Dickman E, DeBoer MD. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. J Clin Endocrinol Metab. 2014;99:1132-41.
22. Baştuğ F, Ağbaş A, Tülpar S, Yıldırım ZNY, Çiçek N, Günay N, et al. Comparison of infants and children with urolithiasis: a large case series. Urolithiasis. 2022;50:411-21.
23. Güven AG, Koyun M, Baysal YE, Akman S, Alimoglu E, Akbas H, et al. Urolithiasis in the first year of life. Pediatr Nephrol. 2010;25:129-34.
24. Serdaroğlu E, Aydoğan M, Özdemir K, Bak M. Incidence and causes of urolithiasis in children between 0-2 years. Minerva Urol Nefrol. 2017;69:181-8.
25. Bargagli M, Ferraro PM, Vittori M, Lombardi G, Gambaro G, Somani B. Calcium and vitamin D supplementation and their association with kidney stone disease: a narrative review. Nutrients. 2021;13:4363.

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Frequency and Trend Analysis of Adverse Childhood Experiences (ACE) in First-year Late Adolescent Students Starting University for the First Time in Türkiye: A Repeated Cross-sectional Study, 2023–2026

Türkiye'de Üniversiteye İlk Kez Başlayan Geç Ergenlik Dönemi Birinci Sınıf Öğrencilerinde Çocukluk Çağı Olumsuz Yaşam Deneyimlerinin Sıklığı ve Eğilim Analizi: Tekrarlı Kesitsel Çalışma, 2023–2026

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Cite this article as: Türe Ş, Silahlı NY, Öz NZ. Frequency and trend analysis of adverse childhood experiences (ACE) in first-year late adolescent students starting university for the first time in Türkiye: a repeated cross-sectional study, 2023–2026. J Curr Pediatr. 2026;24(2):126-135

Abstract

Introduction: Adverse Childhood Experiences (ACEs) refer to potentially traumatic experiences such as abuse, neglect, and household dysfunction that an individual experiences before the age of 18. This study aims to examine the frequency and temporal trends of Adverse Childhood Experiences (ACEs) among first-year late adolescents starting university for the first time between 2023 and 2026.

Materials and Methods: This research was conducted as a repeated cross-sectional study. Data were collected through an anonymous online questionnaire distributed via social media and student networks. Participants voluntarily joined from various regions of Türkiye. At the end of the study, the numbers of participants in 2023, 2024, 2025, and 2026 were 138, 137, 136, and 139, respectively, for a total of 550 students. The ACE-Q 10 scale was used to assess the frequency of adverse childhood experiences (ACEs). Changes over the years were analyzed using the Pearson Chi-square test, the Linear-by-Linear Association test, and multivariable logistic regression analyses.

Results: Fifty-three percent of participants reported experiencing at least one ACE, while 9.6% reported exposure to four or more ACEs. Emotional neglect was the most common type of child abuse across all years, followed by emotional abuse, with physical or medical neglect being the least frequent. Childhood sexual abuse increased significantly from 5.8% in 2023 to 17.4% in 2026 (p-trend=0.001). The prevalence of alcohol or substance abuse problems in the family also increased from 3.6% to 10.1% (p-trend=0.033). The percentage of students with four or more ACE scores increased significantly from 5.8% to 16.5% (p-trend = 0.004).

Conclusion: Among late adolescent students starting university, an increased trend was observed, particularly in cases of sexual abuse and high ACE burden. Although the findings are not nationally representative, they suggest a need for continued monitoring of ACEs and strengthening child protection and trauma-focused preventive programs.

Keywords
Adverse childhood experiences, child abuse, child neglect, students

Anahtar kelimeler
Olumsuz çocukluk deneyimleri, çocuk istismarı, çocuk ihmali, öğrenciler

Received/Geliş Tarihi : 03.06.2026
Accepted/Kabul Tarihi : 10.07.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.24445

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Öz

Giriş: Çocukluk çağı olumsuz yaşam deneyimleri (ÇÇOYD), bireyin 18 yaşına gelmeden önce yaşadığı istismar, ihmal ve aile içi işlev bozukluğu gibi potansiyel olarak travmatik deneyimleri ifade eder. Bu çalışma, 2023 ile 2026 yılları arasında ilk kez üniversiteye başlayan geç ergenlik dönemindeki birinci sınıf öğrencileri arasında ÇÇOYD sıklığını ve zamansal eğilimlerini incelemeyi amaçlamıştır.
Gereç ve Yöntem: Bu araştırma, tekrarlanan kesitsel tipte bir çalışma olarak yürütüldü. Veriler, sosyal medya ve öğrenci ağları aracılığıyla dağıtılan anonim çevrimiçi anket yoluyla toplandı. Katılımcılar Türkiye'nin çeşitli bölgelerinden gönüllü olarak katıldı. Çalışmanın sonunda, 2023, 2024, 2025 ve 2026 yıllarındaki katılımcı sayıları sırasıyla 138, 137, 136 ve 139 olup toplamda 550 öğrenciye ulaşılmıştır. Çocukluk çağı olumsuz yaşam deneyimlerinin sıklığını değerlendirmek için ACE-Q 10 ölçeği kullanıldı. Yıllar içindeki değişiklikler Pearson Chi-square ve Linear-by-Linear Association testi ve çok değişkenli lojistik regresyon analizleri kullanılarak incelendi.
Bulgular: Katılımcıların %53'ü en az bir olumsuz çocukluk çağı olumsuz yaşam deneyimi (ÇÇOYD) yaşadığını bildirirken, %9,6'sı dört veya daha fazla ÇÇOYD'ye maruz kaldığını bildirmiştir. Duygusal ihmal, tüm yıllar boyunca en yaygın çocuk istismarı türü olurken, bunu duygusal istismar takip etmiş, fiziksel veya tıbbi ihmal ise en az sıklıkta görülmüştür. Çocukluk çağı cinsel istismarı, 2023'te %5,8'den 2026'da %17,4'e önemli ölçüde artmıştır (p-trend=0,001). Ailede alkol veya madde bağımlılığı sorunlarının yaygınlığı da %3,6'dan %10,1'e yükselmiştir (p-trend=0,033). Dört veya daha fazla ÇÇOYD puanına sahip öğrencilerin yüzdesi de %5,8'den %16,5'e önemli ölçüde artmıştır (p-trend = 0,004).
Sonuç: Üniversiteye yeni başlayan geç ergenlik dönemindeki öğrenciler arasında, özellikle cinsel istismar ve ÇÇOYD yükü vakalarında artış eğilimi gözlemlenmiştir. Bulgular ulusal düzeyde temsili olamasa da, ÇÇOYD'nin sürekli olarak izlenmesi ve çocuk koruma ile travma odaklı önleyici programların güçlendirilmesi ihtiyacını ortaya koymaktadır.

Introduction

Adverse childhood experiences (ACEs) refer to potentially traumatic experiences such as abuse, neglect, and domestic dysfunction that an individual is exposed to before the age of 18 (1). In recent years, the concept of ACEs has become a key research topic in child health, mental health, and public health. The main reason is that adverse experiences in childhood are not limited to childhood; they also create lifelong physical, psychological, and social effects (1-3).

Studies show that ACE exposure is associated with depression, anxiety, substance use disorders, cardiometabolic diseases, risky health behaviors, and early mortality in adulthood (4,5). Toxic stress caused by ACEs can leave lasting effects on the neuroendocrine system, immune system, and brain development in childhood (6). In particular, chronic activation of the hypothalamic-pituitary-adrenal axis and changes in inflammatory processes underlie lifelong health risks (7).

Experiences within the scope of ACE are generally assessed in two main groups: childhood maltreatment and household dysfunction (1). Emotional, physical, and sexual abuse, and emotional and physical neglect are included in childhood maltreatment. At the same time, domestic violence, parental separation, mental illness in family members, alcohol or substance use problems, and a history of crime are considered household dysfunctions (1-3).

One of the most important findings of ACE studies is the cumulative effect of exposures. It has been shown that individuals with four or more ACEs have a significantly increased risk of mental disorders, chronic diseases, and adverse life outcomes (8). Recent meta-analytic studies report that health outcomes worsen with increasing ACE load, and that a significant dose-response relationship emerges (8-10).

Globally, ACEs are known to be quite common. A recent systematic review and meta-analysis reported that only 42% of children had never experienced an ACE, while 15% had four or more ACEs (11). Similarly, Centers for Disease Control and Prevention (CDC) data show that a large proportion of the adult population has experienced at least one ACE (1). However, ACE prevalence varies across countries, cultures, and socioeconomic conditions (1,11-13).

It is suggested that the negative life events to which children are exposed may have increased following the COVID-19 pandemic. It is stated that factors such as domestic economic problems, increased parental stress, social isolation, and distancing from educational environments during the pandemic period create new risks in terms of child abuse and neglect (14). Therefore, updated ACE assessments are particularly important after 2023, the post-pandemic period.

The period of starting university is a critical stage of life in which the effects of experiences individuals had during childhood and adolescence become visible in academic, social, and psychological areas (14). Recent studies show that the prevalence of ACE is high among university students and that childhood traumas have significant effects on academic success, psychological adjustment, and quality of life (12-17).

Adverse childhood experiences (ACEs) are common

among university students, with similar rates reported across many countries. However, there are almost no longitudinal or repeated cross-sectional trend studies that show an increase in ACE frequency over time (12-17). While studies have examined the prevalence of ACE in Türkiye, we have not found any research evaluating changes over time (12,13). Determining trends in ACE frequency, especially among late adolescent students who have recently started university, can inform the development of preventive public health policies.

This study aimed to determine the frequency of ACE among late-adolescent students starting university for the first time between 2023 and 2026 and to examine trends over time.

Materials and Methods

Study Design and Population

This research was conducted as a repeated cross-sectional study. The study population consisted of approximately 650,000 students starting university for the first time in Türkiye each year between 2023 and 2026. Sample size estimation was performed using an expected ACE prevalence of 12-15%, based on previously reported prevalence estimates among Turkish university students, with a 90% confidence level and a ±5 % margin of error (18). Under these assumptions, the minimum required sample size was calculated to be 124 participants per study year.

To ensure comparable sample sizes and similar levels of statistical precision across the four survey periods, a target of approximately 140 participants was established for each year. Data were collected anonymously via Google Forms, and responses were retained after submission. Therefore, rather than deleting completed questionnaires after data collection, recruitment was prospectively closed when approximately 140 responses had been obtained in each survey period. This approach was adopted to minimize imbalances in sample size between years and to maintain consistency across repeated cross-sectional assessments.

The study used a voluntary online convenience sampling approach rather than probability-based sampling. Data were collected through an anonymous online questionnaire distributed via social media and student networks. Participants voluntarily joined from various regions of Türkiye.Therefore, the sample should not be considered nationally representative, and the findings should be interpreted within the context of the study population.

At the end of the study, the number of individuals reached and included in 2023, 2024, 2025, and 2026 was 138, 137, 136, and 139, respectively, for a total of 550 students. With these numbers, the margins of error at the end of the study, at a 90% confidence level, were ±4.72%, ±4.74%, ±4.76%, and ±4.71 %, respectively.

Data Collection Procedures

Data were collected via an online survey. Participants volunteered for the research, and all data were collected anonymously. The ACE-Q 10 scale was used to determine the frequency of childhood adverse life experiences (ACE). The scale was developed by the CDC and Permanente in 1997, and its Turkish validity and reliability were tested by Gündüz et al. (19) in 2018. Variables within the scope of ACE in the scale were evaluated under two main headings:

Childhood Maltreatment

- Emotional abuse
- Physical abuse
- Sexual abuse
- Emotional neglect
- Physical/Medical negligence

Household Dysfunction

- Domestic violence
- Parental separation/divorce
- Presence of a member of the family with a mental illness
- Alcohol or substance use problem in the family
- Family history of crime or prison

The scale was scored from 0 to 10, with no cutoff points. Higher scores indicated greater exposure to adverse childhood experiences. A score of 0 indicated no ACE exposure, whereas a score of 10 indicated exposure across all ACE domains. (19).

Statistical Analysis

The data obtained in the study were entered into SPSS 22 (Statistical Package for the Social Sciences) and analyzed using descriptive and comparative statistics. Descriptive statistics were presented as frequency and percentage. The normality assumption was assessed by examining the histogram, q-q plot, and skewness and kurtosis values, and by applying the Shapiro-Wilk test. Categorical data were evaluated using the chi-square test. Differences between years were evaluated using the Pearson chi-square test. The Linear-by-Linear Association test was used to determine temporal trends. The statistical significance level was accepted as $p<0.05$. To determine whether observed temporal changes were independent of potential differences in participant characteristics across study years, multivariable logistic

regression analyses were additionally performed. Year of enrollment was entered as an ordinal variable (2023–2026), and the models were adjusted for gender and employment status. Separate models were constructed for childhood sexual abuse, alcohol/substance use problems within the family, and high ACE burden (ACE score ≥4). Adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) were calculated. Statistical significance was set at $p < 0.05$.

Ethics Committee Approval

The authors affirm that all procedures and experiments conducted in this study complied with the ethical standards outlined in the Declaration of Helsinki (1975), as revised in 2008, as well as relevant national regulations. Ethical approval for the study was obtained from the İstanbul Medipol University Clinical Research Ethics Committee (decision no: E-10840098-772.02-7504, date: 29.11.2023).

Results

Participant Characteristics

Of the 550 students participating in the study, 69.6% were female, and 30.4% were male, with a mean age of 19.21 ± 1.77 years. Most participants (83.8%) were not working during their university education. Overall, 53.1% of students reported at least one adverse childhood experience (ACE), 43.1% reported at least one form of childhood maltreatment, and 32.4% reported at least one form of household dysfunction. An ACE score of four or higher was observed in 9.6% of the participants. The general characteristics of all participants were summarized in Table 1.

