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Physician in Chief
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Ankara Bilkent City Hospital, Children's Hospital, Türkiye
Telephone: +90 (312) 552 60 00 / 401506
editorial@turkjpediatrdis.org

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FABRİKA MATBAACILIK
Tic. Sic. No: 393545, Mersis No: 0384 0359 0820 0013
İvedik O.S.B. Mah. 1372 Sk. No: 23 Yenimahalle / *Ankara*, Türkiye
info@fabrikabaskida.com, www.fabrikabaskida.com
Tel: +90 (312) 397 38 78 - Fax: +90 (312) 397 56 31

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Original Articles

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Correlation between mid-upper arm circumference and quality of life: A study in children with cerebral palsy

Beril Dilber, Tülay Kamaşak

Department of Pediatric Neurology, Karadeniz Technical University, Trabzon, Türkiye

ABSTRACT

Objective: This study aimed to evaluate the relationship between mid-upper arm circumference (MUAC) and quality of life in children with cerebral palsy (CP).

Material and Methods: A total of 99 children aged 2–18 years with a diagnosis of CP were included in the study. Nutritional status and quality of life were assessed using anthropometric measurements and the Pediatric Quality of Life Inventory (PedsQL 3.0 CP Module).

Results: This study revealed that mid-upper arm circumference (MUAC) is a reliable indicator not only of nutritional status but also of quality of life in children with cerebral palsy. Anthropometric parameters such as height, weight, MUAC, thigh circumference, and arm length were significantly lower in children with feeding difficulties ($p<0.001$). MUAC was strongly and positively correlated with total PedsQL scores ($r=0.988$, $p<0.001$), indicating a robust association between nutritional status and perceived quality of life. Additionally, as GMFCS level increased, indicating more severe motor impairment, both growth metrics and quality of life scores declined.

Conclusion: MUAC measurement reflects both malnutrition and quality of life in children with CP. Routine clinical use of this parameter in follow-up is recommended.

Keywords: Anthropometry, cerebral palsy, quality of life

INTRODUCTION

Cerebral palsy (CP) is one of the most common causes of physical disability in childhood and is characterized by motor dysfunctions, impaired postural control, abnormal muscle tone, and restricted movement capacity (1). Children with CP frequently experience limitations in physical activity, disrupted body composition, and various nutritional problems. Globally, the prevalence of CP is approximately 2.5 per 1000 live births, and this rate has been reported to increase with advances in neonatal intensive care services and improved survival of very low birth weight (VLBW) infants (2).

Feeding problems in CP arise from multiple factors such as limitations in motor development, tone abnormalities, coordination disorders, loss of proprioceptive sensation, absence of swallowing reflex, and dysfunction of the oral, lingual, and mandibular muscles (3-5). Inadequate trunk control and improper positioning during feeding further exacerbate these issues, potentially leading to prolonged feeding durations, aspiration, poor saliva control, coughing, choking episodes, and disruptions in parent-child interaction (3,5,6).

As a result of these challenges, nutritional difficulties negatively affect growth and development and significantly reduce the quality of life for both the child and the family (4,7). The literature indicates that conditions such as malnutrition, growth retardation, and obesity are more frequently observed in children with neurological problems (NP) compared to healthy children (6-8). Therefore, it is of critical importance to monitor

Correspondence Address:
Beril DİLBER
e-mail: beriltem@gmail.com

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the nutritional status of this patient group in a regular and practical manner.

One of the widely used clinical methods is mid-upper arm circumference (MUAC) measurement, which is a reliable and practical anthropometric parameter for detecting malnutrition (9). Particularly in children aged 6 months to 5 years, MUAC values of <11 cm indicate severe malnutrition, 11–12.5 cm indicate moderate malnutrition, and >12.5 cm are considered normal. Its use of a single fixed cutoff value makes MUAC advantageous for rapid screening and follow-up (9).

Moreover, current health approaches emphasize the necessity of evaluating not only physical symptoms but also the overall quality of life in children. The Pediatric Quality of Life Inventory (PedsQL) is a multidimensional and culturally adapted instrument developed to assess quality of life in children aged 2–18 years (10). PedsQL covers physical, emotional, social, and school functioning domains and can be completed by both the child and the parent. In neurodevelopmental disorders such as CP, children's quality of life is affected multidimensionally, including motor skills, social interaction, and academic performance (11).

The Türkiye version of PedsQL, which has undergone validity and reliability testing, has been successfully used in various clinical pediatric populations in Türkiye (12). This tool allows for comprehensive evaluation not only of disease burden but also of daily life difficulties, psychosocial impacts, and general well-being in individuals with disabilities (10,12).

The aim of this study was to highlight the practicality of using mid-upper arm circumference measurements in monitoring nutritional problems in children with cerebral palsy and to examine the relationship between this measurement and quality of life using the PedsQL scale.

MATERIALS and METHODS

This study included a total of 99 children aged between 2 and 18 years who were diagnosed with cerebral palsy (CP) by a specialist physician at Karadeniz Technichal University between 2020 and 2024 years. Inclusion criteria were a confirmed diagnosis of CP and being within the specified age range. Children with additional genetic and/or neurological disorders other than CP were excluded from the study. Written informed consent was obtained from the parents of all participating children after they were informed about the purpose and methods of the study.

Medical histories were obtained, and clinical evaluations were conducted to determine the type and severity of CP. Feeding problems were assessed through symptoms such as difficulty swallowing, vomiting, aspiration, difficulty chewing, drooling, and inability to retain food in the mouth. Feeding duration, frequency, methods, and associated difficulties were also recorded. The severity of physical limitations and motor dysfunction was assessed using the Gross Motor Function Classification System (GMFCS), which classifies functional levels from I (mildest) to V (most severe). In this study, levels 1 and 2 were classified as mild, level 3 as moderate, and levels 4 and 5 as severe impairment.

Sociodemographic and clinical characteristics of the children were recorded. Anthropometric measurements included body weight, height, mid-upper arm circumference (MUAC), and thigh circumference. The most frequently reported nutritional problems were swallowing difficulties, vomiting, aspiration, chewing disorders, drooling, and inability to retain food in the mouth.

The Pediatric Quality of Life Inventory – Cerebral Palsy Module (PedsQL 3.0 CP) was administered to 45 children with mild-to-moderate CP (GMFCS levels 1–3) who did not have feeding problems, and to their mothers. This scale is a validated instrument developed to assess the quality of life in children and adolescents with disabilities and includes four age-specific forms: 2–4 years (toddler), 5–7 years (young child), 8–12 years (child), and 13–18 years (adolescent). For children aged 8–18, both child self-reports and parent proxy-reports were used. Each form evaluates four subdomains: physical functioning (PF), emotional functioning (EF), social functioning (SF), and school functioning (SchF). In addition to subscale scores, Total Scale Score (TSS) and Psychosocial Health Summary Score (PHSS) are calculated. Scores range from 0 to 100, where higher scores indicate better health status. Since children aged 2–4 years do not attend school, school functioning scores were not calculated for this age group.

Statistical analysis:

Statistical analysis were performed using PASW Statistics (SPSS) version 18.0. Descriptive statistics were presented as mean and standard deviation for continuous variables and as percentages and frequencies for categorical variables. Independent samples t-test was used to compare anthropometric measurements between children with and without feeding problems. Pearson chi-square test used for comparation of categorical variablies. Pearson correlation analysis was conducted to evaluate the relationships between mid-upper arm circumference (MUAC), quality of life scores, and GMFCS levels. The reliability of the PedsQL 3.0 CP module was assessed using Cronbach's alpha coefficients and intraclass correlation coefficients (ICC). A p-value of less than 0.050 was considered statistically significant.

A priori power analysis was conducted using G*Power software to determine the appropriate sample size for detecting medium effect sizes (Cohen's d = 0.5) in independent group comparisons. With an alpha level of 0.050 and desired statistical power of 0.80, the analysis indicated a minimum required sample size of 64 participants. The sample of 99 children in this study was deemed sufficient to detect statistically significant differences between groups.

Table I: Sociodemographic and Clinical Characteristics of the Children

Variable	Values
Age (years)*	8.50±4.49
Gender†	
Male	44 (44.44)
Female	55 (55.56)
Type of involvement†	
Diparetic	19 (19.19)
Hemiparetic	20 (20.20)
Quadriparetic	60 (60.70)
Severity of CP†	
Spastic	59 (59.60)
Dyskinetic	16 (16.16)
Ataxic	9 (9.10)
Hypotonic	7 (7.10)
Mixed	8 (8.10)
GMFCS†	
Level 1	12 (12.12)
Level 2	14 (14.14)
Level 3	21 (21.21)
Level 4	14 (14.14)
Level 5	38 (38.38)
Epilepsy†	
Present	36 (36)
Absent	63 (64)

***:** *mean±SD,* **†:** *n(%)*

RESULTS

A total of 99 children aged between 2 and 18 years who had been diagnosed with cerebral palsy (CP) by a specialist physician were included in this study. The mean age of the participants was 8.50±4.49 years, with 55 (55.56%) being girls and 44 (44.44%) boys. According to the Gross Motor Function Classification System (GMFCS), 12.12% of the children were classified as level I, 14.14% as level II, 21.21% as level III, 14.14% as level IV, and 38.38% as level V. Accordingly, 48.6% were categorized as having mild to moderate impairment (levels I–III), and 51.4% as having severe impairment (levels IV–V).

Regarding clinical subtypes, 19.19% were diparetic, 20.20% hemiparetic, and 60.70% quadriparetic. Sociodemographic characteristics are presented in Table I. Among the participants, 46 (46.46%) had feeding problems, whereas 53 (53.53%) had no such issues.

Feeding problems were significantly more frequent in children with moderate to severe impairment compared to those with mild impairment (p=0.003). In the comparison of anthropometric measurements between children with and without feeding problems, statistically significant differences were found in height (t=-3.161, p<0.001), weight (t=-3.592, p<0.001), mid-upper arm circumference (MUAC) (t=-4.114, p<0.001), thigh circumference (t=-5.337, p < 0.001), and arm length (t= -3.872, p<0.001). No significant difference was observed for age (t =-1.561, p=0.120). These results are presented in Table II.

Among the 52 children with mild to moderate impairment, 41 had weight and height percentiles between the 3rd and 25th percentiles and were provided with enteral nutritional support during a six-month growth follow-up period. Quality of life before and after nutritional support was assessed using the Pediatric Quality of Life Inventory (PedsQL). PedsQL scores obtained from parents of children who received nutritional support were significantly higher compared to those of children who did not receive support (p<0.001). The internal consistency of the scale was analyzed using Cronbach's Alpha coefficient. The overall Cronbach's Alpha value was 0.820 for the child form and 0.880 for the parent form. At the subscale level, Cronbach's Alpha coefficients ranged from 0.560 to 0.830 in the child form, and from 0.570 to 0.850 in the parent form. The item-total correlation coefficients (r) between subscales of child and parent responses ranged from 0.282 to 0.719. The highest correlation was observed in the School Functioning Score subscale (r = 0.719, p < 0.001) (Table III).

In correlation analyses conducted among children with feeding problems, significant positive correlations were found between age and height (r=0.765, p<0.001), age and arm circumference (r=0.682, p=0.002), and age and thigh circumference (r= 0.701, p<0.001). When correlating quality of life scores with anthropometric measurements, mid-upper arm circumference (MUAC) showed the strongest positive correlation (r=0.988, p<0.001), indicating a highly significant relationship. When correlating quality of life scores with anthropometric measurements, mid-upper arm circumference (MUAC) showed the strongest positive correlation (r=0.988, p<0.001), indicating a highly significant relationship.

In children with mild CP (GMFCS levels I–II), after a six-month follow-up, parental satisfaction and PedsQL scores significantly increased in the group receiving enteral nutritional support; furthermore, their response to physical therapy and improvements in motor function were more pronounced compared to those who did not receive support.