Trends in Childhood Abuse and Neglect Experiences

Throughout the four years, the most common type of child abuse was emotional neglect, followed by emotional

Table 1. Participants' sociodemographic and Adverse Childhood Experiences (ACEs) characteristics

Categories		**All participants N (%)**
2023		**138 (25.1)**
2024		137(24.9)
2025		136 (24.7)
2026		139 (25.3)
Gender	**Female**	383 (69.6)
	Male	167 (30.4)
Employment status while at university	**Not working**	461 (83.8)
	Working	89 (16.2)
Childhood maltreatment (CM)		
Emotional abuse		115 (20.9)
Physical abuse		49 (8.9)
Sexual abuse		57 (10.4)
Emotional neglect		167 (30.4)
Physical/Medical neglect		11 (2)
Household dysfunction (HD)		
Domestic violence		32 (5.8)
Parental separation/divorce		56 (10.2)
Presence of a member of the family with a mental illness		114 (20.7)
Alcohol or substance use problem in the family		29 (5.3)
Family history of crime or prison		19 (3.5)
Those who have at least one ACE		292 (53.1)
Those with an ACE score of 4 and above		53 (9.6)
Those that are at least one CM		237 (43.1)
Those with at least one HD		178 (32.4)

abuse, while physical or medical neglect was the least frequent.

The frequency of emotional abuse increased from 17.4% in 2023 to 25.2% in 2026. However, this increase was not statistically significant (p-trend = 0.182).

An increase was also observed in the frequency of physical abuse, from 4.4% to 10.8%, but the linear trend was not significant (p-trend=0.076).

The frequencies of emotional neglect and physical neglect remained largely constant throughout the years. The findings were summarized in detail in Table 2.

A remarkable increase was detected in the frequency of sexual abuse. The rate, which was 5.8% in 2023, increased to 17.4% in 2026, showing a significant linear increase (p=0.008; p-trend=0.001). To determine whether the increase in childhood sexual abuse over time was independent of changes in participant characteristics, a multivariable logistic regression analysis was performed, adjusting for gender and employment status. Year remained a significant predictor of childhood sexual abuse (aOR=1.38, 95% CI: 1.04–1.82, p=0.026). This indicates that the odds of reporting childhood sexual abuse increased by approximately 38% with each successive study year. Employment status was also independently associated with childhood sexual abuse (aOR=2.04, 95% CI: 1.04–4.00, p=0.038), whereas gender was not significantly associated (p=0.342). The findings were summarized in detail in Table 3.

Trends in Household Dysfunction

Parental separation showed a significant difference between years (p = 0.007), but no linear increase or decrease trend was detected.

The frequency of alcohol or substance use problems in the family increased from 3.6% in 2023 to 10.1% in 2026 and showed a significant linear increase (p = 0.029; p-trend = 0.033). In a multivariable logistic regression model adjusted for gender and employment status, year of enrollment was not independently associated with reporting alcohol or substance use problems within the family (aOR=1.26, 95% CI: 0.86–1.85, p=0.233). Employment status showed a borderline association (aOR=2.38, 95% CI: 0.97–5.79, p=0.057), whereas gender was not significantly associated (p=0.463).

There was no significant change over the years in terms of domestic violence, presence of mental illness in the

Table 2. Frequency and trend analysis of Adverse Childhood Experiences (ACEs) over the years in late adolescent students starting university

	2023	2024	2025	2026	Pearson Chi-square	Linear by linear
	Yes N (%)	Yes N (%)	Yes N (%)	Yes N (%)	p-value	P-trend
Childhood maltreatment (CM)						
Emotional abuse	24 (17.4)	30 (21.9)	26 (19.1)	35 (25.2)	0.406	0.182
Physical abuse	6 (4.4)	14 (10.2)	14 (10.3)	15 (10.8)	0.197	0.076
Sexual abuse	8 (5.8)	10 (7.3)	15 (11)	24 (17.4)	**0.008**	**0.001**
Emotional neglect	44 (31.9)	39 (28.5)	41 (30.1)	43 (31.2)	0.935	0.977
Physical/Medical neglect	5 (3.6)	2 (1.5)	1 (0.7)	3 (2.2)	0.367	0.345
Household dysfunction (HD)						
Domestic violence	6 (4.3)	8 (5.8)	7 (5.1)	11 (8)	0.611	0.254
Parental separation/divorce	17 (12.3)	5 (3.7)	12 (8.8)	22 (15.9)	**0.007**	0.167
Presence of a member of the family with a mental illness	25 (18.1)	24 (17.6)	30 (22.1)	35 (25.4)	0.348	0.091
Alcohol or substance use problem in the family	5 (3.6)	6 (4.4)	4 (2.9)	14 (10.1)	**0.029**	**0.033**
Family history of crime or prison	4 (2.9)	4 (3)	5 (3.7)	6 (4.3)	0.902	0.467
Those who have at least one ACE	67 (48.6)	69 (50.4)	74 (54.4)	82 (59)	0.309	0.062
Those with an ACE score of 4 and above	8 (5.8)	11 (8)	11 (8.1)	23 (16.5)	**0.013**	**0.004**
Those that are at least one CM	52 (37.7)	57 (41.6)	59 (43.4)	69 (49.6)	0.240	**0.045**
Those with at least one HD	40 (29)	39 (28.5)	45 (33.1)	54 (38.8)	0.224	0.055

family, and criminal history in the family. The findings were summarized in detail in Table 2 and 3.

Trends in Total ACE Score

The proportion of students with at least one ACE increased from 48.6% in 2023 to 59.0% in 2026. This increase was close to the limit of statistical significance (p-trend = 0.062).

The proportion of students with an ACE score of four or higher increased from 5.8% to 16.5%, showing a significant linear increase (p=0.013; p-trend=0.004).

A significant increase was also found in the proportion of students who experienced at least one childhood abuse (p-trend=0.045). The increase in the rate of experiencing household dysfunction was found to be borderline significant (p-trend=0.055).

To determine whether the increase in high ACE burden over time was independent of changes in participant characteristics, a multivariable logistic regression analysis was performed, adjusting for gender and employment status. Year remained a significant predictor of having an ACE score

Table 3. Multivariable logistic regression analyses of temporal trends in high ACE burden, childhood sexual abuse, and family alcohol/substance use problems, adjusted for gender and employment status

	ACE score of 4 and above			Sexual abuse			Alcohol or substance use problem in the family		
	aOR (%95 CI)	P value	Nagelkerke R-squared	aOR (%95 CI)	p-value	Nagelkerke R-squared	aOR (%95 CI)	P value	Nagelkerke R-squared
Years (2023-2026)	1.41 (1.06-1.87)	**0.019**	0.032	1.38 (1.03-1.82)	**0.026**	0.060	1.26 (0.86-1.85)	0.233	0.046
Female sex	0.80 (0.43-1.47)	0.474		0.73 (0.38-1.39)	0.342		1.39 (0.57-3.35)	0.463	
Working students	1.43 (0.70-2.92)	0.322		2.04 (1.04-4.00)	**0.038**		2.38 (0.97-5.79)	0.057	

aOR: Adjusted odds ratio, CI: Confidence interval, reference categories were male sex and non-working students

Table 4. Examining the frequency of Adverse Childhood Experiences (ACEs) in all participants according to gender and current employment status

	Gender			Employment status while at university		
	Female Yes N (%)	Male Yes N (%)	p-value	Not working Yes N (%)	Working Yes N (%)	p-value
Childhood maltreatment (CM)						
Emotional abuse	74 (19.3)	41 (24.6)	0.165	97 (21)	18 (20.2)	0.862
Physical abuse	28 (7.3)	21 (12.7)	0.044	38 (8.3)	11 (12.4)	0.214
Sexual abuse	43 (11.3)	14 (8.4)	0.310	39 (8.5)	18 (20.5)	**0.001**
Emotional neglect	126 (33)	41 (24.6)	0.048	142 (30.8)	25 (28.4)	0.655
Physical/Medical neglect	5 (1.3)	6 (3.6)	0.080	7 (1.5)	4 (4.5)	0.064
Household dysfunction (HD)						
Domestic violence	22 (5.8)	10 (6)	0.916	24 (5.2)	8 (9.1)	0.154
Parental separation/divorce	39 (10.2)	17 (10.2)	0.984	46 (10)	10 (11.4)	0.699
Presence of a member of the family with a mental illness	85 (22.3)	29 (17.4)	0.189	93 (20.2)	21 (23.9)	0.440
Alcohol or substance use problem in the family	22 (5.8)	7 (4.2)	0.450	19 (4.1)	10 (11.4)	**0.015**
Family history of crime or prison	11 (2.9)	8 (4.8)	0.259	13 (2.8)	6 (6.9)	0.058
Those who have at least one ACE	206 (53.8)	86 (51.5)	0.621	235 (51)	57 (64)	**0.024**
Those with an ACE score of 4 and above	35 (9.1)	18 (10.8)	0.549	39 (8.5)	14 (15.7)	**0.033**
Those that are at least one CM	168 (43.9)	69 (41.3)	0.579	190 (41.2)	47 (52.8)	**0.043**
Those with at least one HD	130 (33.9)	48 (28.7)	0.231	139 (30.2)	39 (43.8)	**0.012**

of four or more (aOR=1.41, 95% CI: 1.06–1.87, p=0.019). This finding indicates that the odds of having a high ACE burden increased by approximately 41% with each successive study year. Neither gender (p=0.474) nor employment status (p=0.322) was significantly associated with having an ACE score of four or more. The findings were summarized in detail in Table 2 and 3.

ACE Distribution by Gender and Employment Status

Physical abuse was more frequent in male students than in female students (12.7% vs. 7.3%; p=0.044). In contrast, emotional neglect was more common in females (33.0% vs. 24.6%; p=0.048).

Childhood sexual abuse (20.5% vs. 8.5%; p=0.001), family history of alcohol or substance use (11.4% vs. 4.1%; p=0.015), at least one ACE score (64.0% vs. 51.0%; p=0.024), and four or more ACE scores (15.7% vs. 8.5%; p=0.033) were significantly higher among students who worked during their university education. The findings were summarized in detail in Table 4.

Discussion

This study examined temporal changes in adverse childhood experiences among late-adolescent students who began university between 2023 and 2026 and reported significant findings. Emotional neglect and abuse were the most common types of child maltreatment each year.

The most striking result of the study was the significant increase observed in the frequency of childhood sexual abuse. The observed increase in childhood sexual abuse remained significant after adjustment for gender and employment status, suggesting that the temporal trend cannot be explained solely by shifts in the demographic composition of the sample. The nearly threefold increase in the frequency of sexual abuse over the four years is a significant warning for child protection systems. This increase may be related not only to the actual rise in frequency but also to increased awareness of sexual abuse and strengthened reporting behaviors. In addition, the change in the risk environments to which children are exposed in the post-pandemic period may also be influential. International reports indicate that children distancing themselves from safe social support systems during the pandemic period may increase the risk of abuse (14).

The marked increase in reported childhood sexual abuse may also reflect broader social changes occurring in Türkiye during the study period. Economic instability and increasing financial pressures on families have been associated with heightened parental stress, family conflict, and reduced supervision of children, all of which may contribute to increased vulnerability to abuse (20). In parallel, adolescents have experienced unprecedented levels of digital exposure. Increased use of social media, online gaming platforms, and digital communication may expand opportunities for online grooming, sexual exploitation, and exposure to inappropriate sexual content (21). It is also possible that increased public discussion of child sexual abuse in traditional and social media has improved awareness and willingness to disclose previously unreported experiences (22). Therefore, the observed increase may reflect a combination of genuine changes in risk exposure and greater recognition and reporting of childhood sexual abuse.

In this study, 53.1% of the students reported experiencing at least one ACE. This rate is largely consistent with the international literature. Current systematic reviews indicate that the prevalence of ACE exceeds 50% among university students and young adults (1,3,12,13). In addition, CDC data reports that approximately two-thirds of adults have experienced at least one ACE in their lives (1). Our findings show that childhood trauma is a widespread public health problem in Turkey as well.

One of the most striking findings of the study is the significant increase in the proportion of students with an ACE score of four or higher over the years. Importantly, the increasing prevalence of high ACE burden (ACE score ≥4) remained significant after adjustment for gender and employment status. This suggests that the observed temporal increase reflects a genuine trend rather than changes in the sample's demographic composition. Having an ACE score of four or higher is considered an indicator of high risk for mental disorders, substance use, suicidal behavior, and chronic diseases (8-10). Therefore, the increase observed in our study should be carefully evaluated in terms of future mental health and public health burdens.

In our study, emotional neglect and abuse were the most common types of child abuse in all four years from 2023 to 2026. Unlike other types of child abuse, emotional neglect and abuse often leave no visible marks, making it an insufficiently addressed problem in societies where violence is socially acceptable. The lack of visible traces of abuse can lead to it going unnoticed in society. Unlike forms of maltreatment that result in visible physical injury, emotional abuse and neglect may be less readily recognized in settings where certain disciplinary practices are culturally normalized or regarded as part of routine child-rearing (23). As a result, these experiences may remain underrecognized by both

families and professionals despite their substantial long-term psychological impact. Continuous emotional abuse and neglect by the family cause chronic stress in the body. Chronic stress, when inflicted by the caregiver and occurring during critical life stages, leads to toxic stress, disrupting the body's balance through biological embedding and negatively impacting psychological resilience (24-26).

An important finding in our study is the increased frequency of alcohol or substance use problems within the family. Although the unadjusted trend analysis suggested an increase in alcohol or substance use problems within the family over time, this association was no longer significant after adjustment for gender and employment status. Therefore, the observed increase should be interpreted cautiously. Substance use within the family not only poses a direct risk of neglect and abuse for children but also creates multifaceted negative effects through insecure family environments, economic difficulties, and psychological stress (27). The literature has shown a strong association between substance use within the family and childhood traumas (27,28).

The higher frequency of physical abuse among male students in our study is consistent with previous research. It is reported that in some cultures, male children are more often subjected to physical punishment for disciplinary purposes (29,30). In contrast, the higher frequency of emotional neglect among female students may be related to gender roles and family expectations (31). However, these differences need to be evaluated within a cultural context.