DISCUSSION

The findings of this study demonstrate that nutritional problems in children with cerebral palsy (CP) affect not only physical growth parameters but also quality of life. In particular, the strong correlation between mid-upper arm circumference (MUAC) and quality of life indicates that this anthropometric measure is not merely a marker of malnutrition, but also a reliable indicator of general health and well-being (9). When examining the relationship between nutritional status and the level of motor impairment, it was found that feeding problems were significantly more frequent in children with more severe functional limitations. These results imply that motor dysfunction in CP impacts not only mobility but also feeding abilities due to compromised oral-motor coordination and feeding

Table II: Anthropometric measurements of all children

	All children	With feeding problems	Without feeding problems	t	p*
Number of patients†	99	46 (46.46)	53 (53.54)	-	-
Age (years)‡	8.50±3.59 (2–18)	8.05±4.80 (2–18)	8.89±4.17 (2–18)	-1.561	0.120
Height (cm)‡	112.20±22.52 (75–182)	110.62±21.67 (75–162)	119.89±21.08 (80–182)	-3.161	<0.001
Weight (kg)‡	23.54±11.77 (7.7–65)	20.94±10.58 (7.7–65)	25.83±11.93 (9.4–65)	-3.592	<0.001
Mid-upper arm circumference (cm)‡	16.82±4.08 (6–38)	15.77±3.33 (6–26)	17.73±4.73 (8.5–38)	-4.114	<0.001
Thigh circumference (cm)‡	24.88±6.72 (7.5–55)	22.61±5.03 (7.5–37)	26.87±4.28 (13–55)	-5.337	<0.001
Arm length (cm)‡	23.5±5.08 (10–38)	21.77±5.03 (10–33)	24.04±4.89 (10–38)	-3.872	<0.001

***:** *Independent samples t-test,* **†:** *n (%),* **‡:** *mean±SD (min-max)*

Table III: Evaluation of PedsQL 3.0 CP module – child and parent reports

Scale	Child (n = 45)			Mother (n=45)			Child–Mother
	α	r	ICC	α	r	ICC	r
PedsQL	0.820	0.933†	0.929	0.880	0.933†	0.929	0.494*
Total Physical Health Score (TPHS)	0.830	0.934†	0.953	0.850	0.934†	0.953	0.488*
Emotional Functioning Score (EFS)	0.560	0.956†	0.922	0.570	0.956†	0.922	0.496
Social Functioning Score (SFS)	0.710	0.980†	0.923	0.760	0.980†	0.923	0.282
School Functioning Score (SFSch)	0.740	0.991†	0.988	0.680	0.991†	0.988	0.719†
Total Psychosocial Health Score (TPHSoc)	0.810	0.962†	0.989	0.800	0.962†	0.989	0.616†

***:** *p < 0.01,* **†:** *p<0.001,* **α:** *Cronbach's alpha (internal consistency);* **r:** *item-total correlation,* **ICC:** *intraclass correlation coefficient*

capacity (3,4). As Chanie et al. (3) emphasized, impairments in gastrointestinal function in children with CP have a direct impact on growth and general health. Similarly, in this study, children with feeding problems had significantly lower values in height, weight, arm circumference, and subcutaneous fat thickness. This finding provides strong evidence for the systemic effects of undernutrition (6,7).

The PedsQL scale used to assess quality of life in this study provided a comprehensive analysis not only of children's physical health, but also of their emotional, social, and academic functioning (10). Especially in neurodevelopmental disorders such as CP, quality of life is determined not only by motor competence but also by multiple factors such as environmental support, psychological resilience, and social participation (11). Therefore, the data obtained from the PedsQL scale are of critical importance in designing multidisciplinary care plans. In our study, the significant increase in PedsQL scores among children receiving enteral nutritional support indicates that such interventions have a beneficial effect not only on weight gain but also on overall quality of life. This finding is also consistent with previous studies (4,10,11).

Moreover, the improvement in quality of life scores as reported by parents of children with CP suggests that the nutritional status of the child is closely linked to the daily quality of life of the family. In this context, it can be said that interventions targeting the child indirectly affect parental well-being. This highlights once again the importance of family-centered approaches in the care of chronically disabled children (10,12–14). However, unlike the study by Aran et al. (15), our study also evaluated the effect of nutritional intervention on quality of life. The significant increase in PedsQL scores among children receiving enteral support demonstrates that the intervention has positive effects not only in physical health but also in psychosocial domains. In this respect, our study offers not only a descriptive but also an interventional perspective.

The negative correlation between the Gross Motor Function Classification System (GMFCS) level and MUAC is also noteworthy. As functional level decreased, MUAC values declined. This suggests a direct relationship between motor abilities and nutritional status and implies that MUAC may reflect functional disability indirectly (9).

Similarly, in a study by Herrera-Anaya E et al. (16), it was reported that malnutrition is prevalent in children with CP, and is caused by factors such as limited dietary diversity, prolonged meal times, and swallowing difficulties, all of which have a direct impact on quality of life. These findings are consistent with the strong correlation identified in our study.

Furthermore, in another study conducted by Namaganda H. et al. (17), it was emphasized that simple anthropometric measures like MUAC play a critical role in the early detection of malnutrition in children with CP in developing countries, and that its impact on quality of life should not be underestimated. However, this study did not clearly establish the direct effect of nutritional status on caregiver-reported quality of life.

The results of this study bring forward several clinical recommendations. First, in the follow-up of children with CP, not only traditional growth indicators such as weight and height, but also practical anthropometric measures like MUAC should be recorded regularly. Second, quality of life instruments such as PedsQL should not only be used for research purposes but also routinely applied to assess treatment responses. Third, early interventions like enteral support have been shown to improve both physical and psychosocial outcomes, underscoring the importance of early screening and intervention strategies (4,10,11).

Our study differs from these previous reports in that it evaluates quality of life not only from the caregiver's perspective, but within a holistic framework encompassing the child's motor impairment and nutritional status. In particular, the use of the PedsQL 3.0 CP module enabled objective comparisons in domains such as daily living activities, school functioning, and social participation.

One of the major contributions of our study is the evaluation of the correlation between child-reported and parent-reported quality of life. The results showed high concordance in physical and school functioning domains, whereas lower correlations were observed in emotional and social areas. This finding confirms frequently reported perception differences in the literature and emphasizes the importance of incorporating both perspectives in quality of life assessments (18-20).

In conclusion, although both studies confirmed a strong relationship between MUAC and quality of life in children with CP, our study contributes more comprehensively to the literature through its evaluation of interventional outcomes, subdomain-level analysis of quality of life, correlation with GMFCS levels, and parent–child agreement. These findings highlight the importance of using MUAC and tools such as PedsQL together in the follow-up of children with CP, both for clinical assessment and for monitoring the impact of interventions. The results reinforce the role of MUAC as a core component of multidisciplinary care. When combined with comprehensive quality of life scales such as PedsQL, this approach can contribute to more effective health service delivery at both the individual and systemic levels.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. Ethics committee approval was obtained from the ethics committee of Karadeniz Technical University with the number 2025/42.

Contribution of the authors

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

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Conflict of interest

The authors declare that there is no conflict of interest.

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Ultrasound as a diagnostic tool for vesicoureteral reflux grade in children: A comparative study with voiding cystourethrography

Nesrin Taş[1], Sare Gülfem Özlü[1], Nagihan Çiftci[1], Mihriban İnözu[1], Özlem Yüksel Aksoy[1], Burcu Yazıcıoğlu[1], Fatma Şemsa Çaycı[1], Avni Merter Keçeli[2], Hüseyin Tuğrul Tiryaki[3]

[1]Department of Pediatric Nephrology, Ankara Bilkent City Hospital, Ankara, Türkiye
[2]Department of Pediatric Radiology, Ankara Bilkent City Hospital, Ankara, Türkiye
[3]Department of Pediatric Urology, Ankara Bilkent City Hospital Ankara, Türkiye

ABSTRACT

Objective: Vesicoureteral reflux (VUR) is a prevalent congenital anomaly in children, with a higher incidence in those with febrile urinary tract infections. Early detection and management of VUR are crucial to prevent reflux nephropathy and its associated complications. This retrospective observational study aimed to evaluate the accuracy and advantages of ultrasonography (USG) in diagnosing VUR grade compared to voiding cystourethrography (VCUG), the gold standard.

Material and Methods: The study included 147 children aged 0-5 years who underwent VCUG for urinary tract infections, as well as antenatal and postnatal hydronephrosis. Patients were categorized into two age groups: 0-24 months (Group 1) and 25-60 months (Group 2). USG findings, including parenchymal thickness, renal pelvis anteroposterior diameter, renal parenchymal echogenicity, and distal ureteral dilatation, were compared between low-grade and high-grade VUR in both groups.

Results: Binary logistic regression analysis revealed that renal pelvis anteroposterior diameter and distal ureteral dilatation were independently associated with high-grade VUR in Group 1. The optimal cut-off value of renal pelvis anteroposterior diameter for predicting high-grade VUR was 5 mm, with 78.0% sensitivity and 76.0% specificity. However, no USG findings were independently associated with high-grade VUR in Group 2.

Conclusion: USG examinations performed by experienced radiologists can effectively decrease radiation exposure in children, especially those with high-grade VUR under two years of age, and may prevent unnecessary radiation exposure in some pediatric patients.

Keywords: Contrast Media, diagnostic imaging, ultrasonography, vesico-Ureteral Reflux, radiography

INTRODUCTION

Vesicoureteral reflux (VUR) is a common congenital anomaly in children. Its reported prevalence varies between 0.4% and 1.8% in healthy children, but it rises to about 30% to 40% in children with febrile urinary tract infections (1). Reflux nephropathy associated with VUR can lead to proteinuria, hypertension, and end-stage renal failure (2). Therefore, it is crucial to identify and manage VUR at an early stage. Urinary system ultrasonography (USG) is the main diagnostic method for initial assessment and subsequent monitoring in children with postnatal hydronephrosis and urinary system infections. Lower grades of VUR typically show normal USG results, and overall, USG is ineffective in detecting VUR. However, USG findings are more frequently associated with higher grades of reflux (3).

The gold standard for diagnosing VUR is voiding cystourethrography (VCUG). This diagnostic approach necessitates catheterization, rendering it an invasive technique that typically elicits substantial distress in pediatric patients and their caregivers. Additionally, the radiation exposure associated with VCUG has emerged as another concern (4). According to the most recent guidelines, VCUG is not advised for children under 2 years old when the USG results are normal and there are unusual or complicated circumstances during the initial urinary tract infection (5).

The objective of this research was to assess the accuracy and additional advantages of USG in diagnosing VUR across various

Correspondence Address:
Nesrin Tas
e-mail: drnesrin2004@yahoo.com

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reflux grades while comparing its performance to VCUG, the recognized gold standard.

METARIALS and METHODS

A retrospective observational analysis was performed from January 2020 to January 2024 at Ankara Bilkent City Hospital Department of Pediatric Nephrology. The research cohort consisted of children aged 0-60 months who were directed to the pediatric nephrology unit for urinary tract infections, as well as antenatal and postnatal hydronephrosis, and subsequently underwent VCUG procedures. The study was conducted by the principles outlined in the Declaration of Helsinki and approved by the Ethics Committee of Bilkent City Hospital (approval no 1236). We excluded patients who had previous genitourinary tract surgery, unilateral renal agenesis, multicystic dysplastic kidney, horseshoe kidney, duplex collecting system, posterior urethral valve, ureterovesical junction obstruction, chronic kidney disease, and neurogenic bladder. Patients whose records were incomplete were eliminated from the study. Patients above 60 months of age were excluded from the study. Each patient was included only once in the analysis. The records of 860 patients were assessed. The research involved 147 individuals and 294 kidney units. The study participants were categorized into two age-based groups. The first group, comprising 105 patients (71.4%), ranged from 0 to 24 months old. The second group, consisting of 42 patients (28.6%), included those between 25 and 60 months of age. Those with non-refluxing renal units were excluded from the study. Group 1 encompassed 175 renal units, while Group 2 had 64 renal units.

The VCUG results were classified from 1 to 5. Grade 1 was assigned when VUR affected only the ureter. Grade 2 indicated VUR extending to the renal pelvis without causing dilatation. Grade 3 dilation indicated mild ureter dilatation and mild to moderate pelvicalyceal dilatation. Grade 4 was characterized by dilatation of the renal pelvis and calyces with moderate ureteral tortuosity, blunting of fornicies. The most severe grade, 5, described VUR extending to the kidney with a tortuous ureter and dilatation ranging from moderate in the renal pelvis to extreme throughout the entire upper urinary tract (6). Reflux severity was categorized as follows: VUR grades 1, 2, and 3 were classified as low-grade, while VUR grades 4 and 5 were considered high-grade.

All images were done by experienced pediatric radiologists. Comprehensive data, including parenchymal thickness (mm), renal pelvis anteroposterior diameter [mm], renal parenchymal echogenicity (Grade 0, 1, and 2), and distal ureteral dilatation (positive or negative), were extracted from the USG images. These parameters were then used to compare Group 1 and Group 2.

Statistical analysis:

Descriptive parameters were expressed as mean and standard deviation for continuous variables and as numbers and percentages for categorical variables. Patients with low-grade and high-grade VUR were compared using independent sample t-tests and chi-squared tests. Variables with p<0.050 were included in the binary logistic regression analysis to identify the independent factors associated with high-grade VUR. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off value of renal pelvic diameter (mm) for predicting high-grade VUR. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 21.0; IBM Corp., Armonk, NY, USA). Odds ratios (ORs) and 95.0% confidence intervals (CIs) were calculated, with statistical significance set at p<0.050.

RESULTS

In this study, 147 patients aged 0–60 months were retrospectively analyzed. The mean age of all patients was 18.4 ± 20.2 months. Seventy (47.6%) patients were female, and 77 (52.4%) were male. VUR was right-sided in 22 (15.0%) patients, left-sided in 33 (22.4%) patients, and bilateral in 92 (62.6%) patients. A total of 239 renal units were examined, of which 139 (58.2%) had undergone surgical intervention (Table I).

Group 1 comprised 175 renal units, while Group 2 consisted of 64 renal units. In Group 1, the number of renal units with low-grade and high-grade VUR were 74 (31.0%) and 101 (42.3%), respectively. In Group 2, the number of renal units with low-grade and high-grade VUR were 40 (16.7%) and 24 (10.0%), respectively.

USG findings [parenchymal thickness (mm), renal pelvis anteroposterior diameter [mm], renal parenchymal echogenicity (Grade 0, 1, and 2), and distal ureteral dilatation (positive or negative)] of renal units with low-grade and high-grade VUR in Groups 1 and 2 are presented in Table II. The mean renal parenchymal thickness and renal pelvis diameter, as well as renal parenchymal echogenicity and distal ureteral dilatation rates, were significantly different in patients with low-grade and high-grade VUR in both groups (all p values were <0.050) (Table II).

Table I: Clinical characteristics of patients, overall and according to age-related groups

Characteristics	0-24 months	25-60 months	All patients
Number of patients*	105 (71.4)	42 (28.6)	147
Age (months)†	6.3±4.9	48.5±9.4	18.4±20.2
Gender*			
Female	38 (25.8)	32 (21.8)	70 (47.6)
Male	67 (45.6)	10 (6.8)	77 (52.4)
VUR laterality*			
Right-side	16 (10.9)	6 (4.1)	22 (15.0)
Left-side	19 (12.9)	14 (9.5)	33 (22.4)
Bilateral	70 (47.6)	22 (15.0)	92 (62.6)

***:** *n (%),* **†:** *mean±SD,* **VUR:** *vesicoureteral reflux*

Table II: Renal and urinary system USG findings in Group 1 and Group 2.

Characteristics	Group 1		p	Group 2		p
	Low-grade	High-grade		Low-grade	High-grade	
Number of Patients*	74 (42.3)	101 (57.7)	-	40 (62.5)	24 (37.5)	-
Renal parenchymal thickness (mm)†	7.9±1.4	6.7±1.9	< 0.010‡	10.0±2.1	8.2±2.7	< 0.010‡
Renal pelvis anteroposterior diameter (mm) †	3.3±3.8	8.5±5.6	< 0.010‡	2.7±2.9	7.5±6.4	< 0.010‡
Renal parenchymal echogenicity*						
Grade 0	61 (52.6)	55 (31.4)	< 0.010 §	34 (53.1)	13 (20.2)	0.010 §
Grade 1	12 (6.9)	34 (19.4)		6 (9.4)	9 (14.1)	
Grade 2	1 (0.6)	12 (6.9)		1 (1.6)	1 (1.6)	
Distal ureteral dilatation*						
Positive	66 (37.7)	62 (35.4)	< 0.010 §	2 (3.1)	7 (10.9)	0.010 §
Negative	8 (4.6)	39 (22.3)		38 (59.4)	17 (26.6)	

***:** *n (%),* **†:** *mean ±SD,* **‡:** *Independent sample t-tests,* **§:** *Chi-squared tests. Groups 1 and 2 represent the renal units of patients aged between 0 – 24 months and 25 – 60 months, respectively were used to compare groups.*

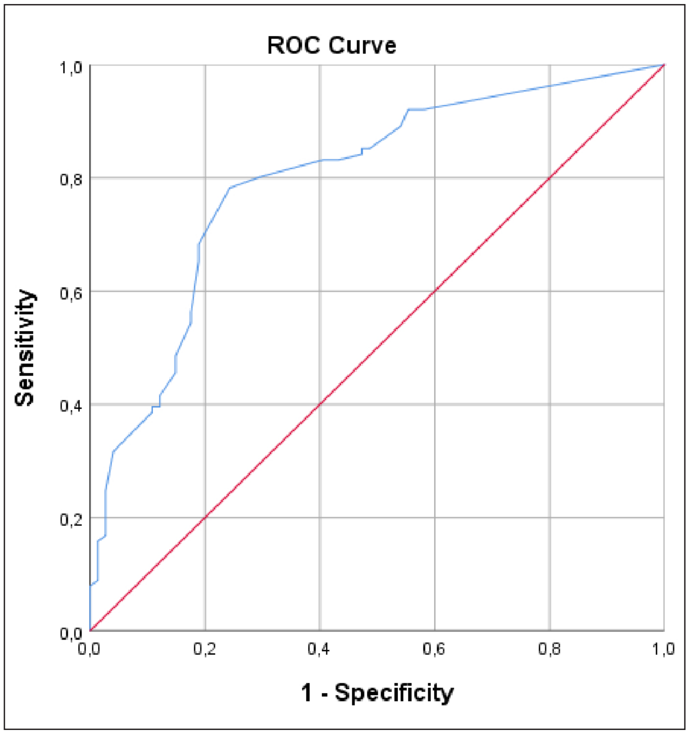

Figure 1: Receiver operating characteristic curve analysis of renal pelvis anteroposterior diameter for predicting patients with high-grade VUR.

Binary logistic regression analysis revealed that renal pelvis anteroposterior diameter (p<0.001; OR:1.2; 95.0% CI:1.12 – 1.35) and distal ureteral dilatation (p=0.010; OR: 4.6; 95.0% CI:1.79–11.67) were independently associated with high-grade VUR in Group 1. Furthermore, ROC curve analysis revealed that the optimal cut-off value of renal pelvis anteroposterior diameter for predicting high-grade VUR was 5 mm, with 78.0% sensitivity and 76.0% specificity (area under the curve: 0.79, standard error: 0.03, p<0.001) (Figure 1). However, binary logistic regression analysis revealed none of the USG findings was independently associated with high-grade VUR in Group 2.

DISCUSSION

Vesicoureteral reflux (VUR), which is primary in nature, is among the most prevalent urological disorders affecting infants and children. The methods for detecting VUR through renal imaging have evolved. There is ongoing debate regarding the optimal initial imaging technique for infants and children with hydronephrosis and urinary tract infections (7). Low-grade VUR generally has a favorable prognosis, with limited adverse effects and a propensity for self-resolution. Conversely, severe cases of reflux necessitate swift detection and intervention to prevent renal injury (8). Consequently, it is essential to correctly diagnose and manage patients with VUR using the most suitable approach at the appropriate time.

Studies on VUR identified after urinary tract infection show varying gender distributions. While some research indicates a female predominance, others report no significant gender difference (9). In our investigation, the gender split was nearly equal, with 47.6% of patients being female and 52.4% male. In a similar study, Chang et al.(10) reported rates of 9.6% for females and 10.7% for males. However, Naseri et al.(11) reported contrasting findings, with 18.37% (77 out of 419) of VUR cases being male, which differs from our results.

The study findings indicated that VUR manifested unilaterally in 37.4% of patients, with 15.0% (22 cases) affecting the right side and 22.4% (33 cases) affecting the left side. The majority of patients, 62.6% (92 cases), exhibited bilateral VUR. In comparison, Naseri et al.'s (11) research identified bilateral VUR in 45.85% of their 410 VUR patients (188 cases). Another investigation by Su et al. (12) reported an even distribution between unilateral and bilateral VUR, with each type occurring in 50.0% of their study participants.

Surgical intervention is often indicated for patients exhibiting grade 4-5 VUR, showing progression of scarring, experiencing febrile urinary tract infections despite prophylactic treatment, or in some cases, due to parental preferences (13). Our study examined 239 kidney units, with mostly endoscopic surgical interventions performed on 139 (58.2%) of them. The majority of these cases exhibited severe VUR. According to published studies, endoscopic injections have shown effectiveness in initial treatments. Ripatti et al. (14) conducted a retrospective analysis of VUR patients over a decade. Their research revealed that out of 1484 children, 1212 underwent endoscopic surgical treatment during these ten years.

Our research revealed that high-grade reflux patients in Groups 1 and 2 displayed a decreased mean renal parenchymal thickness. In contrast, these individuals exhibited significantly higher renal parenchymal echogenicity and a larger anteroposterior renal pelvis diameter. The results of a binary logistic regression analysis showed that in Group 1, the anteroposterior diameter of the renal pelvis and dilation of the distal ureter were independently linked to high-grade VUR. In contrast, for Group 2, no correlation was found between USG findings and high-grade VUR. A study by Doğan et al.(15) examined the effectiveness of USG in performing VCUG procedures with clear indications. The investigation classified subjects into three age ranges: 0-2 years, 3-5 years, and 6-17 years. The USG reports included anteroposterior renal pelvic diameter measurements, kidney parenchyma, kidney dimensions, and ureter size. They found a correlation between VCUG and USG results in all age groups. Using a threshold of >10 mm for the pathologic anteroposterior renal pelvic diameter, the study found sensitivity, specificity, and negative predictive value to be 79.45%, 79.91%, and 71.17%, respectively. For children aged 0-2 years, the USG demonstrated its highest sensitivity and negative predictive value. Our research utilized ROC analysis to determine the optimal renal pelvis anteroposterior diameter threshold in predicting high-grade VUR. The results indicated that a cut-off value of 5 mm yielded the best performance, demonstrating a sensitivity of 78.0% and a specificity of 76.0% in Group 1. In a comparable investigation by Ilıkan, researchers categorized patients into two age groups: those younger than 6 years and those 6 years and older (16). Their findings demonstrated a link between USG and VCUG results for children under 6 years of age, while no such association was found in patients 6 years and above. In a similar study, You et al. (17) examined the effectiveness and predictive capabilities of USG with VUR in patients under 2 years of age. The researchers suggested that USG findings indicating thickened walls and expanded renal collecting systems should be considered indicative of severe VUR. Khater et al. (18) conducted a study that aligns with our findings, demonstrating that patients with high-grade VUR showed statistically significant increases in kidney dimensions, echogenicity, ureteral dilation and wall thickness, as well as renal pelvis diameter and pelvic wall thickness. Additionally, their ROC analysis revealed that USG demonstrated 100% specificity and 78.5% sensitivity in detecting VUR. Nevertheless, research also exists that highlights the potential for USG to cause delays in diagnosing high-grade VUR. The study by Nelson et al. (19) revealed that USG is inadequate as a screening method for identifying genitourinary abnormalities. Their findings suggest that USG and VCUG should be utilized in conjunction, as each technique offers unique and essential information. Some studies suggest that the distal ureter dilatation may play a more significant role in determining the clinical progression of primary VUR than dilation of the upper urinary tract. Consistent with our findings, Hodhod et al. (20), observed that refluxing hydroureter units had a median ureteric diameter of 10 mm, and a significant portion (74%) of refluxing renal units were classified as high-grade.