It is noteworthy that students who work during their university education have a higher ACE load. ACE exposure is associated with economic vulnerability, difficulties in educational processes, and reduced quality of life (1,32). Therefore, the higher ACE rates observed among working students suggest that childhood disadvantages persist into young adulthood.

The toxic stress model currently explains the long-term effects of ACEs. Individuals exposed to continuous traumatic experiences during childhood may develop permanent changes in their neuroendocrine and immunological systems; this can increase their susceptibility to mental and physical illnesses in adulthood (4-7). Recent studies on neurocognitive functions also show that ACEs negatively affect cognitive development in children and adolescents (8-10).

Recent neurodevelopmental research has provided more specific biological explanations for these associations (33-35). Exposure to chronic childhood adversity has been linked to alterations in the connectivity between the prefrontal cortex and the amygdala (34). These neural circuits play a central role in emotional regulation, threat detection, and executive functioning. Dysregulation of these networks may contribute to increased emotional reactivity, impaired impulse control, and vulnerability to anxiety and depressive disorders (33). In addition, accumulating evidence suggests that adverse childhood experiences can influence epigenetic regulation of stress-response systems, including genes involved in the hypothalamic-pituitary-adrenal axis (33,34). These biological changes may be particularly relevant during late adolescence, a developmental period characterized by ongoing maturation of higher-order cognitive and emotional regulatory systems (35).

The period of starting university is a critical life stage during which the effects of experiences from childhood and adolescence become visible in academic, social, and psychological domains (14). It is reported that ACEs are strongly associated with depression, anxiety, stress, and lower life satisfaction in first-year students, and therefore this period is a stage where the effects of ACEs become more pronounced in mental health (16). Therefore, evaluating changes in ACE burden in newly enrolled university students is important for assessing the current state of childhood trauma in society.

The results of our study contain important messages for child protection policies. Current public health approaches recommended by the CDC and the World Health Organization show that parent support programs, economic empowerment policies, safe school environments, and trauma-informed health services are effective in preventing ACEs (36). Conducting ACE screenings in psychological counseling services for university students and supporting high-risk individuals early on may be beneficial. Interventions at this stage can be critical for preventing the transfer of chronic stress to later ages, as late adolescents can receive long-term support in university settings before entering the workforce, i.e., before additional stressors are added.

Study Limitations

This study has some limitations. Collecting data through self-report may introduce recall bias. Also, since the research was conducted only within the university population, the generalizability of the results to the entire youth population is limited. However, the fact that data were collected using similar methods each year is a significant strength of the study for evaluating trends.

Although participants were recruited from different regions of Türkiye, the use of an online convenience

sampling method limits the representativeness of the sample. Therefore, the findings may not be generalizable to all first-year university students in Türkiye.

Conclusion

In conclusion, this study demonstrates the prevalence of ACEs among newly enrolled university students in Turkey, with an upward trend in some ACE indicators. High ACE burdens, increased rates of sexual abuse, and increased frequency of alcohol or substance use problems in the family are particularly noteworthy from a child health and public health perspective. Conducting ACE screenings in psychological counseling services for first-year university students in late adolescence and providing early support to high-risk individuals could be beneficial. Interventions during this period may be critical in preventing the transmission of chronic stress into later life.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the İstanbul Medipol University Clinical Research Ethics Committee (decision no: E-10840098-772.02-7504, date: 29.11.2023).

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Acknowledgements: We sincerely thank all students who participated in this study.

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Centers for disease control and prevention. about adverse childhood experiences (ACEs). Atlanta: CDC; 2026. Available from: https://www.cdc.gov/aces/about/index.html
2. Fujiwara T. Impact of adverse childhood experience on physical and mental health: a life-course epidemiology perspective. Psychiatry Clin Neurosci. 2022;76:544-51.
3. Metzler M, Merrick MT, Klevens J, Ports KA, Ford DC. Adverse childhood experiences and life opportunities: Shifting the narrative. Child Youth Serv Rev. 2017;72:141-9.
4. Wakuta M, Nishimura T, Osuka Y, Tsukui N, Takahashi M, Adachi M, et al. Adverse childhood experiences: impacts on adult mental health and social withdrawal. Front Public Health. 2023;11:1277766.
5. Daníelsdóttir HB, Aspelund T, Shen Q, Halldorsdottir T, Jakobsdóttir J, Song H, et al. Adverse childhood experiences and adult mental health outcomes. JAMA Psychiatry. 2024;81:586-94.
6. Yu J, Haynie DL, Gilman SE. Patterns of Adverse childhood experiences and neurocognitive development. JAMA Pediatr. 2024;178:678-87.
7. Berens AE, Jensen SKG, Nelson C. Biological embedding of childhood adversity: from physiological mechanisms to clinical implications. BMC Medicine. 2017;15.
8. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health. 2017;2:356-66.
9. Bellis M, Hughes K, Ford K, Rodriguez RG, Sethi D, Passmore J. Life course health consequences and associated annual costs of adverse childhood experiences across Europe and North America: a systematic review and meta-analysis. The Lancet. PublicHealth. 2019;4:517-28.
10. Kumar S, Campbell JA, Wang X, Xu Y, Nagavally S, Egede LE. Trends in prevalence of adverse childhood experiences by sociodemographic factors in the United States: behavioral risk factor surveillance system 2009-2022. BMC Public Health. 2024;24:2615.
11. Madigan S, Thiemann R, Deneault AA, Fearon RMP, Racine N, Park J, et al. Prevalence of adverse childhood experiences in child population samples: a systematic review and meta-analysis. JAMA Pediatr. 2025;179:19-33.
12. Sezgin E. The mediating effect of mindfulness on adverse childhood experiences and psychological resilience in Turkish female university students. Frontiers in Psychology. 2025;16.
13. Buyukcebeci A. The effects of adverse childhood experiences on subjective happiness: the serial mediation role of regulatory emotional self-efficacy and future anxiety. BMC Psychology. 2025;13.
14. Hertz M, Heim Viox M, Massetti GM, Anderson KN, Bacon S, Fordyce E, et al. Adverse childhood experiences among US adolescents over the course of the COVID-19 pandemic. Pediatrics. 2023;151:e2022060799.
15. Bhattarai A, King N, Adhikari K, Dimitropoulos G, Devoe D, Byun J, et al. Childhood adversity and mental health outcomes among university students: a longitudinal study. Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie. 2022;68:510-20.
16. Trinh HH, Nguyen TT, Nguyen TQ, Ngo NT, Nguyen ST, Nguyen CV, et al. Impacts of adverse childhood experiences on mental health and satisfaction with life in first-year college students: results from a cross-sectional study in Vietnam. Psychiatry Investigation. 2025;22:939-48.
17. Bartolomé-Valenzuela M, Pereda N, Guilera G. Patterns of adverse childhood experiences and associations with lower mental well-being among university students. Child Abuse Negl. 2024;152:106770.
18. Ulukol B, Kahiloğulları AK, Sethi D. Türkiye'de üniversite öğrencilerinde çocukluk çağı olumsuz yaşam deneyimleri araştırması çalışma raporu-2013. Dünya Sağlık Örgütü Avrupa Bölge Ofisi. 2014.

19. Gündüz A, Yaşar AB, Gündoğmuş I, Konuk E. Adverse childhood events Turkish form: validity and reliability study. Anatolian Journal of Psychiatry. 2018;19:68-75.
20. Koç M, Koçtürk N, Zencir T. Prevalence of the child sexual abuse in Turkey: a scoping review. Toplum ve Sosyal Hizmet. 2023;34:209-26.
21. Marcos V, Fariña F, Isorna M, López-Roel S, Rolán K. Problematic use of the internet and cybervictimization: an empirical study with Spanish adolescents. Behav Sci (Basel). 2025;15:810.
22. Habib G, Urfan Ullah M, Khanum T, Khan A. Role of media in coverage and reporting of child abuse cases. Journal of World Science. 2023;2:529-40.
23. Abdullah A, Thattengat R. Child neglect as a culture-based concept: a systematic review and implications for studying and measuring child neglect. Child Abuse Negl. 2025;161:107261.
24. Fiş NP, Berkem M. Nörotransmitter sistemlerinin gelişimi ve psikopatolojiye yansımaları. Klinik Psikofarmakoloji Bülteni. 2019;19:312-21.
25. Johnson SB, Riley AW, Granger DA, Riis J. The science of early life toxic stress for pediatric practice and advocacy. Pediatrics. 2013;131:319-27.
26. Bick J, Nelson CA. Early adverse experiences and the developing brain. Neuropsychopharmacology. 2016;41:177-96.
27. Dube S, Anda RF, Felitti V, Croft J, Edwards V, Giles W. Growing up with parental alcohol abuse: exposure to childhood abuse, neglect, and household dysfunction. Child abuse & neglect. 2001;25:1627-40.
28. Haugland SH, Carvalho B, Strandheim A, Stea TH. Parental alcohol ıntoxication, adverse childhood experiences, and negative psychological reactions to childhood adversities: cross-sectional and prospective data from the population-based HUNT study. J Child Adolesc Trauma. 2024;17:1225-37.
29. Lansford JE, Alampay LP, Al-Hassan S, Bacchini D, Bombi AS, Bornstein MH, et al. Corporal punishment of children in nine countries as a function of child gender and parent gender. Int J Pediatr. 2010;2010:672780.
30. Heekes S, Kruger CB, Lester S, Ward C. A systematic review of corporal punishment in schools: global prevalence and correlates. Trauma Violence Abuse. 2020;23:52-72.
31. Moody G, Cannings-John R, Hood K, Kemp A, Robling M. Establishing the international prevalence of self-reported child maltreatment: a systematic review by maltreatment type and gender. BMC Public Health. 2018;18.
32. Hardcastle K, Bellis M, Ford K, Hughes K, Garner J, Rodríguez G. Measuring the relationships between adverse childhood experiences and educational and employment success in England and Wales: findings from a retrospective study. Public Health. 2018;165:106-16.
33. Gerin MI, Viding E, Herringa RJ, Russell JD, McCrory EJ. A systematic review of childhood maltreatment and resting state functional connectivity. Dev Cogn Neurosci. 2023;64:101322.
34. Goodpaster CM, Christensen CR, Alturki MB, DeNardo LA. Prefrontal cortex development and its implications in mental illness. Neuropsychopharmacology. 2026;51:114-28.
35. Meredith WJ, Silvers JA. Experience-dependent neurodevelopment of self-regulation in adolescence. Dev Cogn Neurosci. 2024;66:101356.
36. CDC. A Public Health Approach to adverse childhood experiences. 2024. Available from: https://www.cdc.gov/aces/php/public-health-strategy/index.html

ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Evaluation of Complete Blood Count Parameters and Hematological Inflammatory Indices at Diagnosis in Childhood Nephrotic Syndrome

Çocukluk Çağı Nefrotik Sendromunda Tanı Anındaki Tam Kan Sayımı Parametreleri ve Hematolojik Enflamatuvar İndekslerin Değerlendirilmesi

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Cite this article as: Akacı O, Bostancı M, Duran. Duran Sİ. Evaluation of complete blood count parameters and hematological ınflammatory ındices at diagnosis in childhood nephrotic syndrome. J Curr Pediatr. 2026;24(2):136-144

Abstract

Introduction: Nephrotic syndrome is associated with immüne inflammatory activation and alterations in platelet-related parameters. This study aimed to compare complete blood count parameters, platelet/mean platelet volüme related indicators, and hematological inflammatory indices between children with nephrotic syndrome and healthy controls, and to evaluate their relationship with steroid response and relapse frequency.

Materials and Methods: This retrospective case-control study included 72 children with nephrotic syndrome and 40 healthy controls. Laboratory data obtained at the time of diagnosis, before steroid treatment, were analyzed. Complete blood count parameters, platelet/mean platelet volüme related indicators, and hematological inflammatory indices, including neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, systemic immüne inflammation index, and systemic inflammatory response index, were evaluated. Patients with nephrotic syndrome were further classified as steroid sensitive or steroid resistant. Steroid sensitive patients were also compared according to relapse frequency.

Results: Hemoglobin, white blood cell count, absolute neutrophil count, red cell distribution width, and platelet count were significantly higher in the nephrotic syndrome group than in the control group, whereas mean platelet volume was significantly lower. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immüne inflammation index were also significantly higher in the nephrotic syndrome group. No significant differences were found between steroidsensitive and steroid resistant nephrotic syndrome groups in complete blood count parameters, platelet/mean platelet volüme related indicators, hematological inflammatory indices, or biochemical parameters. Among steroid sensitive patients, platelet count, platelet-to-lymphocyte ratio, and systemic immüne inflammation index were significantly higher in the frequent relapse group than in the infrequent relapse group. Correlation analyses showed limited associations, mainly between platelet count and albumin or total cholesterol levels.

Conclusion: Complete blood count derived indices may provide practical supportive information regarding inflammatory and platelet related alterations in children with nephrotic syndrome. Platelet count, mean platelet volume, platelet-to-lymphocyte ratio, and systemic immüne inflammation index differed particularly in

Keywords
Nephrotic syndrome, child, complete blood count, mean platelet volüme, platelet-to-lymphocyte ratio, systemic immune-inflammation index

Anahtar kelimeler
Nefrotik sendrom, çocuk, tam kan sayımı, ortalama trombosit hacmi, trombosit-lenfosit oranı, sistemik immün-enflamasyon indeksi

Received/Geliş Tarihi : 01.07.2026
Accepted/Kabul Tarihi : 23.07.2026
Published Date/ Yayınlanma Tarihi : 04.08.2026

DOI:10.4274/jcp.2026.80008

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patient control comparisons. At the same time, platelet related indices were also higher among steroid sensitive patients with frequent relapses. These parameters should be interpreted as complementary indicators rather than standalone diagnostic or prognostic markers.