This study has various constraints, including its retrospective design. Additionally, the research is limited by a restricted number of patients in the sample. Furthermore, it is important to consider that the investigation was conducted at only one medical facility. Another limitation is that the degree of ureter dilation can vary with age, making it an unreliable indicator. Consequently, children who have not yet been toilet-trained may exhibit false ureter dilation. Additionally, bladder distention can alter the condition.

CONCLUSION

In conclusion, our results indicate that under two years of age, the anteroposterior diameter of the renal pelvis and dilation of the distal ureter were independently linked to high-grade VUR. A ROC analysis indicated that a cut-off value of 5 mm yielded the best performance, demonstrating a sensitivity of 78.0% and a specificity of 76.0% in this age group. For children, especially those under two years of age, the use of USG examinations performed by experienced radiologists can effectively decrease radiation exposure. This strategy may prevent some pediatric patients from being subjected to unnecessary radiation.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Bilkent City Hospital (approval no 1236).

Contribution of the authors

Taş N and Özlü SG: participated in study design, analysis, and manuscript preparation. ***Çiftci N, İnözü M, Aksoy ÖY, Yazıcıoğlu B, Çaycı FŞ, and Tiryaki HT:*** were involved in patient follow-up and analysed the manuscript. The ultrasonographic analysis was performed by ***Keçeli AM.***

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Psychiatric aspects of children in the transplantation process: 6-year outcomes from a tertiary hospital

Hatice Ünver, Hatice Ezgi Bırık, Neşe Perdahlı Fiş

Department of Child and Adolescent Psychiatry, Marmara University, İstanbul, Türkiye

ABSTRACT

Objective: Pediatric patients undergoing transplantation are at increased risk for a variety of psychiatric problems. The aim of this study was to analyse the data of children and adolescents referred to the child and adolescent psychiatry unit of a tertiary hospital and who were in the process of transplantation.

Material and Methods: This retrospective observational study, planned using the hospital information system and patient records, included clinical data over a 6-year period. Patients were assessed according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition.

Results: This study included the data of 64 patients (n= 30, 46.9% girls) in the transplantation process. Of the patients, 46 (71.9%) were undergoing kidney transplantation, 13 (20.3%) bone marrow transplantation, two (3.1%) liver transplantation, two (3.1%) lung transplantation, and one (1.6%) heart transplantation. The duration of pre-transplant illness was approximately 5.21±4.17 years. The most common reason for admission to child psychiatry unit was pre-transplant psychiatric and intelligence assessment. Thirty-two (50%) patients were diagnosed with any mental illness. The most common diagnoses were depression and adjustment disorder. No association was found between the duration of pre-transplant illness and the mean psychiatric diagnosis (r= -0.101, p= 0.603).

Conclusion: The data from this study will help to guide mental health and psychosocial care in this population. Prospective longitudinal studies of children are needed to determine optimal psychiatric assessment.

Keywords: Adjustment disorder, bone marrow transplant, children, depressive disorder, kidney transplant

INTRODUCTION

Chronic illnesses and transplantation processes in children and adolescents are complex and influence the individual's functioning in terms of family, school and peer relationships. Patients are affected by many mental health problems such as depression, anxiety, attention deficit hyperactivity disorder and have more developmental and neurocognitive delays compared to healthy controls. Addressing these concerns is associated with positive transplant outcomes (1-3).

Patients with chronic kidney illness have a reduced quality of life and a higher risk of hospitalisation, heart problems and death (4). Although kidney transplantation is difficult for these patients, it is better than hemodialysis and peritoneal dialysis in terms of quality of life. In addition, kidney transplant patients have lower levels of anxiety and depression than haemodialysis and peritoneal dialysis patients (5). There are studies in the literature on children undergoing kidney, bone marrow and heart transplantation, with kidney transplantation being the most common area of research (1-3,6-9). Studies have evaluated pre-transplant and post-transplant processes, and some pre-transplant factors, including the patient's psychiatric history, have been associated with poorer outcomes. The presence of psychiatric factors and psychosocial problems such as anxiety/depression, low self-esteem, social and peer difficulties, emotional and behavioural problems have also been associated with an increased risk of non-adherence. Notably, several aspects of family functioning, including parental psychopathology, also place patients at increased risk for psychiatric and post-transplant concerns. In particular,

Correspondence Address:
Hatice Ünver
e-mail: drhaticeunver@gmail.com

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duration of pre-transplant illness, lower intelligence scores and learning disabilities, age, prolonged school absence, attention and neurocognitive difficulties may increase the risk of mental health problems (1-3). Intelligence is also an important factor and may affect the transplant process, but intellectual disability alone is not a contraindication to transplantation (10). Another study of children who received a kidney transplant reported that these children had more emotional and behavioural problems and a lower quality of life than the healthy control group (7). Psychosocial support should be provided after transplantation. Monitoring patients to determine the level of risk and intervention needed to address neurocognitive factors is important to promote academic functioning and success, adherence to treatment, and overall functioning (6,7).

Similar processes occur in heart transplant patients, suggesting the need for pre- and post-transplant psychiatric assessment and the importance of a multidisciplinary approach and inter-institutional collaboration in the child and adolescent age group (8). In bone marrow transplant patients, children often describe fears of life-threatening illness, along with fears of illness and death, feelings of being a burden to the family, low self-esteem, helplessness and vulnerability. During transplantation, the main problems are anxiety, depression, overdependence and regression, along with anger, reduced tolerance to procedures and periodic refusal to cooperate. Children also experience high levels of anxiety due to fear of procedures and express concern when complications occur; as they become more seriously ill, they often ask not to be left alone. Despite this, children suffering from the stress of a bone marrow transplant have fewer and less severe overt psychiatric disorders than might be expected. Adjustment disorder with depressed mood, separation anxiety disorder and major depressive disorder make up the majority of cases (9).

This study aimed to evaluate the sociodemographic and clinical characteristics, psychiatric diagnoses, and follow-up processes of pediatric patients referred to child and adolescent psychiatry during kidney, bone marrow, heart, liver, or lung transplantation.

MATERIALS and METHODS

This retrospective observational study was conducted at Marmara University Pendik Research and Training Hospital, a tertiary care center. Data were collected through the hospital information management system and patient medical records. The study sample included pediatric patients who were referred to the Child and Adolescent Psychiatry Clinic for consultation from the organ transplantation unit, bone marrow transplantation unit, or from the pediatric nephrology and hematology outpatient clinics within the same institution. Our clinic is an outpatient unit, we do not have an inpatient unit. Kidney and bone marrow transplants are performed in our hospital; patients in the process of lung, heart and liver transplantation are referred to our clinic from other hospitals for child and adolescent psychiatric assessment as consultations. The data in this retrospective study includes the period between 2018 and the first half of 2024. Psychiatric interviews were conducted in the services where the patients were hospitalised. Other interviews were conducted in outpatient clinics with patients who were admitted as outpatients. Interviews with foreign patients were conducted with the help of an interpreter. In our outpatient clinic, patients are assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version-Turkish Adaptation (K-SADS-PL). The K-SADS-PL is a semi-structured diagnostic interview developed by Kaufman et al. (11). The Turkish version has undergone validity and reliability studies by Gökler et al. (12).

Patients' psychiatric disorders were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Patients with suspected cognitive problems were assessed using the Wechsler Intelligence Scale for Children-Revised (WISCR). According to the test results, a total intelligence section score of 90 and above was classified as normal, 70-89 as borderline, and 55-70 as mild intellectual disability. Since this study was a retrospective study, no consent was obtained, but necessary permissions were obtained and patient privacy was taken into consideration. Sociodemographic form is a form created by the researchers. Participants' age and sex, school, psychiatric history, family psychiatric history, intelligence level, time and reason for consultation, pre-transplant diagnoses, psychiatric diagnoses, psychopharmacological treatments and information about their follow-up were recorded.

Statistical Analysis

The analysis of the data was conducted utilising the IBM Statistical Package for the Social Sciences, version 20.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). Sociodemographic data, primary childhood illness, transplanted organ/tissue, duration of illness, psychiatric diagnoses and treatment modality were analysed using descriptive statistics. Descriptive statistics, expressed as mean and standard deviation, were used to analyse the study data. The correlation between the duration of illness in children and the mean psychiatric disorders was examined using Spearman correlation analysis. A $p<0.050$ was considered significant.

RESULTS

The study sample consisted of 64 patients, 30 of whom were girls (46.9%). Two patients were Syrian. The mean age of the patients was 12.70±3.41 years. The mean number of siblings of the patients was 2.38±0.80. Thirty-two (50%) patients were able to attend school, while the other half could not attend school due to their illness. Sixteen (25%) patients had a history of psychiatric outpatient treatment. Previous psychiatric

Table I: Primary pediatric diagnosis (with ICD-10 codes) for transplant

Transplated organ, tissue	Disease-ICD 10 codes	Number of patients*
Kidney	Chronic kidney disease (N18.1-9), Kidney transplant status (Z94.0), Malignant neoplasm of kidney (C64), Nephrotic syndrome (N04)	46 (71.9)
Bone marrow	Neutropenia (D70) Severe combined immunodeficiency (D81) Malignant neoplasm of unspecified part of adrenal gland (C74.9) Hodgkin lymphoma (C81) Leukemia (C91, C94, C95) Aplastic anemia (D61)	13 (20.3)
Liver	Fibrosis and cirrhosis of liver (K74) Metabolic disorders (E70-88)	2 (3.1)
Lung	Cystic fibrosis (E84) Primary ciliary dyskinesia/Cartagener syndrome	2 (3.1)
Heart	Cardiomyopathy (I42)	1 (1.6)

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

Table II: The reasons for admissions/referrals, psychiatric diagnoses distribution and intelligence level of sample

The reasons for admissions/referrals (n)	64
Intelligence assessment	13
Depressive symptoms	6
Anxiety	6
Hyperactivity-attention problems	10
Pre-transplant psychiatric assessment	42
Noncompliance with treatment/medication	11
Food refusal	2
Presence of psychiatric diagnosis*	32 (5)
Number of diagnoses †	2.25±1.09
Presence of major depresive disorder (F32)*	12 (37.5)
Presence of adjustment disorder (F43)*	12 (37.5)
Presence of attention deficit hyperactivity disorder (F90)*	7 (21.9)
Presence of dyslexia (F81)*	1 (3.1)
Intelligence level*	57
Normal intelligence	44 (68.8)
Intellectual disability (F70)	9 (14.1)
Borderline mental functioning	4 (6.3)

***:** *n(%),* **†:** *mean±SD*

diagnoses were; three (4.7%) patients had depression, two (3.1%) patients had adjustment disorder, three (4.7%) patients had attention deficit hyperactivity disorder, eight (10.9%) patients had mild intellectual disability and one (1.6%) patient had dyslexia. Patients diagnosed with intellectual disability and dyslexia were in special education. Twenty-three patients (35.9%) had a history of mental illness in one of their parents.

In the sample, 46 (71.9%) patients were in the process of kidney transplantation, 13 (20.3%) patients were in the process of bone marrow transplantation, two (3.1%) patients were in the process of liver transplantation, two (3.1%) patients were in the process of lung transplantation, and one (1.6%) patient was in the process of heart transplantation. The primary pediatric diagnosis (with ICD-10 codes) for transplantation is shown in Table I.

Of the patients, 44 (68.8%) had normal intelligence (intelligence score according to WISCR test; 90-110), four (6.3%) had borderline mental functioning (70-89) and nine (14.1%) had intellectual disability (mild level-55-70). For seven patients, no record of intelligence level could be found in the files or in the system. There were no patients with moderate or severe intellectual disability in the sample. Looking at the distribution of patients per year, 32 (50) patients were assessed in 2018, 14 in 2019, 13 in 2020 and eight patients per year between 2021-2024.

Forty-two (65.6%) of the patients were referred to our clinic before transplantation, six (9.4%) were evaluated after transplantation and 16 (25%) were evaluated both before and after transplantation. Patients were evaluated 2.61±2.03 times in our outpatient clinic. Thirty-two (50%) patients (16 of them were girls) were diagnosed with any mental illness, while 32 (50%) did not meet the diagnostic criteria for any mental illness. The patients who were diagnosed had an average of 2.25±1.09 diagnoses. The reasons for admission/referral and the distribution of diagnoses (with ICD-10 codes) are shown in Table II.

Psychopharmacological treatment was planned for 16 (50%) patients with a psychiatric diagnosis. As the transplant unit did not consider the use of psychotropic medications to be appropriate due to the patients' chronic conditions (due to drug interactions and side effects such as bleeding, immunosuppression related to the primary diagnosis), approval was not given. The most commonly prescribed treatment was serotonin reuptake blockers in 12 patients (75%). Twenty-one of the 32 patients (65.2%) were followed up in our clinic. The duration of pre-transplant illness was approximately 5.21±4.17 years. No association was found between the duration of pre-transplant illness and the mean psychiatric diagnosis (r= -0.101, p= 0.603).

DISCUSSION

According to the results of our study, many psychiatric disorders can be diagnosed in children during the transplantation process. Psychiatric disorders can influence pre-transplantation and post-transplantation outcomes. It is important to evaluate patients' mental health before and after transplantation.

Half of the children in our sample group were unable to attend school during the period they were admitted to our clinic. The school environment contributes to the academic, social and personal development of children and adolescents, and absence from school has a negative effect on children and adolescents with any chronic illness (13). It is important that patients continue their education at home or in hospital schools during the early post-transplant period. The implementation of individualised education plans and other school services, including computerised training programmes, should be considered.

Having a mental illness prior to transplant is a risk factor for stressful situations that may develop during and after the transplant process (14). Untreated psychiatric morbidities may worsen and reduce medical compliance after transplantation, which may lead to rejection of the transplanted organ or tissue. In our sample, 25% of patients had a history of outpatient psychiatric treatment. Conversely, anxiety, depression and post-traumatic stress disorder have been reported in parents of children undergoing transplantation. Parents' mental health issues can influence their children's mental well-being at all stages of the transplant process (7,15). One third of our sample group had a parent who was diagnosed with a mental illness. We could not obtain data on whether the diagnosis occurred before or after transplantation. Nevertheless, parents should receive psychological support, such as family or cognitive behavioural therapy.

The patients referred to our clinic did not have a moderate or severe intellectual disability. They may not have been on the waiting list as potential recipients because they were unable to adapt to the post-transplant process. The relationship between intellectual disability and organ transplantation in children is multifaceted, encompassing clinical, ethical, and policy dimensions. Historically, children with intellectual disability have faced significant barriers to accessing life-saving transplants, often due to misconceptions about their quality of life and potential outcomes. However, recent studies and policy shifts are challenging these assumptions and advocating for more equitable treatment. A study found that children with intellectual disability had similar graft survival rates and lower rates of acute rejection compared to those without intellectual disability (10). Another study reported that children with intellectual disability had comparable short-term graft and patient survival rates to those without intellectual disability (11). Additionally, a study conducted in Japan suggests that kidney transplantation is not contraindicated in patients with intellectual disabilities. However, it was also emphasised that researchers cannot determine which patients are unsuitable for transplantation (12). Further multidisciplinary and prospective studies are needed to enable such predictions to be made. However, it is clear that children with intellectual disabilities and their families require additional support throughout this process. Intellectual disability can make the process more stressful for children and may lead to more non-compliance and behavioural problems. If intellectual disability has a genetic aspect, their parents may also be affected.

Half of our sample group had a diagnosis of mental illness. Consistent with other studies, the most common diagnoses were depression, adjustment disorder and intellectual disability (2,3,6,18). Studies have reported that the rate of having a psychiatric diagnosis during the transplant process is around 60% (18,19). In our study, half of our sample had a psychiatric diagnosis. Major depression and adjustment disorder are the most common psychiatric diagnoses among hospitalised patients have been associated with an increased incidence of suicide attempts and completions (20). The presence of comorbid psychiatric disorders in the post-transplant period is an important risk factor for graft rejection. Non-compliance with treatment/medication was also the reason for referral in some patients. Psychiatric disorders may contribute to non-compliance with treatment/medication. Patients with psychiatric disorders already have a low rate of medication compliance and an increased health risk (21). Furthermore, psychopharmacological treatment could not be applied to all patients with mental illness. Drug interactions and side effects such as bleeding or immunosuppression caused by primary pediatric illnesses were evaluated interclinically. For this special group, cognitive behavioural therapy, dialectical behavioural therapy and mindfulness-based therapies should be considered as an alternative to psychopharmacological treatments. Cognitive behavioural therapy is one of the most evidence-based treatments for anxiety and depression in children who are in the transplant process. It helps children cope with medical anxiety, anticipatory fear, and treatment-related stress, enhances adherence to complex post-transplant regimens by addressing maladaptive thoughts and behaviors, builds coping skills for pain, uncertainty, and hospitalization (22). Dialectical behavioural therapy may be effective in reducing self-harming behaviors, emotional volatility, and non-adherence and offer structured modules on distress tolerance, emotion regulation, mindfulness, and interpersonal effectiveness- all critical in managing post-transplant stress (23). Mindfulness-based therapies reduce preoperative anxiety and postoperative stress, improves pain management, sleep, and emotional well-being (24).

This study has important limitations. Firstly, the data were retrospective. As the study included data from a single centre, the sample size was small. Patients were not reassessed for the study, and self-report psychiatric scales were not used. There was also a lack of socio-demographic information. Further statistical analysis could not be performed using the available data. Information on post-transplant processes and follow-up data on graft function could not be obtained.

CONCLUSION

Studies have shown that interdisciplinary interventions involving psychiatrists, physicians, nurses, dieticians, and social workers in the transplant population are associated with improved outcomes, including delay in ilness progression, improved patient education and preparedness, and reduced mortality (25). However, clinical data from large transplant centres are limited. This study includes data from a small sample, therefore the results cannot be generalised, but the results of this study can contribute to the literature, consequently it includes data from a 6-year experience.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. Ethical approval was obtained from the Ethics Committee of the Medical Faculty of Marmara University (09.02.2024/178).

Contribution of the authors

All the authors made substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data; participated in drafting the article and revising it; and gave final approval of the submitted version. Ünver H and Perdahlı Fiş N: has the study conception, designed the study; Ünver H: has drafting of the manuscript; performed analyses and interpretation of data, , Bırık HE: involved in the acquisition of data and made critical revisions. All authors participated in the interpretation of data and contributed significant intellectual content to the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Efficacy and safety of levetiracetam treatment in childhood epilepsy

Arife Toksöz[1], Serap Teber[2]

[1]Department of Pediatric Immunology and Allergy, Ankara Etlik City Hospital, Ankara, Türkiye
[2]Department Pediatric Neurology, Ankara University, Ankara, Türkiye

ABSTRACT

Objective: Levetiracetam (LEV) is a second-generation antiepileptic drug widely used in pediatric epilepsy due to its favorable pharmacokinetics, efficacy, and tolerability. This study aimed to evaluate the long-term efficacy and safety of LEV treatment in children with epilepsy.

Material and Methods: A retrospective review was conducted on pediatric patients diagnosed with epilepsy and treated with LEV at a tertiary pediatric neurology center. Treatment efficacy was assessed based on seizure frequency reduction of more than 50% or complete seizure freedom. The occurrence and types of adverse effects were also analyzed. Statistical analyses included chi-square tests, independent t-tests, and logistic regression models.

Results: A total of 101 patients were included in the study. LEV was initiated as the first antiepileptic drug in 9.9% of patients. By the end of the follow-up, 34.7% remained on LEV treatment, and 11.9% discontinued LEV. LEV was effective in 72.3% of patients, with 38.0% achieving complete seizure freedom. The drug was significantly more effective in patients older than four years and those with a lower pre-treatment seizure frequency. The mean LEV dose was 24.8 mg/kg/day in the effective group and 33.8 mg/kg/day in the ineffective group. Adverse effects were observed in 45.5% of patients, with the most common being drowsiness, irritability, and fatigue. Patients with a prior history of adverse reactions to other antiepileptic drugs had a significantly higher likelihood of developing side effects with LEV.

Conclusion: Levetiracetam (LEV) is an effective and well-tolerated treatment option for childhood epilepsy, with high efficacy rates and a manageable safety profile. Older children, those receiving lower doses, and those with a lower pre-treatment seizure burden demonstrated better treatment outcomes. Careful monitoring is necessary for patients with a history of adverse reactions to other anti-epileptic drugs.

Keywords: Antiepileptic drugs, children, epilepsy, levetiracetam, seizure control, safety, tolerability

INTRODUCTION

Epilepsy is defined as the occurrence of two or more unprovoked seizures at least 24 hours apart (1). As the second most common neurological disorder after headaches, it is a chronic disease affecting 0.5–1% of children under 16 years of age (2,3). The primary goal of antiepileptic treatment is to achieve seizure freedom without adverse effects.

Levetiracetam [(S)-α-ethyl-2-oxo-1-pyrrolidineacetamide] is a water-soluble pyrrolidine derivative and a new-generation antiepileptic drug introduced in 2000 (4). The U.S. Food and Drug Administration (FDA) initially approved LEV in 1999 as an adjunctive therapy for drug-resistant partial epilepsy in adults, extending its approval in 2005 to include individuals over four years of age (5,6). Currently, LEV is indicated as adjunctive therapy for myoclonic seizures in adults and adolescents (≥12 years) with juvenile myoclonic epilepsy, partial seizures in adults and infants (≥1 month) with epilepsy, and primary generalized tonic-clonic seizures in adults and children (≥5 years) with idiopathic generalized epilepsy (7).

This study aimed to evaluate the long-term efficacy and safety of LEV treatment in children with epilepsy.

Correspondence Address:
Arife TOKSÖZ
e-mail: arifetoksoz@gmail.com

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MATERIALS and METHODS

This retrospective chart review included 101 patients who were diagnosed with epilepsy and started on levetiracetam (LEV) treatment in the Pediatric Neurology Clinic of Ankara Child Health and Diseases Hematology-Oncology Training and Research Hospital between 01.01.2010 and 30.12.2011.

Epilepsy was defined as two or more unprovoked seizures occurring at least 24 hours apart. Treatment efficacy was determined based on a reduction of over 50% in seizure frequency or complete seizure freedom with LEV.

Statistical Analyses

Data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including mean, standard deviation, frequency, and percentage, were used to summarize the data. Pearson's chi-square test and the independent t test were used to compare groups. All statistical analyses were two-tailed, with a significance level set at 0,050 and a 95% confidence interval.

RESULTS

A total of 101 patients were included in the study, of whom 41 (40.6%) were female and 60 (59.4%) were male. The mean age of the participants was 12.6 ± 4.7 years (range, 1.5–23 years) (Table I).. LEV was initiated as the first antiepileptic drug in 10 (9.9%) of the 101 patients. By the end of the treatment period, 35 (34.7%) patients were on LEV monotherapy, while LEV was discontinued in 12 (11.9%) patients. Table II presents the clinical characteristics associated with LEV treatment, observed adverse effects, and seizure outcomes at final follow-up.

Levetiracetam was found to be effective in 72.3% (73/101) of patients. No statistically significant differences were observed between LEV efficacy and patients' sex, age, or age at diagnosis. In patients with effective LEV treatment (n=73), the mean age at initiation was 11.25±3.94 years, which was significantly higher than the mean age of 8.86±5.43 years observed in those with an ineffective response (n=28) (p=0.040). The mean LEV dose was 24.8±9.6 mg/kg/day in the effective group, whereas it was 33.8±9.05 mg/kg/day in the ineffective group, with a statistically significant difference (p=0.001). Details regarding LEV treatment efficacy are presented in Table III.

LEV treatment was discontinued in 12 out of our 101 patients. Among these, 5 (41.7%) discontinued due to lack of efficacy, 4 (33.3%) due to side effects, and 3 (25%) due to increased seizure frequency. The mean duration of LEV use in these patients was 9.5±8.2 months.