Öz

Giriş: Nefrotik sendrom, immün inflamatuar aktivasyon ve trombositle ilgili parametrelerdeki değişikliklerle ilişkilidir. Bu çalışmanın amacı, nefrotik sendromlu çocuklar ile sağlıklı kontrol grubu arasında tam kan sayımı parametrelerini, trombosit/ortalama trombosit hacmi ile ilgili göstergeleri ve hematolojik inflamatuar indeksleri karşılaştırmak ve bunların steroid yanıtı ve nüks sıklığı ile ilişkisini değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif vaka-kontrol çalışmasına nefrotik sendromlu 72 çocuk ve 40 sağlıklı kontrol katılımcısı dahil edildi. Tanı anında steroid tedavisi öncesinde elde edilen laboratuvar verileri analiz edildi. Tam kan sayımı parametreleri, trombosit/ortalama trombosit hacmi ile ilgili göstergeler ve nötrofil-lenfosit oranı, trombosit-lenfosit oranı, monosit-lenfosit oranı, sistemik immün inflamasyon indeksi ve sistemik inflamatuar yanıt indeksi dahil olmak üzere hematolojik inflamatuar indeksler değerlendirildi. Nefrotik sendromlu hastalar ayrıca steroid duyarlı veya steroid dirençli olarak sınıflandırıldı. Steroid duyarlı hastalar ayrıca nüks sıklığına göre karşılaştırıldı.

Bulgular: Hemoglobin, lökosit sayısı, mutlak nötrofil sayısı, kırmızı kan hücresi dağılım genişliği ve trombosit sayısı nefrotik sendrom grubunda kontrol grubuna kıyasla istatistiksel olarak anlamlı derecede yüksekken, ortalama trombosit hacmi ise istatistiksel olarak anlamlı derecede düşüktü. Nötrofil-lenfosit oranı, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi de nefrotik sendrom grubunda istatistiksel olarak anlamlı derecede yüksekti. Steroid duyarlı ve steroid dirençli nefrotik sendrom grupları arasında tam kan sayımı parametreleri, trombosit/ortalama trombosit hacmi ile ilgili göstergeler, hematolojik inflamasyon indeksleri veya biyokimyasal parametreler açısından anlamlı bir fark saptanmadı. Steroid duyarlı hastalar arasında sık nüks eden grupta trombosit sayısı, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi, seyrek nüks eden gruba kıyasla anlamlı derecede daha yüksekti. Korelasyon analizleri esas olarak trombosit sayısı ile albümin veya toplam kolesterol düzeyleri arasında sınırlı ilişkiler olduğunu gösterdi.

Sonuç: Tam kan sayımından elde edilen indeksler, nefrotik sendromlu çocuklarda inflamatuar ve trombositle ilgili değişiklikler konusunda pratik ve destekleyici bilgiler sağlayabilir. Trombosit sayısı, ortalama trombosit hacmi, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi, özellikle hasta-kontrol karşılaştırmalarında farklılık göstermiştir. Aynı zamanda, trombositle ilgili indeksler, sık nüks görülen steroid duyarlı hastalarda da daha yüksek bulunmuştur. Bu parametreler, tek başına tanı veya prognostik belirteçler olarak değil tamamlayıcı göstergeler olarak yorumlanmalıdır.

Introduction

Nephrotic syndrome is one of the most common glomerular diseases of childhood and is characterized by nephrotic-level proteinuria, hypoalbuminemia, edema, and, frequently, hyperlipidemia (1,2). In idiopathic nephrotic syndrome of childhood, the majority of cases are steroid-responsive, and this clinical presentation is most often associated with minimal change disease. In contrast, steroid-resistant nephrotic syndrome is less common. Focal segmental glomerulosclerosis is more commonly detected in this group, and steroid resistance is an important clinical indicator for long-term renal prognosis (3). It is believed that abnormalities in T- and B-cell responses, cytokine-mediated mechanisms, and structural and functional changes in the glomerular filtration barrier contribute to the pathogenesis of the disease. Therefore, immune and inflammatory processes are closely associated with the development and clinical course of childhood nephrotic syndrome (1,4,5). This interaction between inflammation and hemostasis has heightened interest in platelet parameters in nephrotic syndrome. Indeed, an increased risk of thromboembolism has been identified in nephrotic syndrome, and this risk is associated with multiple mechanisms, including loss of anticoagulant factors, increased procoagulant factors, hemoconcentration, and altered platelet activation (6).

Complete blood count parameters and the hematological inflammatory indices derived from these parameters are considered practical auxiliary indicators that may reflect systemic inflammation, given their ease of access and low cost (7). Mean platelet volume is a parameter that reflects platelet size and is considered to be associated with platelet activation. Red blood cell distribution width, on the other hand, has been linked to anisocytosis, systemic inflammation, and oxidative stress (7,8). Similarly, indices derived from a complete blood count such as the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII) are also considered as auxiliary markers that may reflect inflammatory processes. (9).

Studies have evaluated platelet indices and inflammatory markers derived from complete blood counts in childhood nephrotic syndrome. However, the findings reported in these

studies vary across different centers and patient groups (5,6,9-12). This study aimed to compare complete blood count parameters and hematological inflammatory indices at the time of diagnosis in patients followed at our clinic for nephrotic syndrome with those of a control group.

Materials and Methods

This study was conducted among pediatric patients diagnosed with nephrotic syndrome and followed up at the Pediatric Nephrology Clinic of Bursa Yüksek İhtisas Training and Research Hospital between 2016 and 2024. All patients with childhood nephrotic syndrome identified in the clinic records during the study period who had complete blood count data available at diagnosis were included, and no eligible patient was excluded. All laboratory parameters were obtained from blood samples collected at the patients' initial admission, before the initiation of any treatment, including corticosteroids, albumin infusion, or diuretic therapy. The control group consisted of cases evaluated during routine well-child examinations. When selecting control cases, care was taken to ensure they had no history of active infection, chronic disease, regular medication use, kidney disease, or hematological disease. Cases with missing baseline laboratory data or laboratory measurements taken at times other than the time of diagnosis were excluded from the study. Nephrotic-range proteinuria was defined as 24-hour urinary protein excretion ≥1,000 mg/m^2/day (≥40 mg/m^2/h). Complete remission was defined as negative or trace proteinuria on urine dipstick for three consecutive days. SSNS was defined as complete remission within four weeks of standard-dose corticosteroid treatment, whereas SRNS was defined as failure to achieve complete remission within four weeks (2,3).

Data Collection

Data were obtained retrospectively by reviewing patient records and the hospital information system. For each case, age, sex, and study group were recorded. In patients with nephrotic syndrome, the age at diagnosis, response to steroid therapy, and disease subtype were also assessed. At the time of diagnosis, the following complete blood count parameters were recorded: hemoglobin (Hb), white blood cell count (WBC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count (PLT), mean corpuscular volume (MCV), red blood cell distribution width (RDW), and mean platelet volume (MPV). Since monocyte counts were present only in the nephrotic syndrome group, the monocyte-to-lymphocyte ratio (MLR) and the systemic inflammatory response index (SIRI) were not included in the case-control comparison. In patients with nephrotic syndrome, serum albumin, creatinine, blood urea nitrogen (BUN), total protein, sodium, potassium, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), very low-density lipoprotein cholesterol (VLDL), erythrocyte sedimentation rate (ESR), and 24-hour urinary protein excretion were recorded. Hematological inflammatory indices were calculated using complete blood count components. In this context, NLR, PLR, MLR, SII, and SIRI were evaluated. SII was calculated using the formula PLT × ANC / ALC, while SIRI was calculated using the formula ANC × monocyte count / ALC. The platelet-to-MPV ratio was also calculated as a platelet- and MPV related indicator.

Statistical Analysis

The study size was determined by the number of eligible patients available in the clinic records during the study period. Therefore, no a priori sample size calculation was performed. Statistical analysis of the data was performed using SPSS. The normality of continuous variables was assessed using the Shapiro-Wilk test. Variables that followed a normal distribution were presented as mean ± standard deviation, while those that did not follow a normal distribution were presented as median and interquartile range (IQR). Categorical variables were expressed as counts and percentages. The main comparison in the study was made between the nephrotic syndrome group and the healthy control group. In secondary analyses, the SSNS and SRNS groups were compared. Within the SSNS subgroup, patients with frequent and infrequent relapses were evaluated separately.

For comparisons between the two groups, the Student's t-test was used for continuous variables that followed a normal distribution, and the Mann-Whitney U test was used for continuous variables that did not follow a normal distribution. For comparisons of categorical variables, the chi-square test was used, or Fisher's exact test was used when the expected cell counts were insufficient. In the correlation analyses, the Pearson or Spearman correlation coefficient was calculated based on the variables' distributional characteristics. Effect sizes were calculated as Hedges' g for comparisons performed using the independent-samples t-test, r for Mann-Whitney U tests, and the Phi coefficient for 2 × 2 categorical comparisons. A p-value of <0.05 was considered statistically significant.

Ethics Committee Approval

Approval for this study was obtained from the Ethics Committee of Bursa Specialized Training and Research Hospital (No. 2011-KAEK-25-2020/10-04, date: 23.11.2011). Due to the retrospective design, data were obtained from patient charts and hospital records. All patient data were anonymized prior to analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

A total of 112 children were included in the study. Of these, 72 were in the nephrotic syndrome group, and 40 were in the control group. When the nephrotic syndrome group was evaluated based on steroid response, 57 patients were classified as SSNS and 15 as SRNS. In the SSNS group, based on relapse frequency, 25 patients were classified as frequent relapsers and 32 as infrequent relapsers.

Demographic Characteristics

The mean age in the nephrotic syndrome group was 11.12 ± 4.05 years, and in the control group, 9.37 ± 3.62 years. There was a statistically significant difference in age between the groups (p=0.025). The gender distribution was 25 girls and 47 boys in the nephrotic syndrome group and 14 girls and 26 boys in the control group. There was no significant difference in gender distribution between the groups. The median age at diagnosis in the nephrotic syndrome group was 4.00 (3.00–6.00) years. Demographic characteristics are presented in Table 1.

Comparison of Complete Blood Count Parameters

A comparison of complete blood count parameters between the nephrotic syndrome group and the control group is presented in Table 2. The between-group effect was moderate for hemoglobin (r = 0.36), small for WBC, ANC, and RDW (r = 0.25-0.28), and large for platelet count and MPV (Hedges' g = 1.12 and -0.92, respectively).

Table 1. Demographic characteristics of the study groups

Nephrotic syndrome vs control			
Variable	**Nephrotic syndrome (n=72)**	**Control (n=40)**	**p**
Age (years)	11.12 ± 4.05	9.37 ± 3.62	0.025
Sex, Female/Male (n)	25/47	14 / 26	0.976
Age at diagnosis (years)	4.00 (3.00-6.00)		
SSNS and SRNS subgroups			
Variable	**SSNS (n=57)**	**SRNS (n=15)**	**p**
Age (years)	11.03±4.09	11.47 ± 4.05	0.713
Sex, Female/Male (n)	23/34	2/13	0.069

Data are presented as mean ± standard deviation, median (interquartile range), or number. SSNS: steroid-sensitive nephrotic syndrome; SRNS: steroid-resistant nephrotic syndrome

Table 2. Complete blood count parameters in the nephrotic syndrome and control groups

Variable	**Nephrotic syndrome**	**Control**	**p**
Hemoglobin (g/dL)	13.30 (11.95-14.05)	12.0 (11.02-12.97)	<0.001
WBC (mm^3)	10100 (7710-13125)	8400 (7020-9915)	0.003
Neutrophil (mm^3)	5600 (3890-7790)	4230 (2580-5145)	0.008
Lymphocyte (mm^3)	3060 (2425-4375)	3082 (2362-4395)	0.949
Platelet (mm^3)	408704 ± 123927	281712 ± 89493	<0.001
MCV (fL)	78.57 ± 5.15	77.48 ± 4.37	0.262
RDW (%)	14.00 (13.30-14.80)	13.43 (12.61-13.98)	0.005
MPV (fL)	8.37 ± 1.14	9.36 ± 0.93	<0.001
Platelet/MPV ratio	46188 (39892-58918)	26820 (22868-36448)	<0.001

Data are presented as mean ± standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; MCV: mean corpuscular volume; RDW: red cell distribution width; MPV: mean platelet volume

In the nephrotic syndrome group, hemoglobin, WBC, ANC, RDW, and platelet count were significantly higher than in the control group. However, MPV was significantly lower in the nephrotic syndrome group. The p-values were as follows: p <0.001 for hemoglobin, p = 0.003 for WBC count, p = 0.008 for ANC count, p = 0.005 for RDW, and p < 0.001 for both platelet count and MPV. The platelet-to-MPV ratio was also significantly higher in the nephrotic syndrome group compared to the control group (p <0.001). The platelet-to-MPV ratio also showed a large effect size (r = 0.60).

Hematological Inflammatory Indices

A comparison of hematological inflammatory indices between the nephrotic syndrome and control groups is presented in Table 3. The NLR was significantly higher in the nephrotic syndrome group compared to the control group (p=0.034). Similarly, PLR and SII values were also significantly higher in the nephrotic syndrome group (p <0.001 for both). The effect size was small for NLR (r = 0.20) and moderate for PLR and SII (r = 0.34 and r = 0.35, respectively). Since monocyte data were not available for the control group, MLR and SIRI were not included in the patient-control comparison and were reported only in the nephrotic syndrome subgroup analyses.

Comparison of the SSNS and SRNS Subgroups

The SSNS (n=57) and SRNS (n=15) groups were compared for demographic characteristics, complete blood count parameters, platelet- and MPV related indicators, hematological inflammatory indices, and biochemical parameters. There were no significant differences between the groups in age, age at diagnosis, or gender distribution. Hemoglobin, WBC, neutrophil, lymphocyte, monocyte, and platelet counts, as well as MCV, RDW, and MPV values, were similar between the two groups. No significant differences were observed in platelet or MPV related indicators or in hematological inflammatory indices, including NLR, PLR, MLR, SII, and SIRI. Serum albumin, total protein, lipid profile, creatinine, and other biochemical parameters were similar between the groups (Table 4). The corresponding effect sizes were predominantly negligible or small.