Side effects were observed in 46 patients (45.5%), including drowsiness, irritability, fatigue, aggression, dizziness, insomnia, headache, vomiting, and loss of appetite. Among all patients, 19 (18.8%) had previously experienced side effects from another antiepileptic drug (AED) and 13 of these 19 (68.4%) also developed side effects with LEV. Among these 19 patients, adverse effects were observed in 6 patients (31.6%) with valproic acid, 6 patients (31.6%) with carbamazepine, 3 patients (15.8%) with lamotrigine, 2 patients (10.5%) with clonazepam, 1 patient (5.3%) with oxcarbazepine, and 1 patient (5.3%) with primidone. Table III presents the factors influencing the

Table I: Demographic, clinical, and laboratory characteristics, imaging, and electroencephalographic findings of the patients

Gender*	
Female	41 (40.6)
Male	60 (59.4)
Age (years)†	12.6±4.7 (1.5-23)
Age at epilepsy diagnosis (years) †	5.5±4.5 (0.1-17)
Seizure Classification*	
Generalized Seizure	77 (76.2)
Focal Seizure	24 (23.8)
Mental and motor developmental delay	48 (47.5)
History of febrile convulsions	19 (18.8)
History of past illness	72 (71.3)
Use of other medications	35 (34.7)
History of hospitalization	65 (64.4)
Academic Performance*	
Regular education	47 (46.5)
Special education	46 (45.5)
Not attending school	8 (8)
Family history of epilepsy	33 (32.7)
Family history of neurological disorders	38 (37.6)
Pathological findings on systemic examination	4 (4)
Neurological Examination Findings*	
Mental retardation	57 (56.4)
Motor retardation	43 (42.6)
Microcephaly	29 (28.7)
Syndromic appearance	13 (12.9)
Abnormal EEG *	75 (74.2)
Abnormal MRI*	72 (71.2)
Etiology*	
Unknown	46 (45.5)
Hypoxic-ischemic encephalopathy	13 (12.9)
Structural CNS abnormalities	8 (7.9)
Specific epileptic syndromes	7 (6.9)
Thromboembolism – Infarct	6 (5.9)
CNS infections	5 (5)
Metabolic disorders	5 (5)
Chromosomal anomalies	3 (3)
CNS tumor	3 (3)
Intracranial hemorrhage	3 (3)
Intrauterine infection	1 (1)
Trauma	1 (1)

***:** *n (%),* **†:** *mean±SD (min-max),* **EEG:** *Electroencephalography,* **MRI:** *Magnetic Resonance Imaging,* **CNS:** *Central Nervous System*

Table II: Clinical features related to lev treatment, adverse effects, and follow-up seizure outcomes

Seizure Frequency Before LEV Treatment*	
1 or fewer seizures per year	4 (4)
Less than 1 seizure per 6 months	11 (10.9)
1 or fewer seizures per month	36 (35.6)
More than 1 seizure per month	50 (49.5)
Seizure Duration Before LEV Treatment*	
<1 minute	29 (28.7)
1–5 minutes	34 (33.7)
5–30 minutes	35 (34.7)
Status epilepticus	3 (3)
LEV Treatment Details†	
Age at LEV initiation (years)	10.5±4.5 (0.6-20.5)
Order of LEV usage	3.7±2.1 (1-10)
Initial LEV dose (mg/kg/day)	10.8±4.2 (5-25)
Final LEV dose (mg/kg/day)	27.3 ±10.2
Duration of LEV treatment (months)	21.7±15.08
Adverse Effects of LEV Treatment*	
Any adverse effect observed	46 (45.5)
No adverse effect	55 (54.5)
Types of Adverse Effects Observed*	
Drowsiness / Excessive sleep	14 (13.9)
Irritability	13 (12.9)
Fatigue	9 (8.9)
Aggressiveness*	6 (5.9)
Dizziness	5 (5)
Insomnia	4 (4)
Reduction in aggressiveness	4 (4)
Headache	3 (3)
Vomiting	3 (3)
Loss of appetite	2 (2)
Other	11 (11)
Seizure Frequency at Final Follow-up After LEV Treatment*	
Seizure-free	39 (38)
>50% reduction in seizure frequency	34 (34)
<50% reduction in seizure frequency	8 (8)
No change in seizure frequency	12 (12)
Increased seizure frequency	8 (8)

:** *n (%),* **†:** *mean±SD (min-max),* ***LEV: *Levetiracetam*

development of side effects in patients who were initiated on LEV treatment.

DISCUSSION

Levetiracetam is considered a favorable option for the treatment of childhood epilepsy due to its efficacy and tolerability. Recent studies report LEV efficacy rates ranging from 44% to 94% (8-10). A retrospective study conducted by Tekgül H. et al. (11) in Türkiye, involving 351 pediatric epilepsy patients aged 6 months to 18 years, demonstrated that LEV was effective in 65% of cases following a 12-month follow-up period. Similarly, our findings indicate that LEV was effective in 72.3% of patients. The variability in reported LEV efficacy may be attributed to the significant heterogeneity of study populations.

Initially approved for drug-resistant focal epilepsy in adults, LEV was suggested to be more effective in partial epilepsy. However, multiple studies have found no significant difference in efficacy between generalized and partial epilepsy (12-18). In the present analysis, when end-of-treatment efficacy was evaluated based on seizure type, LEV was effective in 55 of 77 (71.4%) patients with generalized epilepsy and in 18 of 24 (75%) patients with partial epilepsy. No statistically significant difference in efficacy was observed between patients with generalized and partial epilepsy.

A multicenter, double-blind, randomized study comparing patients receiving 4000 mg/day and 2000 mg/day of LEV to those receiving a placebo found LEV to be more effective at a dose of 2000 mg/day, while no significant difference was observed between the 4000 mg/day group and the placebo group (19). In contrast, some studies suggest that higher LEV doses are more effective, whereas others report no significant relationship between LEV dose and efficacy (16,20,21). Additionally, a review by Sourbron et al. (22) highlighted that in children aged 2 months to 12 years, LEV clearance is 30-70% higher compared to adults, indicating that higher LEV doses may be required in this age group. Consistent with these findings, our results demonstrated that the mean LEV dose was significantly lower in patients for whom LEV was effective than in those for whom it was ineffective (p=0.001).

Although studies on LEV efficacy in younger age groups are limited, a retrospective analysis of 122 epilepsy patients under four years old reported a reduction in seizure frequency in 57% of patients, primarily those with partial epilepsy requiring lower LEV doses. Hu et al. (24) studied 120 patients aged four months to four years with refractory epilepsy, finding that after a mean follow-up of 13 months, 38.4% achieved a ≥50% seizure reduction, and 12.5% became seizure-free. Kanmaz et al. (25) examined 67 neonates treated with LEV, reporting that after one year, 76% achieved seizure freedom with LEV monotherapy, and 63.8% showed positive neurodevelopmental outcomes. Arzimanoglou et al. (26) found a 71.8% LEV efficacy rate in 100 infants aged 1-11 months, while Zhao et al. (27) reported a 41% seizure-free rate over 12 months in 78 patients (aged 2-24 months) receiving LEV monotherapy (23-25). In the present study, LEV was effective in 28.6% of patients who started treatment at ≤4 years and in 75.5% of those who started at >4 years (p=0.017). The small sample size for patients under four years old (7/101) may have limited our evaluation, underscoring the need for larger cohorts in future prospective studies.

Studies investigating the relationship between seizure frequency before LEV treatment and LEV efficacy have shown that patients experiencing two or more seizures per month prior to LEV initiation had a poorer response to treatment (23). In this analysis, LEV was significantly more effective in patients who had one or fewer seizures per month before treatment (p =0.012).

Although LEV is generally well tolerated, literature reviews indicate that side effects occur in 7% to 55% of patients (12-

Table III: Efficacy data of LEV in patients initiated on treatment and factors influencing adverse effects

Group	n	Effective Response to LEV Treatment		Patients experiencing adverse effects	
		n (%)	p*	n (%)	p*
Generalized Epilepsy Focal Epilepsy	72 24	55 (71.4) 18 (75)	0.936	-	-
LEV Initiation Age ≤ 4 years LEV Initiation Age > 4 years	7 94	2 (28.6) 71 (75.5)	0.017	2 (28.6) 44 (46.8)	0.450
Pre-Treatment Seizure Frequency ≤ 1 per month Pre-Treatment Seizure Frequency > 1 per month	51 50	43 (84.3) 30 (60)	0.012	22 (43.1) 24 (48)	0.624
LEV Initiated as Adjunctive Therapy LEV Initiated as First-Line Therapy	91 10	63 (69.2) 10 (100)	0.058	41 (45.1) 5 (50)	0.998
Initial Dose <10 mg/kg/day Initial Dose ≥10 mg/kg/day	60 41	44 (73.3) 29 (70.7)	0.952	27 (45) 19 (46.3)	0.894
Final Dose <40 mg/kg/day Final Dose ≥40 mg/kg/day	89 12	65 (73) 8 (66.7)	0.733	40 (44.9) 6 (50)	0.983
LEV Treatment Order ≤ 4 LEV Treatment Order ≥ 5	76 25	56 (73.7) 17 (68.0)	0.769	34 (44.7) 12 (48)	0.958
LEV Treatment Duration ≤ 12 months LEV Treatment Duration > 12 months	37 64	-	-	16 (43.2) 30 (46.9)	0.724
Normal Neurological Examination Abnormal Neurological Examination	51 50	41 (80.4) 32 (62)	0.106	-	-
Normal EEG Abnormal EEG	26 75	22 (84.6) 51 (68)	0.113	-	-
Normal MRI Abnormal MRI	29 72	23 (79.3) 50 (69.4)	0.449	-	-

:** *Pearson Chi-Square test,* ***EEG: *Electroencephalography,* ***MRI:*** *Magnetic Resonance Imaging,* ***LEV:*** *Levetiracetam*

18). In the current study, at least one side effect was observed in 46 patients (45.5%). Additionally, 19 patients (18.8%) had previously experienced side effects from another AED before LEV initiation. Among these, 13 (68.4%) also developed side effects with LEV (p=0.049), suggesting a predisposition to adverse reactions. This finding highlights the importance of reviewing patients' prior AED histories before initiating LEV treatment.

CONCLUSION

This study demonstrated that levetiracetam is an effective, well-tolerated, and safe treatment for childhood epilepsy. Although it may cause side effects or an increase in seizures, these effects were generally mild and transient, not necessitating treatment discontinuation in most patients. Efficacy was higher in children over four years of age, those receiving lower doses, and those with less frequent seizures before treatment. The risk of side effects was found to be higher in patients who had previously experienced side effects from another AED.

Additional information

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Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by The study was approved by the Education Planning and Coordination Committee of the Ankara Children's Health and Diseases Hematology Oncology Education and Research Hospital. (06.02.2012, reference number: 95).

Contribution of the authors

Study conception and design: ***AT, ST***; data collection: ***AT***; analysis and interpretation of results: ***AT, ST***; draft manuscript preparation: ***AT, ST***. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Assessment of enteral nutrition in preterm infants with patent ductus arteriosus undergoing medical treatment

Berrak Naz Kırgıl[1], Abdullah Kurt[2], Burak Ceran[3], Evrim Alyamaç Dizdar[3], Cüneyt Tayman[3], Hazım Alper Gürsu[4]

[1]Department of Pediatrics, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye
[2]Department of Neonatology, Ankara Bilkent City Hospital, Ankara Yıldırım Beyazıt University, Ankara, Türkiye
[3]Department of Neonatology, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye
[4]Department of Pediatric Cardiology, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye

ABSTRACT

Objective: The aim of this study was evaluate the effect of enteral nutrition during treatment in preterms under 32 weeks of gestation with patent ductus arteriosus receiving medical treatment.

Material and Methods: Preterm newborns born before 32 weeks of gestation who received medical treatment for patent ductus arteriosus were categorized into three groups based on their enteral feeding status during treatment: Group A (not fed), Group B (fed <60 ml/kg/day), and Group C (fed ≥60 ml/kg/day). Gastrointestinal system problems and neonatal morbidities were compared with nutritional status. In this retrospective study, 105 patients were included.

Results: Gastrointestinal intolerance was more common in group A, which was never fed (p=0.017) and the time to full enteral nutrition was the longest in this group (p=0.024). In the most fed group C, the time to regain birth weight was the longest (p=0.002). Daily weight gain was the lowest in patients in group A (p=0.022) and mortality was the most common in this group (p=0.003). There was no statistically significant difference in the incidence of bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular hemorrhage and sepsis between fed and unfed infants.

Conclusion: No statistically significant adverse effects of enteral feeding were observed in preterms treated medically for patent ductus arteriosus. This study shows that enteral feeding does not increase gastrointestinal or neonatal morbidities, and that feeding during treatment appears to be safe.

Keywords: Enteral feeding, newborn, patent ductus arteriosus, preterm infant

INTRODUCTION

Patent ductus arteriosus (PDA) is the most common cardiovascular disorder in preterm neonates. Its incidence has been reported to be 79% in extremely low birth weight babies (1). Physiologically, almost all infants have an open duct at birth. The ductus arteriosus connects the proximal left pulmonary artery to the descending aorta just distal to the origin of the left subclavian artery, near where it arises from the main pulmonary artery (2). After birth, the duct closes functionally within 12-24 hours and anatomically within 2-3 weeks (3,4). Low oxygen and high prostaglandin sensitivity in the ductus of preterm infants lead to impaired closure or reopening of the closed ductus by decreasing constriction (5,6). An unclosed duct steals blood flow from the descending aorta to the pulmonary arteries and consequently decreases organ perfusion. Hypoperfusion has been clinically associated with necrotizing enterocolitis, cerebral ischemia, intraventricular hemorrhage, and pulmonary hemorrhage in newborns (7-9). Therefore, hemodynamically significant ductal patency can be treated conservatively, medically, or surgically.

The aim of medical treatment is the inhibition of prostaglandin synthesis (10). The prostaglandin-H2 synthetase enzyme, which has two active sites, cyclooxygenase (COX) and peroxidase

Correspondence Address:
Berrak Naz Kırgıl
e-mail: berraknazbozelli@gmail.com

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(POX), produces circulating prostaglandins that regulate ductal patency (11,12). Among nonsteroidal anti-inflammatory drugs, indomethacin and ibuprofen exert their therapeutic effects by acting on the COX site, while paracetamol targets the POX site. Nonsteroidal anti-inflammatory drugs have many effects on COX, particularly in the cerebral, gastrointestinal, and renal regions (12,13). Surgical ligation is performed in infants with pharmacologically resistant PDA or in those with contraindications to medical therapy (14,15).

In the literature, there are many studies investigating the enteral nutrition status of babies with PDA receiving medical treatment (16-18). There is no complete consensus in the literature on this subject. The optimal management of enteral feeding in preterm infants with a hemodynamically significant patent ductus arteriosus (hsPDA) has long been a subject of considerable debate. Notably, substantial differences of opinion persist among neonatologists regarding this issue. In this study, we investigated the effects of enteral nutrition during treatment and neonatal morbidities in preterm infants with patent ductus arteriosus receiving medical treatment.

MATERIALS and METHODS

The study group consisted of <32-week preterm newborns who received treatment for patent ductus arteriosus between September 2019 and December 2021 at Ankara Bilkent City Hospital Pediatric Neonatology Clinic. Echocardiography (ECHO) was performed in all patients at 72 hours after the postnatal period. HsPDA was diagnosed according to the clinical and ECHO criteria (19). A pediatric cardiologist performed the ECHO examination. Doppler ECHO was performed using a GE Vivid 7 Pro 10S transducer (GE Healthcare, Salt Lake City, Utah). HsPDA was initially treated with either paracetamol or ibuprofen. Patients diagnosed with hsPDA by echocardiography received ibuprofen as the first line for treatment. Paracetamol was administered when ibuprofen was contraindicated. All patients were re-evaluated with clinical and echocardiographic findings after the first course. Patients with persistent hsPDA at the end of the evaluation were treated with the second and third courses. Surgical ligation was performed in patients with persistent hsPDA despite 3 courses of paracetamol or ibuprofen treatment.

Patients receiving PDA treatment were categorized according to their nutritional status during treatment into three groups: Group A was never fed, Group B was fed <60 ml/kg/d, and Group C was fed ≥60 ml/kg/d. All patients were fed with breast milk during hospitalization.

In our study, several clinical parameters- such as birth weight, gestational age, gender, mode of delivery, preterm premature rupture of membrane (PPROM), antenatal steroid usage and Apgar scores - were retrospectively obtained from hospital records and patient charts. We also evaluated nutritional and respiratory outcomes such as time to regain birth weight, days to full enteral feeding, total parenteral nutrition requirement and duration, surfactant use, oxygen requirement and duration, mechanical ventilation use, gastrointestinal bleeding and major morbidities (pulmonary hemorrhage, respiratory distress syndrome [RDS], necrotizing enterocolitis [NEC] stage ≥2, bronchopulmonary dysplasia [BPD], intraventricular hemorrhage [IVH], retinopathy of prematurity [ROP]), as well as discharge weight.

Preterm newborns born at or after 32 weeks of gestation, as well as those with genetic anomalies, pre-existing gastrointestinal problems, or who died before completion of treatment, were excluded from the study.

Statistical analyses

The data were evaluated using the IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA). In the descriptive statistics section, categorical variables are presented as numbers, percentages, and continuous variables are presented as medians (interquartile range). The conformity of continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Mann Whitney-U test was used for comparisons of continuous variables that did not conform to normal distribution. Pearson Chi-Square, Chi-Square with Yates correction, and Fisher exact chi-square tests were used to compare categorical variables. In this study, the statistical significance level was set as $p<0.050$.

RESULTS

A total of 105 neonates were included in the study and categorized into three groups: Group A (n =7), Group B (n = 50), and Group C (n=48). The median gestational age at birth was 28 weeks (26.4–29.8), and the median birth weight was 1075 g (755–1400 g). The median gestational age was significantly lower in Group A [27 weeks (24.4–27.0)] compared to Group C [28 weeks (27.0–29.4)] (p=0.022). In addition, the median birth weight was lowest in Group A [760 g (570–910)] compared to Group B [1050 g (700–1436)] (p=0.024) and Group C [1115 g (860–1400)] (p=0.004). Antenatal steroid administration was more prevalent in Group B (70%) than in Group C (47%) (p =0.044). No statistically significant differences were observed among the groups in terms of 5-minute APGAR scores, PPROM incidence, surfactant use, or the occurrence of RDS (Table I).

Gastrointestinal system intolerance was significantly lower in Group C (35%) compared to Group A (85%) (p=0.017) and Group B (68%) (p=0.020). The median time to transition to full enteral nutrition was significantly shorter in Group C [12 days (11–16)] compared to Group A [29 days (17–29)] (p=0.024) and Group B [17 days (11.5–25.5)] (p=0.023). The median time to regain birth weight was significantly shorter in Group B [8 days (6–11.5)] compared to Group C [12 days (9.2–14)] (p=0.02). The median TPN duration was highest in Group B [15 days

Table I: Descriptive characteristics of patients according to nutritional status

	Group A	Group B	Group C	p		
				B vs A	C vs A	C vs B
Number of patients	7	50	48	-	-	-
Birth week*	27 (24.4- 27.0)	28 (26.2-30)	28 (27- 29.4)	0.066	0.022	0.762[a]
Birth weight (grams)*	760 (570-910)	1055 (700-1436)	1115 (860-1400)	0.024	0.004	0.462[a]
Gender†						
Male	1 (14)	24 (4)	30 (62)	0.122	0.035	0.215[b]
Female	6 (85)	26 (52)	70 (37)			
Birth by C/S†	7 (100)	48 (9)	40 (83)	-	-	0.049[b]
5th minute APGAR*	7 (6-7)	7 (5-7)	6 (6-7)	0.960	0.855	0.953[a]
PPROM†	0 (0)	6 (12)	9 (18)	-	-	0.518[b]
Antenatal steroid†	3 (42)	35 (70)	23 (47)	0.206	1.000	0.044[b]
Surfactant use†	6 (85)	44 (88)	41 (85)	1.000	1.000	0.937[b]
RDS†	6 (85)	45 (90)	42 (87)	0.562	1.000	0.943[b]

****:** Median (IQR), **†:** n(%), **[a]:** Mann Whitney U test was applied, **[b]:** Chi Square test was applied, **C/S:** Ceserrian Section, **PPROM:** Preterm premature rupture of membranes, **RDS:** Respiratory distress syndrome*

Table II: Effects of nutritional status in preterms receiving PDA treatment

	Group A	Group B	Group C	p		
				B vs A	C vs A	C vs B
Number of patients	7	50	48	-	-	-
GIS intolerance*	6 (85)	34 (68)	17 (35)	0.662	0.017	0.002[b]
NEC (stage 2 ≥) within 7 days of treatment*	2 (28)	7 (14)	3 (6)	0.304	0.116	0.318[b]
Time to reach full enteral transition (days)†	29 (17-29)	17 (11.5-25.5)	12 (11-16)	0.208	0.024	0.023[a]
Time to reach birth weight (days)†	9 (4-11)	8 (6-11.5)	12 (9.2-14)	0.661	0.050	0.002[a]
TPN duration (days)†	12 (8-29)	15 (10-24.5)	12 (9-14.7)	0.567	0.810	0.047[a]
Daily weight gain (grams)†	15 (6-15.2)	17.5 (13.8-21.4)	17.8 (14.2-22.2)	0.029	0.022	0.823[a]
GIS bleeding*	1 (14)	5 (10)	1 (2.1)	0.562	0.240	0.205[b]
Pulmonary hemorrhage*	3 (42)	9 (18)	6 (12)	0.154	0.078	0.635[b]

****:** n(%), **†:** Median(IQR), **[a]:** Mann Whitney U test was applied, **[b]:** Chi Square test was applied, **GIS:** Gastrointestinal System, **NEC:** Necrotizing Enterocolits, **TPN:** Total Parenteral Nutrition*

Table III: Neonatal morbidities in preterms receiving PDA treatment

	Group A	Group B	Group C	p		
				B vs A	C vs A	C vs B
Number of patients	7	50	48	-	-	-
IVH*	4 (57)	13 (26)	14 (29)	0.180	0.200	0.901[b]
ROP*	2 (28)	16 (32)	29 (60)	1.000	0.220	0.009[b]
BPD*	3 (42)	36 (72)	38 (79)	0.191	0.061	0.555[b]
Proven sepsis*	4 (57)	26(52)	20(41)	1.000	0.686	0.411[b]
NEC (stage 2 ≥)*	2 (28)	11 (22)	4 (8.3)	0.653	0.163	0.110[b]
Surgical NEC*	1 (1)	3 (6)	3 (6)	0.417	0.429	1.000[b]
Duration of invasive ventilation (days)†	10 (7-28)	11 (6-20.2)	23.5 (4.25-3)	0.817	0.343	0.215[a]
Oxygen duration (days)†	12 (8-74)	39 (21-60.2)	69 (31.2-93.7)	0.576	0.042	0.003[a]
Discharge day (days)†	78 (76-78)	66 (51-83)	78 (55-111.5)	0.203	0.831	0.091[a]
Mortality*	4 (57)	15 (30)	3 (6.3)	0.206	0.003	0.006[b]

****:** Median (IQR), **†:** n(%), **[a]:** Mann Whitney U test was applied, **[b]:** Chi Square test was applied, **IVH:** Intraventricular hemorrhage, **ROP:** Retinopathy of Prematurity, **BPD:** Bronchopulmonary Dysplasia, **NEC:** Necrotizing Enterocolitis*

(10–24.5)] compared to Group C [12 days (9–14.5)] (p=0.047). The median daily weight gain was lowest in Group A [15 g (6–15.2)] compared to Group B [17.5 g (13.8–21.4)] (p=0.029) and Group C [17.8 g (14.2–22.2)] (p=0.022). No statistically significant differences were observed among the groups with respect to NEC (stage ≥ 2) within 7 days of treatment, GIS bleeding, or pulmonary hemorrhage (Table II).

The effect of nutrition on neonatal morbidities is shown in Table III. ROP incidence was highest in Group C (60%) compared to Group B (32%) (p=0.009). The median duration of oxygen therapy was highest in Group C [69 days (31.2–93.7)] compared to Group A [12 days (8–74)] (p=0.042). Mortality was lowest in Group C (6.3%) compared to Group A (57%) (p=0.003) and Group B (30%) (p =0.006). No statistically significant differences were observed among the groups with regard to IVH, BPD, proven sepsis, NEC (stage ≥ 2), surgical NEC, invasive ventilation duration, or length of hospital stay.