Comparison of Frequent Relapses in the SSNS Group

SSNS patients were compared between those with frequent relapses (n=25) and those with infrequent relapses (n=32). In the frequent relapse group, platelet count, PLR, and SII values were significantly higher. The effect size was moderate for platelet count and SII (Hedges' g = 0.56 and r = 0.30, respectively) and large for PLR (Hedges' g = 0.83). No significant differences were observed between the groups in terms of other complete blood count parameters, MPV, NLR, MLR, SIRI, MPV/platelet ratio, and the evaluated biochemical parameters (Table 5).

Correlation Analyses

In the nephrotic syndrome group, the relationships between hematological markers and disease parameters were evaluated using Spearman's correlation analysis. A significant negative correlation was found between platelet count and serum albumin (rho = -0.36; p = 0.002). A significant positive correlation was found between platelet count and total cholesterol (rho = 0.30; p = 0.012). There was a significant positive correlation between the MPV/platelet ratio and serum albumin (rho = 0.36; p = 0.002). No significant correlations were found between NLR, PLR, SII, SIRI, and MPV values and serum albumin, 24-hour urinary protein excretion, total cholesterol, and erythrocyte sedimentation rate (Supplementary Table 1).

Discussion

In this retrospective case-control study, hematological changes at the time of diagnosis in childhood nephrotic syndrome were evaluated using platelet- and MPV related markers, as well as inflammatory indices derived from the complete blood count. Our findings indicate that in patients with nephrotic syndrome, platelet-related markers particularly platelet count, PLR, and SII are higher than in healthy controls, whereas MPV is lower. However, the evaluated hematological and biochemical parameters showed no significant differences between the SSNS and SRNS subgroups.

Table 3. Hematological inflammatory indices in the nephrotic syndrome and control groups

Variable	Nephrotic syndrome	Control	p
NLR	1.96 (0.91-3.26)	1.29 (0.80-1.93)	0.034
PLR	125 (89-181)	84 (67-109)	<0.001
SII×10^9/L	750.2 (310.5-1318.3)	355.2 (187.0-541.6)	<0.001

Data are presented as median (interquartile range). NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index

The higher platelet count, PLR, and SII observed in frequent relapsers within the SSNS group may represent a preliminary pattern; however, given the small subgroup size, this finding requires confirmation in larger prospective studies. In correlation analyses, however, the fact that only certain platelet-based parameters show a limited association with albumin and lipid profiles suggests that these indicators should not be considered, on their own, as strong markers of disease activity or severity.

It has long been recognized that nephrotic syndrome is associated with immune-mediated mechanisms, particularly within the spectrum of steroid-responsive and minimal change disease. Impaired podocyte integrity, abnormalities in T- and B-cell responses, circulating permeability factors, and anti-nephrin autoantibodies which have been identified in recent years are among the primary mechanisms involved in this pathogenesis (13). Studies have shown that childhood nephrotic syndrome is associated with changes in the CD4/

Table 4. Comparison of demographic, hematological, inflammatory, and biochemical parameters between the SSNS and SRNS subgroups

Variable	SSNS (n=57)	SRNS (n=15)	p
Demographic			
Age (years)	11.03 ± 4.09	11.47 ± 4.05	0.713
Age at diagnosis (years)	4.00 (3.00-6.00)	3.50 (2.50-4.50)	0.345
Complete blood count			
Hemoglobin (g/dL)	13.15 (12.23-14.03)	13.4 (11.4-13.9)	0.882
WBC (mm^3)	10100 (7780-13088)	10600 (7655-13105)	0.794
Neutrophil (mm^3)	5600 (3930-7890)	5570 (3102-6830)	0.983
Lymphocyte (mm^3)	2835 (2408-4400)	3240 (2730-3905)	0.632
Monocyte (mm^3)	530 (408-792)	630 (415-770)	0.905
Platelet (mm^3)	409071 ± 128228	407333 ± 110414	0.962
MCV (fL)	78.38 ± 5.35	79.27 ± 4.41	0.557
RDW (%)	14.00 (13.38-14.80)	13.70 (13.15-14.40)	0.356
MPV (fL)	8.34 ± 1.10	8.50 ± 1.32	0.627
Platelet/MPV related			
Platelet/MPV ratio	48000 (39950-61666)	45567 (39716-51772)	0.529
Inflammatory indices			
NLR	2.04 (0.98-3.32)	1.61 (0.83-2.38)	0.451
PLR	126 (88-180)	114 (95-180)	0.784
MLR	0.19 (0.13-0.27)	0.16 (0.12-0.20)	0.490
SII $\times 10^9$/L	766.5 (385.6-1272.3)	532.5 (279.7-1215.6)	0.730
SIRI$\times 10^9$/L	1072 (485-1785)	899 (421-2592)	0.719
Biochemical			
Albumin (g/dL)	1.80 (1.50-2.32)	2.00 (1.57-2.05)	0.632
Total protein (g/dL)	4.49 ± 0.97	4.75 ± 0.69	0.339
Total cholesterol (mg/dL)	352 ± 127	356 ± 93	0.919
Triglyceride (mg/dL)	179 (134-243)	168 (132-309)	0.510
LDL (mg/dL)	213 (166-307)	235 (139-342)	0.707
HDL (mg/dL)	65.8 (52.5-87.5)	79.5 (53.3-91.7)	0.769
VLDL (mg/dL)	38.00 (27.40-49.75)	33.7 (25.02-53.75)	0.559
Creatinine (mg/dL)	0.39 (0.28-0.51)	0.39 (0.35-0.51)	0.464

Data are presented as mean ± standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; MCV: mean corpuscular volume; RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammatory response index; SSNS: steroid-sensitive nephrotic syndrome; SRNS: steroid-resistant nephrotic syndrome

Table 5. Comparison of hematological, inflammatory, and biochemical parameters according to relapse frequency within the SSNS group

Variable	Frequent relapse (n=25)	Infrequent relapse (n=32)	p
Hemoglobin (g/dL)	13.5 (12.7-14.2)	13.0 (11.8-13.9)	0.167
WBC (mm^3)	10085 (7780-13012)	10100 (7838-13268)	0.947
Neutrophil (mm^3)	6000 (4330-8202)	4975 (3895-7722)	0.389
Lymphocyte (mm^3)	2630 (2272-3685)	3315 (2500-4772)	0.070
Platelet (mm^3)	449542 ± 137562	378719 ± 113637	**0.040**
MPV (fL)	8.41 ± 1.07	8.28 ± 1.14	0.674
RDW (%)	14.00 (13.70-14.38)	14.00 (13.17-15.12)	0.974
NLR	2.41 (1.19-3.98)	1.90 (0.93-2.44)	0.081
PLR	186 ± 106	117 ± 60	**0.003**
SII×10^9/L	1259.5 ± 868.6	1169.6 (423.5-1858.1)	**0.025**
SIRI×10^9/L	1345 (703-1861)	939 (468-1657)	0.271
MLR	0.20 (0.14-0.27)	0.17 (0.12-0.26)	0.436
MPV/Platelet (×10^3)	0.02 (0.02-0.02)	0.02 (0.02-0.03)	0.156
Albumin (g/dL)	1.88 ± 0.54	1.96 ± 0.59	0.631
Cholesterol (mg/dL)	391 ± 120	324 ± 125	0.051
24-hour protein (mg/day)	1180 (625-3056)	1049 (792-1930)	0.813

Data are presented as mean ± standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammatory response index; SSNS: steroid-sensitive nephrotic syndrome

CD8 ratio, CD19+ B lymphocytes, and natural killer (NK) cells, supporting the notion that the disease develops against a background of immune dysregulation (5, 14). For this reason, inflammation indices derived from peripheral blood cells have become a focus of interest in nephrotic syndrome. NLR, PLR, MLR, SII, and SIRI provide indirect information about the systemic inflammatory response. These indices do not require additional testing and are easily calculated from a complete blood count. Their low cost has led to their widespread use in research on various inflammatory diseases.

In our study, NLR, PLR, and SII were higher in the nephrotic syndrome group than in the control group. However, in the absence of CRP data and a case-control comparison of ESR, these indices cannot be interpreted as reflecting inflammation alone. They may represent overlapping processes, including inflammation, hemoconcentration, and hematological changes associated with hypoalbuminemia and hyperlipidemia. This finding is consistent with observations reporting increased leukocyte and neutrophil counts in children with nephrotic syndrome, as well as with studies suggesting that NLR and PLR may be associated with relapse or an adverse clinical course in steroid-responsive nephrotic syndrome (9,11). However, because no monocyte data were available for the control group, the MLR and SIRI indices could not be included in the case-control comparison. Therefore, these two indices were interpreted only within the context of subgroup analyses within the nephrotic syndrome group.

The platelet-related findings in our study are largely consistent with the literature. Previous clinical studies have consistently shown that platelet counts are elevated in children with nephrotic syndrome. This finding may be associated with platelet hyperactivity, an increased tendency toward aggregation, and increased activation dependent surface markers (4,6,8,15). This increase may be associated with multifactorial mechanisms, including plasma protein loss, hyperlipidemia, and hemoconcentration, that are observed in nephrotic syndrome. However, the causal relationship between platelet changes and thromboembolic events remains unclear (6).

Our findings regarding mean platelet volume reflect the heterogeneity in the literature. In our study, MPV was lower in the nephrotic syndrome group. While Gulleroğlu et al. (15) reported similarly low MPV during the active phase, Göknar et al. (4) found higher MPV in children with nephrotic syndrome than in the control group. The fact that MPV may increase or decrease in inflammatory conditions suggests that this parameter may be influenced by the type and stage

of the disease, as well as by platelet production dynamics (8). For this reason, it is difficult to explain the low MPV findings in our study by a single mechanism.

The marked differences in platelet count and MPV were also reflected in the ratios derived from these two parameters. In our study, the platelet-to-MPV ratio was higher in the nephrotic syndrome group. Nickavar et al. (10) reported higher platelet counts in children with steroid-resistant nephrotic syndrome and suggested that certain platelet indices may be associated with steroid resistance. In contrast, our study found no significant difference in platelet count or MPV between the SSNS and SRNS groups. This finding may be related, in particular, to the limited number of patients in the SRNS group. In our study, RDW was higher in the nephrotic syndrome group. It has been reported that RDW may have prognostic value in systemic inflammation and various clinical conditions (7,8). However, this increase in RDW should not be interpreted as a finding specific to nephrotic syndrome.

No significant differences were found between the steroid-sensitive and steroid-resistant subgroups of nephrotic syndrome in complete blood count parameters, platelet- and MPV related markers, and hematological inflammatory indices. This finding indicates that these parameters do not distinguish the steroid response phenotype in the current patient group. However, the literature has reported that platelet count and certain platelet indices may be associated with steroid resistance (4,10,11).

These differences may stem from variations in subgroup definitions, patient characteristics, and sample size. In our study the SRNS group comprising only 15 patients limits the statistical power of the subgroup comparisons. Therefore, the failure to detect a difference between the SSNS and SRNS groups should not be interpreted as indicating that hematological indices at the time of diagnosis are entirely inadequate for distinguishing the steroid-response phenotype.

In our study, platelet count, PLR, and SII were higher in patients with frequent relapses within the SSNS group. Although this pattern is consistent with previous studies (9,12), the limited subgroup size precludes considering it a confirmed association with relapse tendency. This preliminary observation should be explored in larger prospective studies.

Correlation analyses should be considered supporting findings rather than the study's main message. NLR, PLR, MLR, SII, SIRI, and MPV did not show significant correlations with albumin, 24-hour proteinuria, total cholesterol, or erythrocyte sedimentation rate. In contrast, platelet count was negatively correlated with albumin and positively correlated with total cholesterol. This finding suggests that an increase in platelet count may be associated with a nephrotic syndrome characterized by hypoalbuminemia and hyperlipidemia (15). However, due to the limited magnitude of the correlation coefficients and the possibility of multiple comparisons, these data are insufficient to draw definitive conclusions.

Among the strengths of the study are the focus on laboratory parameters at the time of diagnosis before treatment and the joint evaluation of numerous indices derived from the complete blood count within the same patient group. The separate analysis of platelet and MPV related indicators, combined with the examination of clinically meaningful subgroups such as steroid-sensitive/resistant and frequent/infrequent relapsers, lends the findings a stronger clinical context.

Study Limitations

The main limitations of the study are its retrospective, single-center design, limited sample size, and, in particular, the small number of patients in the SRNS group. The lack of monocyte data in the control group prevented the evaluation of MLR and SIRI in a case-control comparison. CRP data were unavailable, and ESR data were not available for the control group; therefore, these hematological indices could not be directly compared with conventional inflammatory markers in the case-control analysis. Certain platelet indices, such as PDW and plateletcrit, are also missing from the dataset. The significant age difference between the patient and control groups represents a potential confounding factor, particularly because hemoglobin, WBC, and RDW may vary with age, and this effect could not be fully controlled for because of the retrospective design. Additionally, complete blood count parameters can be influenced by infection, hydration status, time of sample collection, and technical factors. Because the study covered an eight-year period, possible changes in hematology analyzers, reagent lots, or laboratory reference ranges may have introduced measurement variability, particularly for instrument-dependent parameters such as MPV and RDW.

Conclusion

In conclusion, indices derived from a complete blood count may provide practical information about hematological changes in children with nephrotic syndrome, but they should not be interpreted as specific measures of

inflammation. Our findings indicate that platelet and MPV related indicators, in particular, showed differences in the patient-control comparison. However, these indices should not be evaluated as diagnostic or prognostic markers on their own; they should be interpreted alongside clinical findings and standard laboratory parameters.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Ethics Committee of Bursa Specialized Training and Research Hospital (approval number: 2011-KAEK-25-2020/10-04, date: 23.11.2011).

Footnotes

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

Financial Disclosure: The authors declared that this study received no financial support.

Supplementary Table 1: https://d2v96fxpocvxx.cloudfront.net/51ec7646-9122-48c7-a1d9-90e9cb16981b/content-images/c14e01df-6a4b-49cf-ae09-99e5223469c1.pdf

References

1. Floege J, Gibson KL, Vivarelli M, Liew A, Radhakrishnan J, Balk EM, et al. Executive summary of the KDIGO 2025 clinical practice guideline for the management of nephrotic syndrome in children. Kidney Int. 2025;107:806-8.
2. Trautmann A, Boyer O, Hodson E, Bagga A, Gipson DS, Samuel S, et al. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-sensitive nephrotic syndrome. Pediatr Nephrol. 2023;38:877-919.
3. Trautmann A, Vivarelli M, Samuel S, Gipson D, Sinha A, Schaefer F, et al. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome. Pediatr Nephrol. 2020;35:1529-61.
4. Göknar N, Küçükkoç M, Demir AD, Vehapoglu A, Öktem F. Çocukluk çagi nefrotik sendromunda ortalama trombosit hacminin önemi/ the ımportance of mean platelet volume in children with nephrotic syndrome. dicle Tip Dergisi. 2016;43:275.
5. Deng Y, Ou YY, Mo CJ, Huang L, Qin X, Li S. Peripheral blood lymphocyte subsets in children with nephrotic syndrome: a retrospective analysis. BMC Nephrol. 2023;24:7.
6. Eneman B, Levtchenko E, van den Heuvel B, Van Geet C, Freson K. Platelet abnormalities in nephrotic syndrome. Pediatr Nephrol. 2016;31:1267-79.
7. Sunkonkit K, Chai-Adisaksopha C, Natesirinilkul R, Phinyo P, Trongtrakul K. Admission red blood cell distribution width and mean platelet volume as predictors of mortality in the pediatric ıntensive care unit: a five-year single-center retrospective study. J Clin Med. 2025;14:3839.
8. Korniluk A, Koper-Lenkiewicz OM, Kaminska J, Kemona H, Dymicka-Piekarska V. Mean platelet volume (MPV): new perspectives for an old marker in the course and prognosis of inflammatory conditions. Mediators Inflamm. 2019;2019:9213074.
9. Maimaititusvn G, Jvnaiti N, Kulaixi M, Liu F. Predictive value of early neutrophil-to-lymphocyte ratio and C-reactive protein in pediatric steroid-sensitive nephrotic syndrome. Front Nephrol. 2025;5:1524231.
10. Nickavar A, Moharerpour SS, Abiry E. Predictive value of platelet indices in children with idiopathic nephrotic syndrome. Immunopathologia Persa. 2019;6:e04-e.
11. Döven SS, Kayacan H, Erdoğan S, Delibaş A. Nefrotik sendromlu hastalarda trombosit indekslerinin değerlendirilmesi. Mersin Üniversitesi Sağlık Bilimleri Dergisi.2020;13:200-7.
12. Yazilitas F, Kargin Cakici E, Karakaya D, Gungor T, Celikkaya E, Bulbul M. Evaluation of immature granulocyte percentage and count in pediatric nephrotic syndrome. Postgrad Med. 2024;136:36-43.
13. Chan EY, Boyer O. Childhood idiopathic nephrotic syndrome: recent advancements shaping future guidelines. Pediatr Nephrol. 2025;40:2431-42.
14. Printza N, Papachristou F, Tzimouli V, Taparkou A, Kanakoudi-Tsakalidou F. Peripheral CD19+ B cells are increased in children with active steroid-sensitive nephrotic syndrome. NDT Plus. 2009;2:435-6.
15. Gulleroglu K, Yazar B, Sakalli H, Ozdemir H, Baskin E. Clinical importance of mean platelet volume in children with nephrotic syndrome. Ren Fail. 2014;36:663-5.

ÖZGÜN ARAŞTIRMA ORIGINAL ARTICLE

Nöral Tüp Defekti Olan Yenidoğanlarda Tiroid Fonksiyon Testlerinin Değerlendirilmesi: Tek Merkez Deneyimi

Evaluation of Thyroid Function Tests in Newborns with Neural Tube Defects: A Single Center Experience

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Cite this article as: Bağcı O, Saltan Aydın S, Ören A, Akacı O, Yazıcı A, Tunç G, et al. Evaluation of thyroid function tests in newborns with neural tube defects: a single center experience. J Curr Pediatr. 2026;24(2):145-151

Öz

Giriş: Nöral tüp defektleri (NTD), yenidoğan döneminde multidisipliner yaklaşım gerektiren, ek konjenital anomaliler ve nörogelişimsel morbidite ile ilişkili önemli bir konjenital gelişim kusurudur. Bu çalışmada, yenidoğan yoğun bakım ünitemizde izlenen NTD tanılı olguların perinatal özelliklerinin ve tiroid fonksiyon testlerinin (TFT) değerlendirilmesi, NTD olan yenidoğanlarda hipotiroidi sıklığının belirlenmesi amaçlandı.

Gereç ve Yöntem: Bu tek merkezli retrospektif çalışmaya, Ocak 2019-Haziran 2024 tarihleri arasında üçüncü basamak yenidoğan yoğun bakım ünitesinde NTD tanısı ile izlenen hastalar dahil edilmiştir. Hastaların ilk bir yıl içindeki TFT değerlendirmeye alınmıştır. Demografik, klinik ve laboratuvar verilerine tıbbi kayıtlardan ulaşıldı.

Bulgular: Dışlama kriterleri ve eksik veriler sonrası toplam 49 olgu değerlendirildi. Olguların 30'u (%61,2) kız, 19'u (%38,8) erkekti. Ortalama gebelik haftası 37±3 hafta, ortalama doğum ağırlığı 2887±670 g, ortalama anne yaşı 27,5±6 yıl idi. Doğumların 43'ü (%87,8) sezaryen ile gerçekleşmişti. Otuz olgu (%61,2) term, 19 olgu (%38,8) prematüre doğmuştu. Nöral tüp defektleri lokalizasyonu en sık lomber ve lumbosakral bölgede saptandı. Hidrosefali en sık eşlik eden anomalilerden biri olup 27 olguda (%55,1) mevcuttu ve 20 olguya ventriküloperitoneal şant uygulandı. Olguların 25'inde tiroid fonksiyon testleri postnatal ilk hafta içinde çalışılmıştı. İlk hafta değerlendirilen olguların 5'inde (%20,0), tüm kohortun ise %10,2'sinde hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu saptandı. Hipotiroidi saptanan tüm olguların ilk hafta içinde opere edildiği ve tiroid fonksiyon testlerinin postoperatif dönemde çalışıldığı görüldü. Üç olguya levotiroksin tedavisi başlandı. İlk tiroid fonksiyon testi normal olan olgularda izlemde hipotiroidi gelişmedi.

Sonuç: Bu çalışmada NTD tanılı yenidoğanlarda hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu, toplum temelli konjenital hipotiroidi prevalansına göre daha yüksek oranda saptanmıştır. Tetkiklerin operasyon sonrası dönemde çalışılması hipotiroidinin postoperatif sürece ve povidon-iyot kullanımına bağlı olabileceğini düşündürürken takibinde hipotiroidisi devam eden hastalar, etiyolojiye yönelik farklı nedenlerin de olduğunu göstermektedir.

Anahtar kelimeler
Konjenital hipotiroidi, nöral tüp defekti, povidon-iyot, tiroid fonksiyon testi, yenidoğan

Keywords
Congenital hypothyroidism, neural tube defect, povidone-iodine, thyroid function test, neonate

Geliş Tarihi/Received : 08.07.2026
Kabul Tarihi/Accepted : 27.07.2026
Yayınlanma Tarihi/Published Date : 04.08.2026

DOI:10.4274/jcp.2026.66563

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Abstract

Introduction: Neural tube defects (NTDs) are major congenital malformations that require multidisciplinary management during the neonatal period and are associated with additional congenital anomalies and adverse neurodevelopmental outcomes. This study aimed to evaluate the perinatal characteristics and thyroid function tests (TFTs) of newborns with NTDs admitted to our neonatal intensive care unit (NICU) and to determine the frequency of hypothyroidism in this population.

Materials and Methods: This single-center retrospective study included neonates diagnosed with NTDs and admitted to a tertiary NICU between January 2019 and June 2024. TFT results obtained during the first year of life were evaluated. Demographic, clinical, and laboratory data were retrieved from the medical records.

Results: After exclusion of patients with missing data, 49 neonates were included. Of these, 30 (61.2%) were female and 19 (38.8%) were male. The mean gestational age was 37±3 weeks, mean birth weight was 2887±670 g, and mean maternal age was 27.5±6 years. Forty-three infants (87.8%) were delivered by cesarean section. Thirty (61.2%) were born at term and 19 (38.8%) were preterm. The most common NTD locations were the lumbar and lumbosacral regions. Hydrocephalus was the most frequent associated anomaly, affecting 27 infants (55.1%), and 20 underwent ventriculoperitoneal shunt placement. TFTs were performed within the first postnatal week in 25 infants. Among the infants evaluated during the first postnatal week, 5 (20.0%) had thyroid function test abnormalities consistent with hypothyroidism, corresponding to 10.2% of the entire cohort. All infants with hypothyroidism underwent surgery within the first week of life, and TFTs were obtained postoperatively. Levothyroxine treatment was initiated in three infants. None of the infants with normal initial TFTs developed hypothyroidism during follow-up.

Conclusion: In this study, TFT abnormalities consistent with hypothyroidism were more frequently observed in newborns with NTD than the reported population-based prevalence of congenital hypothyroidism. Because TFTs were obtained after surgery, postoperative factors, including povidone-iodine exposure, may have contributed to thyroid dysfunction. However, persistent hypothyroidism during follow-up in some patients suggests that additional etiological factors should also be considered.

Giriş

Nöral tüp defektleri (NTD), embriyonik gelişimin 3.-4. haftalarında nöral tüpün kapanmasındaki bozukluk sonucu ortaya çıkan, santral sinir sistemini ve vertebral kolonu etkileyen majör konjenital malformasyonlardır. NTD'ler, konjenital kalp defektlerinden sonra en sık görülen majör konjenital anomaliler arasında yer almaktadır (1). Dünya genelinde NTD prevalansının yaklaşık 1,53-2,3/1000 doğum olduğu bildirilmektedir (2). Türkiye'de ise ulusal ve bölgesel verilere göre prevalans yaklaşık 2,7-3/1000 doğum düzeyinde olup, bazı bölgelerde daha yüksek oranlar rapor edilmiştir (3,4).

Nöral tüpün kapanması embriyonik dönemde servikal bölgeden başlayarak kraniyal ve kaudal yönde ilerler. Kapanma sürecinin etkilendiği anatomik bölgeye bağlı olarak anensefali, ensefalosel, meningosel, miyelomeningosel ve spina bifida gibi farklı NTD çeşitleri ortaya çıkabilir. NTD'lerin etiyolojisi multifaktöriyeldir; genetik yatkınlık, folat metabolizması, maternal beslenme durumu ve çevresel faktörler birlikte rol oynar. Maternal folat eksikliği, gebelik öncesi diyabet, obezite, valproik asit başta olmak üzere antiepileptik ilaç kullanımı, pestisit ve radyasyon maruziyeti, sigara kullanımı, iç ortam hava kirliliği, ailede NTD öyküsü ve daha önce NTD'den etkilenmiş gebelik öyküsü, NTD gelişimiyle ilişkilendirilen başlıca risk faktörleri arasındadır (3). Perikonsepsiyonel dönemde folik asit desteğinin NTD riskini azalttığı gösterilmiş olup, bu nedenle gebelik planlayan tüm kadınlara günlük 400-800 µg folik asit takviyesi önerilmektedir (5).

Tiroid hormonları fetal ve neonatal dönemde beyin gelişimi, somatik büyüme, enerji metabolizması ve nörogelişim açısından kritik öneme sahiptir. Konjenital hipotiroidi erken tanı ve tedavi edilmediğinde kalıcı entelektüel yetersizlik ve motor gelişim bozukluklarına yol açabilir. Güncel kılavuzlar, tüm yenidoğanlarda konjenital hipotiroidi taramasının yapılmasını; tarama pozitifliği veya klinik şüphe varlığında serum TSH ve serbest T4 düzeyleriyle tanının doğrulanmasını ve tedavi gerektiren olgularda levotiroksin tedavisine en kısa sürede başlanmasını önermektedir (6,7).

Yenidoğan döneminde tiroid fonksiyon testleri postnatal yaş, gebelik haftası, prematürite, kritik hastalık, cerrahi stres, ilaç maruziyeti ve iyot dengesi gibi birçok faktörden etkilenmektedir (6). Bununla birlikte NTD tanılı yenidoğanlarda tiroid fonksiyon testlerinin değerlendirildiği çalışmalar sınırlıdır. Bu çalışmada, üçüncü basamak yenidoğan yoğun bakım ünitesinde NTD tanısı ile izlenen olguların demografik ve klinik özelliklerinin değerlendirilmesi, tiroid fonksiyon testlerinin incelenmesi ve hipotiroidi sıklığının belirlenmesi amaçlanmıştır.

Gereç ve Yöntem

Bu gözlemsel, tek merkezli, retrospektif çalışmada, üçüncü basamak bir yenidoğan yoğun bakım ünitesinde Ocak

2019-Haziran 2024 tarihleri arasında nöral tüp defekti (NTD) tanısı ile izlenen yenidoğanların dosya kayıtları incelendi.

Çalışmaya, yenidoğan döneminde NTD tanısı ile yatırılan ve yaşamının ilk yılı içinde tiroid fonksiyon testi çalışılmış olan hastalar dahil edildi. Tiroid fonksiyon testlerine veya klinik verilerine ulaşılamayan olgular çalışma dışı bırakıldı.

Hastaların cinsiyet, anne yaşı, gebelik haftası, doğum ağırlığı, doğum şekli, NTD lokalizasyonu, hidrosefali varlığı, ventriküloperitoneal şant gereksinimi, operasyon günü, hastanede yatış süresi, tiroid fonksiyon testlerinin zamanı, TSH ve serbest T4 (sT4) değerleri, hipotiroidi varlığı, levotiroksin tedavisi kaydedildi.

Gebelik haftası 37 haftanın altında olan olgular prematüre, 37 hafta ve üzerinde olan olgular term olarak kabul edildi. Nöral tüp defektleri lokalizasyonu servikal, torakolomber, lomber, lumbosakral, sakral, sakrokoksigeal olarak sınıflandırıldı.

Serum TSH ve serbest T4 (sT4) düzeyleri, Roche Cobas c801 analizörü (Roche Diagnostics, Mannheim, Germany) kullanılarak Elecsys® elektro-kemilüminesans immünoassay (ECLIA) yöntemi ile ölçüldü. Postnatal yaşa özgü referans aralıkları esas alındı. Buna göre 1-6 gün için TSH; 0,7–15,2 mIU/L, sT4; 0,86–2,49 ng/dL, 7-90 gün için TSH; 0,42–6,32 mIU/L, sT4; 1,21–2,29 ng/dL, 3-12 ay için TSH; 0,73-8,35 mIU/L ve sT4; 0,92-1,99 ng/dL referans aralıkları kullanıldı. Postnatal yaşa uygun referans aralıklarına göre yüksek TSH ve/veya düşük sT4 varlığı hipotiroidi ile uyumlu TFT bozukluğu olarak değerlendirildi. Levotiroksin tedavisi başlanan olgular tedavi gerektiren hipotiroidi olarak ayrıca kaydedildi. Hastalar TFT bozukluğu saptanan ve saptanmayan olgular olarak iki gruba ayrılarak karşılaştırıldı.

Bu çalışma için etik kurul onayı, Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'ndan alındı (karar no: 2024-TBEK-2024/08-05, tarih: 28.08.2024).

İstatistiksel Analiz

İstatistiksel analiz SPSS programı kullanılarak yapılmıştır. Sürekli değişkenlerin normal dağılıma uygunluğu Kolmogorov-Smirnov ve Shapiro-Wilk testleri ile değerlendirilmiştir. Normal dağılım gösteren değişkenler ortalama±standart sapma, normal dağılım göstermeyen değişkenler medyan ve uygun aralık değerleri ile ifade edilmiştir. Kategorik değişkenler sayı ve yüzde olarak verilmiştir. Gruplar arası karşılaştırmalarda normal dağılım gösteren sürekli değişkenler için bağımsız örneklem t-testi, normal dağılım göstermeyen değişkenler için Mann-Whitney U testi kullanılmıştır. Kategorik değişkenlerin karşılaştırılmasında ki-kare testi veya beklenen hücre sayısının düşük olduğu durumlarda Fisher exact test kullanılmıştır. Tüm istatistiksel analizlerde iki yönlü testler kullanıldı ve $p<0,05$ değeri istatistiksel olarak anlamlı kabul edildi. Hipotiroidi saptanan hasta sayısının az olması nedeniyle Hipotiroidi saptanan olgu sayısının az olması nedeniyle grup karşılaştırmaları keşifsel (exploratory) nitelikte değerlendirilmiş olup, çok değişkenli lojistik regresyon analizi yapılmamıştır.

Bulgular

Çalışma döneminde YDYBÜ'mizde NTD ile toplam 68 hasta izlendi. Dışlama kriterleri sonrasında 49 hastanın verileri değerlendirildi. Olguların 30'u (%61,2) kız, 19'u (%38,8) erkekti. Ortalama anne yaşı 27,56±6,10 yıl, ortalama gebelik haftası 37±3 hafta ve ortalama doğum ağırlığı 2887±670 g idi. Olguların 43'ü (%87,7) sezaryen, 6'sı (%12,3) normal spontan vajinal yol ile doğmuştu. Otuz olgu (%61,2) term, 19 olgu (%38,8) prematüreydi. On altı olgu (%32,7) postnatal ilk 3 gün içinde, 33 olgu (%67,3) ise sonraki günlerde opere edildi. Ortalama hastanede yatış süresi 13±12 gün olarak saptandı. Olguların demografik ve perinatal özellikleri Tablo 1 'de gösterilmiştir.

Nöral tüp defektlerinin lokalizasyonu değerlendirildiğinde, olguların en sık lumbosakral (%34,7; n=17), lomber (%30,6; n=15) ve torakolomber (%26,5; n=13) bölgelerde yerleştiği saptandı. Daha nadir olarak iki olguda (%4) servikal, birer olguda ise (%2) sakral ve sakrokoksigeal yerleşim mevcuttu. Eşlik eden klinik bulgular incelendiğinde, olguların %55,1'inde (n=27) hidrosefali bulunduğu, %40,8'ine (n=20) ise ventriküloperitoneal şant uygulandığı belirlendi (Tablo 2).

Tiroid fonksiyon testleri değerlendirildiğinde, olguların 25'inde (%51,0) tiroid fonksiyon testleri postnatal ilk hafta içinde çalışılmıştı. İlk hafta değerlendirilen olguların 5'inde (%20,0), tüm kohortun ise %10,2'sinde hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu saptandı. Bu olguların

Tablo 1. Olguların demografik ve perinatal özellikleri

Toplam olgu sayısı	**49**
Cinsiyet, kız n (%)	30 (61,2)
Anne yaşı, yıl (ortalama ± SD)	27,56 ± 6,10
Gebelik yaşı, hafta (ortalama ± SD)	37 ± 3
Doğum ağırlığı, g (ortalama ± SD)	2887 ± 670
Sezaryen doğum n (%)	43 (87,7)
Prematüre doğum n (%)	19 (38,8)
İlk 3 gün opere edilen olgu n (%)	16 (%32,7)
Hastanede yatış süresi, gün (ortalama ± SD)	13± 12

SS: Standart sapma

%6,2'sine (n=3) levotiroksin tedavisi başlandı. Ayrıca, olguların %26,5'inde (n=13) yaşamın ilk ayı içerisinde tiroid fonksiyon testi değerlendirmesinin yapılmadığı belirlendi (Tablo 3).

Tiroid fonksiyon testi bozukluğu saptanan ve saptanmayan olgular karşılaştırıldığında, cinsiyet dağılımı açısından gruplar arasında istatistiksel olarak anlamlı bir fark saptanmadı (p=0,142). Benzer şekilde, anne yaşı (p=0,951), gebelik haftası (p=0,855) ve doğum ağırlığı (p=0,339) bakımından da hipotiroidi olan ve olmayan olgular arasında istatistiksel olarak anlamlı farklılık izlenmedi (Tablo 4).

Tiroid fonksiyon testi bozukluğu saptanan beş olgunun tümü kız cinsiyetindeydi. Gebelik haftaları 34+2 ile 38+6 hafta, doğum ağırlıkları ise 1850-3420 g arasında değişmekteydi. Nöral tüp defekti lokalizasyonu iki olguda torakolomber, iki olguda lomber ve bir olguda lumbosakral düzeydeydi. Üç olguda hidrosefali bulunurken, bu olguların tamamına ventrikülоperitoneal şant uygulanmıştı. Operasyonlar yaşamın 1-3. günleri arasında gerçekleştirilmiş, tiroid fonksiyon testleri ise postnatal 6-8. günlerde değerlendirilmişti. İlk değerlendirmede TSH düzeyleri 18,1-60,9 mIU/L, serbest T4 (sT4) düzeyleri ise 0,54-0,89 ng/dL arasında saptandı. Beş olgunun üçünde levotiroksin tedavisi başlandı, iki olgu ise tedavisiz izleme alındı. Birinci ay kontrolünde tedavi başlanmayan iki olgunun TSH düzeylerinin normal sınırlara gerilediği (1,08 ve 0,42 mIU/L) ve sT4 düzeylerinin normal olduğu görüldü. Buna karşın levotiroksin tedavisi başlanan üç olgudan ikisinde birinci ayda TSH düzeyleri sırasıyla >100 mIU/L ve 70,8 mIU/L olarak yüksek seyretmeye devam ederken, sT4 düzeyleri düşük (<0,40 ng/dL ve 0,46 ng/dL) bulundu. Diğer tedavi alan olguda ise TSH düzeyi 0,29 mIU/L'ye gerilemiş ve sT4 düzeyi 1,90 ng/dL olarak normal aralıkta saptanmıştır (Tablo 5).

Tablo 2. Nöral tüp defekti lokalizasyonu ve eşlik eden klinik özellikler

NTD lokalizasyonu	n (%)
Lomber	15 (30,6)
Lumbosakral	17 (34,7)
Torakolomber	13 (26,5)
Servikal	2 (4)
Sakral	1 (2)
Sakrokoksigeal	1 (2)
Eşlik eden klinik bulgular	
Hidrosefali var	27 (55,1)
Şant uygulanan	20 (40,8)

NTD: Nöral tüp defekti

Tablo 3. Tiroid fonksiyon testi bozukluğu ve tedavi gereksinimi

	n (%)
İlk hafta TFT değerlendirilen	25 (51,0)
İlk hafta TFT bozukluğu saptanan	5 (20)
Tüm kohortta TFT bozukluğu saptanan	5 (10,2)
Levotiroksin tedavisi başlanan	3 (6,1)
İlk 1 ay içinde tiroid fonksiyon testi bakılmayan	13 (26,5)

TFT: Tiroid fonksiyon testi

Tartışma

Çalışmamızda 49 olgunun %10,2'sinde, postnatal ilk hafta içinde değerlendirilen olguların ise %20'sinde hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu saptanmış ve %6,1'ine levotiroksin tedavisi başlanmıştır. Konjenital hipotiroidi, yenidoğan döneminin en sık görülen endokrin hastalıklarından biridir. Dünya genelinde yaklaşık 1/3000-1/4000 canlı doğumda bildirilirken, güncel tarama programlarında TSH eşiklerinin düşürülmesi ve hafif biyokimyasal formların da saptanabilmesiyle bazı popülasyonlarda bildirilen sıklık 1/2000-1/3000 canlı doğuma kadar yükselmiştir (6-7). Türkiye'de ise ulusal yenidoğan tarama programının 2008-2010 verilerine göre konjenital hipotiroidi sıklığı yaklaşık 1/650 olarak bulunmuş ve dünya ortalamasına göre daha yüksek olduğu bildirilmiştir (8). Çalışmamızda saptanan hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu oranları hem dünya hem de ülkemizden bildirilen toplum temelli konjenital hipotiroidi sıklıklarına kıyasla yüksek bulunmuştur.

Tablo 4. TFT bozukluğu olan ve olmayan olguların karşılaştırılması

Değişken	TFT bozukluğu yok (n=44)	TFT bozukluğu var (n=5)	p değeri
Kız Cinsiyet n (%)	25 (57)	5 (100)	0,142[a]
Anne yaşı, yıl ortalam ±SS	27,58 ± 6,17	27,40 ± 6,19	0,951[b]
Gebelik haftası ortanca min-max	38 (36-39)	37 (35-38)	0,855[c]
Doğum ağırlığı, g ortalam ±SS	2919,19 ± 673,74	2613,00 ± 640,58	0,339[b]

a: Fisher's exact test, b: Bağımsız örneklem t testi, c: Mann–Whitney U testi, TFT: Tiroid fonksiyon testi

Tablo 5. TFT bozukluğu saptanan olguların ayrıntılı klinik özellikleri

Olgu	Cinsiyet	GH	DA, g	NTD lokalizasyonu	Hidrosefali	Şant	Operasyon günü	Tetkik günü	TSH	sT4	Levotiroksin	1. ay TSH	1. ay sT4
1	K	38+6	3420	Torakolomber	Var	Var	2	7	41,2	0,89	Hayır	1,08	1,16
2	K	35+5	2110	Lumbosakral	Yok	Yok	2	6	18,9	0,70	Evet	>100	<0,40
3	K	38	2685	Lomber	Var	Var	1	7	19,3	0,89	Hayır	0,42	1,34
4	K	34+2	1850	Torakolomber	Var	Var	3	8	60,9	0,69	Evet	0,29	1,90
5	K	38	3000	Lomber	Yok	Yok	3	7	18,1	0,54	Evet	70,8	0,46

GH: Gebelik haftası, **DA:** Doğum ağırlığı, **NTD:** Nöral tüp defekti, **TFT:** Tiroid fonksiyon testleri, **TSH:** Tiroid stimülan hormon, **sT4:** Serbest tiroksin

Nöral tüp defekti tanılı yenidoğanlarda hipotiroidi sıklığını bildiren sınırlı sayıda çalışma olmakla birlikte, mevcut veriler bulgularımızı desteklemektedir. Yorulmaz ve Konak, Konya bölgesinde izlenen 186 NTD tanılı yenidoğanı değerlendirdikleri çalışmalarında 14 olguda konjenital hipotiroidi saptamış ve NTD'li hastalarda konjenital hipotiroidi sıklığını %7,5 olarak bildirmiştir (9). Nöral tüp defektleri spektrumunda yer alan frontoetmoidal ensefalomeningosel hastalarında yapılan başka bir çalışmada da tiroid fonksiyon testi çalışılan 37 hastanın 3'ünde santral hipotiroidi ile uyumlu bulgular saptanmış, diabetes insipidus ve büyüme hormonu eksikliği gibi diğer hipotalamo-hipofizer bozukluklar da bildirilmiştir (10). Benzer şekilde Perrone ve ark. (11), meningomyelosel tanılı 56 çocukta hipofiz, tiroid, adrenal ve gonadal fonksiyonları değerlendirmiştir. Çalışmada 6 olguda normal sT4 düzeyleri ile hafif TSH yüksekliği saptanmış, bazı olgularda TRH uyarısına TSH yanıtının abartılı, uzamış veya gecikmiş olduğu bildirilmiştir. Ayrıca santral puberte prekoks, hiperprolaktinemi ve gonadotropin yanıtlarında bozukluk gibi hipotalamo-hipofizer aksın etkilenimini düşündüren bulgular da gösterilmiştir (11). Bu bulgular, çalışmamızda NTD tanılı yenidoğanlarda saptanan tiroid fonksiyon testi bozukluklarının, daha geniş bir endokrin etkilenimin parçası olabileceğini düşündürmektedir.

Nöral tüp defektleri ile tiroid fonksiyonları arasındaki ilişkiyi açıklayabilecek mekanizmalar tam olarak bilinmemektedir. Sak ve ark. (12), NTD tanılı fetusların amniyotik sıvılarında serbest T4 düzeyinin kontrol grubuna göre anlamlı olarak daha düşük, total oksidan durum ve paraoksonaz-1 aktivitesinin ise daha yüksek olduğunu bildirmiştir. Bu bulgu, NTD'li olgularda tiroid hormon metabolizması, oksidatif stres ve intrauterin çevresel faktörler arasında olası bir ilişki olabileceğini düşündürmektedir. Bizim çalışmamız intrauterin mekanizmaları doğrudan değerlendirmemektedir. Ancak postnatal dönemde saptanan TFT bozukluklarının yalnızca cerrahi sonrası iyot maruziyetiyle açıklanamayabileceğini, bazı olgularda altta yatan farklı biyolojik mekanizmaların da rol oynayabileceğini düşündürmektedir.

Konjenital hipotiroidili olgularda ek konjenital anomalilerin beklenenden daha sık görülebildiği bildirilmiştir (13). Bu birlikteliğin ortak embriyolojik gelişim süreçleri, genetik yatkınlık ve intrauterin çevresel faktörlerle ilişkili olabileceği düşünülmektedir. Çalışmamız bu mekanizmaları doğrudan değerlendirmemekle birlikte, NTD gibi majör konjenital anomalisi olan yenidoğanlarda tiroid fonksiyonları testlerinin gözden kaçırılmaması gerektiğini desteklemektedir. Özellikle nörogelişimsel morbidite riski yüksek olan bu hasta grubunda, eşlik eden hipotiroidinin erken tanınması klinik açıdan önem taşımaktadır.

Çalışmamızda TFT bozukluğu saptanan tüm olgular yaşamın ilk üç günü içinde opere edilmişti ve testler postoperatif dönemde çalışılmıştı. Yenidoğanlarda, özellikle prematüre ve hasta bebeklerde, iyot içeren topikal antiseptiklerin cilt yoluyla emilimi geçici veya kalıcı tiroid fonksiyon bozukluğuna yol açabilmektedir (14-15). Nöral tüp defektleri tanılı yenidoğanların önemli bir kısmı yaşamın ilk günlerinde cerrahi girişim geçirmekte ve bu süreçte povidon-iyot gibi iyot içeren antiseptiklere maruz kalabilmektedir. Bu nedenle postoperatif dönemde TSH ve sT4 düzeylerinin izlenmesi klinik açıdan önemlidir. Çalışmamızdaki bulgular, saptanan TFT bozukluklarının tümünün kalıcı konjenital hipotiroidi olarak değerlendirilmemesi gerektiğini de göstermektedir. Levotiroksin başlanmayan iki olguda birinci ay kontrolünde tiroid fonksiyon testlerinin normale dönmesi, bazı olgularda geçici postoperatif veya iyot ilişkili tiroid fonksiyon bozukluğu gelişmiş olabileceğini düşündürmektedir. Bu nedenle NTD'li yenidoğanlarda anormal TFT saptandığında, tek bir ölçümle kalıcı hipotiroidi tanısı koymak yerine postnatal yaş, klinik durum, operasyon öyküsü, olası iyot maruziyeti ve izlem testleri birlikte değerlendirilmelidir.

Konjenital hipotiroidi ile ilişkili perinatal faktörler literatürde farklı çalışmalarda değerlendirilmiştir. Zhou ve ark. (16), konjenital hipotiroidili olgularda perinatal risk

faktörlerini inceledikleri çalışmalarında düşük doğum ağırlığı ve preterm doğumun özellikle geçici konjenital hipotiroidi için risk faktörü olduğunu, ek doğumsal anomalilerin ise kalıcı konjenital hipotiroidi ile daha yakın ilişkili olduğunu bildirmiştir. Jo ve ark. (17) ise konjenital hipotiroidi insidansını gebelik haftası, doğum ağırlığı ve gestasyon haftasına göre doğum ağırlığı açısından değerlendirmiş, prematüre ve düşük doğum ağırlıklı bebeklerde tiroid fonksiyon bozukluklarının daha sık görülebileceğini vurgulamıştır. Waller ve ark.'nın (18) Kaliforniya yenidoğan tarama verilerine dayanan çalışmasında ise doğum ağırlığının, etnik köken ve cinsiyetin konjenital hipotiroidi riskiyle ilişkili olabileceği gösterilmiştir. Ayrıca bazı epidemiyolojik çalışmalarda ileri anne yaşı ve kız cinsiyetin konjenital hipotiroidi ile ilişkili olabileceği bildirilmiştir (19).

Çalışmamızda hipotiroidi ile uyumlu TFT bozukluğu saptanan ve saptanmayan olgular karşılaştırıldığında anne yaşı, gebelik haftası ve doğum ağırlığı açısından istatistiksel olarak anlamlı fark saptanmadı. TFT bozukluğu saptanan olguların tamamının cinsiyeti kızdı ancak bu fark istatistiksel olarak anlamlı bulunmadı. Çalışmamızda anlamlı fark saptanmaması, NTD'li yenidoğanlarda hipotiroidi açısından bu faktörlerin etkisiz olduğunu göstermekten çok, örneklem büyüklüğünün ve TFT bozukluğu saptanan olgu sayısının az sayıda olması ile açıklanabilir.

Ülkemizde NTD sıklığının halen dünya ortalamasına kıyasla yüksek seyretmesi, çalışmamızın klinik önemini artırmaktadır. Bu durumun nedenleri arasında perikonsepsiyonel folik asit kullanımının yetersizliği, gebeliklerin önemli bir kısmının plansız gerçekleşmesi, zorunlu folik asit fortifikasyon programlarının yaygın olmaması, bölgesel ve sosyoekonomik farklılıklar, maternal eğitim düzeyi ve genetik/çevresel yatkınlıklar yer almaktadır (4,5,9). NTD'li yenidoğanlarda hidrosefali, şant gereksinimi, motor defisit, nörojen mesane, ortopedik sorunlar, üriner sistem komplikasyonları ve uzun dönem rehabilitasyon gereksinimi klinik süreci zorlaştırmaktadır (9,20). Bu bebekler nörogelişimsel açıdan riskli bir grup olduğundan, eşlik eden hipotiroidinin gözden kaçması mevcut morbiditeye önlenebilir ek katkıda bulunabilir. Bu nedenle NTD tanılı yenidoğanlarda, özellikle erken cerrahi geçiren ve iyot içeren antiseptiklere maruz kalma olasılığı bulunan olgularda, postoperatif dönemde TSH ve sT4 düzeylerinin takip edilmesi önemlidir.

Çalışmanın Kısıtlılıkları

Çalışmamızın başlıca kısıtlılıkları retrospektif ve tek merkezli tasarımlı olmasıdır. Eş zamanlı sağlıklı veya cerrahi girişim geçirmeyen kontrol grubu bulunmadığından, toplum prevalansı ile yapılan karşılaştırma dolaylıdır. İyot içeren antiseptik maruziyetinin miktarı ve süresi tüm olgularda ayrıntılı olarak değerlendirilememiştir. Maternal tiroid hastalığı, maternal iyot durumu, ilaç kullanımı ve yenidoğanın aldığı diğer tedaviler gibi tiroid fonksiyonlarını etkileyebilecek değişkenlere retrospektif olarak eksiksiz ulaşılamamıştır. Ayrıca hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu saptanan olgu sayısının yalnızca beş olması nedeniyle grup karşılaştırmaları keşifsel (exploratory) nitelikte olup Tip II hata olasılığı yüksektir. Bu nedenle elde edilen sonuçlar dikkatli yorumlanmalıdır.

Sonuç

Nöral tüp defekti tanılı yenidoğanlarda özellikle erken postoperatif dönemde tiroid fonksiyon testlerinde bozukluklar görülebilmektedir. Çalışmamızda yaşamın ilk haftasında saptanan hipotiroidi ile uyumlu tiroid fonksiyon testi bozukluğu oranı, toplum temelli konjenital hipotiroidi prevalansından yüksek bulunmuş ve Türkiye'den bildirilen NTD serilerindeki hipotiroidi sıklığı ile benzerlik göstermiştir. Bununla birlikte, bu bulgunun gerçek bir risk artışını mı yoksa cerrahi süreç ve iyot maruziyetine bağlı geçici tiroid fonksiyon bozukluklarını mı yansıttığının ortaya konulabilmesi için prospektif, kontrollü ve daha geniş örneklemli çalışmalara gereksinim vardır. Nöral tüp defektli yenidoğanların nörogelişimsel açıdan yüksek riskli bir grup olması nedeniyle, tiroid fonksiyonlarının düzenli olarak izlenmesi; hipotiroidinin erken tanınması, uygun tedavinin zamanında başlanması ve önlenebilir nörogelişimsel olumsuzlukların azaltılması açısından önem taşımaktadır.

Etik

Etik Kurul Onayı: Bu çalışma için etik kurul onayı, Sağlık Bilimleri Üniversitesi, Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'ndan alındı (karar no: 2024-TBEK-2024/08-05, tarih: 28.08.2024).

Dipnot

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar tarafından finansal destek almadıkları bildirilmiştir.

Kaynaklar

1. Practice Bulletin No. 187: Neural tube defects. Obstet Gynecol. 2017;130: e279-90.
2. Blencowe H, Kancherla V, Moorthie S, Darlison MW, Modell B. Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis. Ann N Y Acad Sci. 2018;1414:31-46.

3. Çaylan N, Yalçin SS, Tezel B, Aydin Ş, Üner O, Kara F. Evaluation of neural tube defects from 2014 to 2019 in Turkey. BMC Pregnancy Childbirth. 2022;22:340.
4. Tunçbilek E, Boduroğlu K, Alikaşifoğlu M. Neural tube defects in Turkey: prevalence, distribution and risk factors. Turk J Pediatr. 1999;41:299-305.
5. Kancherla V. Neural tube defects: a review of global prevalence, causes, and primary prevention. Childs Nerv Syst. 2023;39:1703-10.
6. Van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L et al. Congenital hypothyroidism: a 2020-2021 consensus guidelines update-an ENDO-European Reference Network Initiative Endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. Thyroid. 2021;31:387-419.
7. Rose SR, Wassner AJ, Wintergerst KA, Yayah-Jones NH, Hopkin RJ, Chuang J et al. Congenital hypothyroidism: screening and management. Pediatrics. 2023;151: e2022060419.
8. Dilli D, Çzbaş S, Acıcan D, Yamak N, Ertek M, Dilmen U. Establishment and development of a national newborn screening programme for congenital hypothyroidism in Turkey. J Clin Res Pediatr Endocrinol. 2013;5:73-9.
9. Yorulmaz A, Konak M. Short-term results of patients with neural tube defects followed-up in the Konya region, Turkey. Birth Defects Res. 2019;111:261-9.
10. Wacharasindhu S, Asawutmangkul U, Srivuthana S. Endocrine abnormalities in patients with frontoethmoidal encephalomeningocele. A preliminary study. Horm Res. 2005;64:64-7.
11. Perrone L, Del Gaizo D, D'Angelo E, Rea L, Di Manso G, Del Gado R. Endocrine studies in children with myelomeningocele. J Pediatr Endocrinol. 1994;7:219-23.
12. Sak S, Agacayak E, Tunc SY, Icen MS, Findik FM, Sak ME et al. Amniotic fluid paraoxonase-1 activity, thyroid hormone concentration and oxidant status in neural tube defects. J Obstet Gynaecol Res. 2016;42:1080-5.
13. Reddy PA, Rajagopal G, Harinarayan CV, Vanaja V, Rajasekhar D, Suresh V et al. High prevalence of associated birth defects in congenital hypothyroidism. Int J Pediatr Endocrinol.2010;2010:940980.
14. Aitken J, Williams FL. A systematic review of thyroid dysfunction in preterm neonates exposed to topical iodine. Arch Dis Child Fetal Neonatal Ed. 2014;99:F21-8.
15. Smerdely P, Lim A, Boyages SC, Waite K, Wu D, Roberts V et al. Topical iodine-containing antiseptics and neonatal hypothyroidism in very-low-birthweight infants. Lancet. 1989;2:661-4.
16. Zhou J, Luo J, Lin J, Zeng Y, Qiu X, Zhu W et al. Perinatal risk factors for congenital hypothyroidism: a retrospective cohort study performed at a tertiary hospital in China. Medicine (Baltimore). 2020;99:e20838.
17. Jo HY, Yang EH, Kim YM, Choi SH, Park KH, Yoo HW et al. Incidence of congenital hypothyroidism by gestational age: a retrospective observational study. J Yeungnam Med Sci. 2023;40:30-6.
18. Waller DK, Anderson JL, Lorey F, Cunningham GC. Risk factors for congenital hypothyroidism: an investigation of infant's birth weight, ethnicity, and gender in California, 1990-1998. Teratology. 2000;62:36-41.
19. Kirmızibekmez H, Güven A, Yildiz M, Cebeci AN, Dursun F. Developmental defects of the thyroid gland: relationship with advanced maternal age. J Clin Res Pediatr Endocrinol. 2012;4:72-5.
20. Çakır SÇ, Dorum BA, Özkan H, Taşkapılıoğlu Ö, Köksal N, Tütüncü Toker R ve ark. Nöral tüp defektli yenidoğanların kısa dönem sonuçları. Güncel Pediatri. 2018;16:117-26.

ERRATUM

J Curr Pediatr. 2025;23(3):172-180

DOI: 10.4274/jcp.2026.e001

DOI: 10.4274/jcp.2025.90958

Tuhan H, Singin B, Donbaloğlu Z, Özdem S, Parlak M. Can asprosin be used as a diagnostic biomarker for non-alcoholic fatty liver disease in obese children? J Curr Pediatr. 2025;23(3):172-180

The errors were made inadvertently by the authors.

The funding information was inadvertently omitted from the final published version of the article.
The funding statement was included in the initially submitted manuscript but was removed from the blinded version during the double-blind peer-review process. However, it was inadvertently not reinserted into the final version of the manuscript.

The Financial Disclosure statement was published as follows:

The authors declared that this study received no financial support.

The Financial Disclosure statement should be corrected as follows:

This research was funded by the Scientific Research Projects Coordination Unit of Akdeniz University (project no. TSA-2023-6059).