DISCUSSION

Patent ductus arteriosus is the most common cardiovascular disease in preterm newborns. In the preterm population, where ductal closure is delayed, ductus-related systemic hypoperfusion effects and related complications are observed. Gastrointestinal system problems are one of these complications. There is no consensus in the literature regarding nutritional management in infants with PDA. In a study by Louis et al.(17) in 415 preterms receiving indomethacin for PDA treatment, patients were divided into three groups: never fed, ≤60 ml/kg/d, and >60 ml/kg/d fed. The effect of enteral feeding on the gastrointestinal system and neonatal morbidities were evaluated, it was found that enteral feeding volume change during and after treatment did not affect the incidence of NEC, gastrointestinal system intolerance, or prematurity-related morbidities. In the same study, the duration of transition to full enteral nutrition and total parenteral nutrition (TPN) duration was found to be the longest in patients receiving low enteral feeding volume (17). Kelleher et al. (20) investigated the incidence of spontaneous intestinal perforation in 15751 LBW infants who received prophylactic indomethacin treatment in the first 3 days of life to prevent PDA and IVH. Infants who received early enteral feeding reached full enteral nutrition on a shorter day, and the total duration of parenteral nutrition was found to be less, regardless of indomethacin treatment (20). In our study, the duration of transition to full enteral nutrition was found to be the longest in group A and the shortest in group C, and a statistically significant difference was found (C vs A p=0.024, C vs B p=0.023). The shortest duration in group A may be related to the highest mortality rate in group A patients.

In a study by Clyman et al. (16) with 177 preterms with PDA receiving indomethacin or ibuprofen, patients were divided into two groups as trophic fed and non-fed, and the effect of nutrition on gastrointestinal effects and morbidities were evaluated. The study showed that there was no significant difference in NEC rates or other neonatal morbidities between the two groups, but it took 2.8 days to reach full enteral nutrition in the trophically fed group (16). In this study, gastrointestinal intolerance was found in 85.7% of patients in group A, 68.0% in group B, and 35.4% in group C (A vs C p=0.017, B vs C p=0.002). In this study, there was no statistically significant difference in NEC incidence among the groups. However, NEC was observed more often in infants who were fed less. Daily weight gain was highest in group C and lowest in group A. Although the time to reach birth weight was the longest in group C, the patients in group C had the highest discharge weight. The discharge weight was 2210 g in group B and 2784 g in group C patients. The longer time to reach birth weight in the most fed group may also be related to the long-term preterm morbidities of the patients. In this group, ROP, ventilation time, oxygen exposure, and discharge times were higher in other groups resulting in a prolonged hospital stay. This study contributes to the literature in this regard. The main limitation of this study is its retrospective design. Because of the small number of patients, further and larger scale studies are needed.

CONCLUSION

PDA can be associated with severe gastrointestinal complications such as feeding intolerance, gastrointestinal perforation, and necrotizing enterocolitis, which pose a major challenge in the nutritional management of preterm infants. Guidelines should be developed to clearly define the administration and course of enteral nutrition and target nutrient intake before, during, and after the medical treatment of PDA. In preterm infants with PDA, fluid restriction is used in the management of PDA, but this may lead to inadequate nutrient intake. This may lead to long-term adverse effects such as impaired growth and development in preterm infants.

The results of this study suggest that feeding during medical therapy does not significantly affect mesenteric blood flow and splanchnic oxygenation after enteral feeding in infants with PDA. We may recommend that enteral feeding should not be interrupted; rather, it should be initiated or continued in infants with PDA.

In preterm infants who received medical treatment, it was observed that gastrointestinal system intolerance and mortality were less, the transition time to full enteral feeding was shorter, and daily weight gain was higher in those who received enteral feeding during treatment. In this study, it was not observed that feeding increased the incidence of BPD, IVH, sepsis, and NEC. In addition, feeding during PDA treatment did not have a negative effect on the duration of invasive ventilation, inotrope use, or discharge day. This study shows that feeding during the medical treatment of PDA is beneficial and does not increase gastrointestinal and neonatal morbidities.

Ethics committee approval

This study was granted ethical approval by Ankara Bilkent City Hospital Ethics Committee under reference number E2-21-1162 on December 22, 2021.

Contribution of the authors

Study conception and design: ***BNK,AK,CT;*** data collection: ***BNK, AK, EAD, HAG;*** analysis and interpretation of results: ***BNK, AK ,BC ,EAD, HAG;*** draft manuscript preparation: ***BNK, BC, CT.*** All authors reviewed the results and approved the final version of the article

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The authors declare that there is no conflict of interest.

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Original Article

Evaluation of basic life support training provided to mothers of preterm infants

Okan Şahin[1], Sabriye Korkut[2], Sara Erol[2]

[1]Department of Pediatrics, Ankara City Hospital, University of Health Sciences, Ankara, Türkiye
[2]Department of Neonatology, Ankara City Hospital, University of Health Sciences, Ankara, Türkiye

ABSTRACT

Objective: Preterm infants admitted to neonatal intensive care units (NICUs) are at an increased risk of requiring basic life support (BLS). This study aimed to evaluate the impact of BLS training on the knowledge and anxiety levels of mothers of preterm infants.

Material and Methods: This prospective descriptive study included mothers of preterm infants born at less than 37 weeks of gestation who were either discharged from the NICU or being treated in the mother-infant adaptation unit. Participants were provided with BLS training using visual materials. A questionnaire assessing knowledge levels and the State-Trait Anxiety Inventory (STAI Form TX-1 and TX-2) were administered before and after the training. Pre- and post-training questionnaire responses and anxiety scores were analyzed.

Results: A total of 100 mothers participated in the study. Post-training knowledge levels regarding BLS significantly improved ($p<0.001$). State and trait anxiety scores significantly decreased after the training ($p<0.001$). Mothers with a university education had higher pre-training knowledge scores compared to those with primary or secondary education ($p<0.001$); however, post-training knowledge levels were similar across all educational groups ($p = 0.600$).

Conclusion: BLS training increased knowledge levels and reduced anxiety among mothers of preterm infants. Therefore, developing and disseminating appropriate BLS training programs for parents may play a crucial role in improving public health. Moreover, reducing parental anxiety through such training could contribute to enhancing the quality of neonatal care.

Keywords: Preterm, mother, parent, basic life support, education, anxiety

INTRODUCTION

Basic life support (BLS) involves life-saving interventions performed without the use of medications, such as establishing airway patency, providing ventilation support, and performing chest compressions to maintain circulation. These interventions are simple yet effective measures applied to preserve vital functions until professional healthcare personnel arrive at the scene (1). Therefore, it is critical for the general population to possess basic knowledge about BLS. Regular BLS training for lay rescuers has been shown to improve survival rates and reduce long-term sequelae in cases of out-of-hospital cardiac arrest (2).

Globally, each year, 15 million babies are born preterm, which is estimated to be about 11% of all deliveries (3). The risk of mortality and both short- and long-term morbidity increases as gestational age decreases (4). The risk of mortality is increased in neonates who are premature and/or have low birth weight for gestational age, and this risk continues until the second month of life (5). Even after discharge from the neonatal intensive care

Correspondence Address:
Okan Şahin
e-mail: drokan3865@gmail.com

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unit (NICU), preterm infants remain at risk for mortality. Studies have shown that 1-2% of preterm infants experience mortality after discharge until their corrected ages of 22 to 26 months (6). Therefore, discharge decisions for these infants should consider the caregivers' ability to assess vital signs, recognize pathological findings, and perform BLS procedures with adequate skill and confidence (7).

Caring for a high-risk infant post-discharge is a significant source of anxiety for parents. Non-healthcare professionals may experience heightened anxiety due to the fear of being unable to respond appropriately to a life-threatening situation requiring BLS. Parental education on this topic not only improves post-discharge care but also helps alleviate parental anxiety (8).

The primary objective of this study was to investigate the impact of BLS training on the knowledge and anxiety levels of mothers of preterm infants. Secondary objectives included assessing the influence of maternal and infant characteristics on these knowledge and anxiety levels following BLS training.

MATERIALS and METHODS

This prospective descriptive study was conducted between September 2023 and December 2023 at the NICU of Ankara City Hospital. The study included mothers of preterm infants born at less than 37 weeks of gestational age who were either discharged from the NICU or being treated in the mother-infant adaptation unit.

Sample Size: A previous study showed that 40% of parents were knowledgeable about basic life support (BLS), specifically chest compressions and ventilation. To detect a significant 50% increase in knowledge levels following BLS training, the required sample size was calculated as 97 participants, with 80% power and a 0.05 alpha level. Considering potential data loss, the study included 100 participants.

Inclusion Criteria: Mothers of preterm infants born at less than 37 weeks of gestational age at Ankara Bilkent City Hospital who voluntarily agreed to participate in the study.

Exclusion Criteria: Mothers unable to communicate due to language problems or cognitive impairment. Participants who initially enrolled but later withdrew from the study.

BLS Training and Questionnaire Administration: The BLS training was conducted by study physicians and neonatal nurses in either the mother-infant adaptation unit or neonatal outpatient clinic. Training sessions were planned for one or two participants at a time and included visual materials such as images and infant mannequins. The content and BLS algorithm were designed based on the 2020 American Heart Association (AHA) Pediatric BLS and Cardiopulmonary Resuscitation guidelines (9).

Each BLS training session lasted approximately 30 minutes and included hands-on practice using infant mannequins and visual slides. The BLS knowledge questionnaire used in this study was developed by the researchers based on current guidelines. The BLS knowledge questionnaire was originally developed to reflect the full content of BLS education.

Before the training, participants completed a questionnaire comprising:

Seven questions about demographic characteristics.

Ten questions assessing BLS knowledge.

The same BLS-related 10-question section was administered again after the training. No time limit was imposed for answering the questionnaire, and responses were recorded in written form.

Assessment of Anxiety Levels: To evaluate anxiety levels, the following two forms were administered to participants both before and after the training: State Anxiety Inventory (STAI Form-I): A 20-item scale assessing transient anxiety experienced in response to specific situations or events. Trait Anxiety Inventory (STAI Form-II): A 20-item scale assessing a person's general predisposition to anxiety (10).

State anxiety reflects temporary feelings of tension and worry triggered by particular situations, while trait anxiety represents a more enduring sense of nervousness and stress.

In addition to the survey responses, a study form was completed containing infants' demographic data and length of stay in the Neonatal Intensive Care Unit.

Statistical analyses

The normality of data distribution was assessed using the Shapiro-Wilk test. Descriptive statistics for non-normally distributed variables were expressed as medians (25th percentile–75th percentile). The Wilcoxon signed-rank test was used for paired comparisons of two dependent groups. Chi-square tests were applied for comparisons of categorical variables between groups. Spearman's correlation analysis was conducted to examine relationships between continuous variables, with correlation coefficients reported as Rho. A p-value of <0.050 was considered statistically significant for all tests.

RESULTS

A total of 100 mothers of premature infants participated in the study. The demographic characteristics of the mothers and their infants are presented in Table I. Among the participants, 25% had previously received BLS training, 11% had prior experience with BLS, and 7% had previously applied BLS to their own child. Additionally, 3% of the participants were healthcare workers.

The knowledge level of the mothers participating in the study increased after the BLS training, and both state and trait anxiety scores decreased ($p<0.001$) (Table II).

The BLS knowledge level was compared according to education level. The knowledge level of university graduate mothers before

Table I: Characteristics of mothers and newborns

Variable	n (%)
Maternal Age (years)	
18-24	27 (27)
25–35	55 (55)
>36	18 (18)
Number of Children	
1	15 (15)
2–3	46 (46)
≥ 4	39 (39)
Education Level	
Primary	8 (8)
Secondary	51 (51)
University	41 (41)
Gestational Age (weeks)	
34–36	55 (55)
32–33	19 (19)
28–31	19 (19)
<28	7 (7)
Birth Weight (grams)	
>2500	27 (27)
2500–1500	46 (46)
1500–1000	16 (16)
<1000	11 (11)
Duration of NICU Stay (days)	
Median (IQR)	15 (5–45)

Data are presented as number (percentage) or median (interquartile range). ***NICU:*** *Neonatal Intensive Care Unit*

Table II: Comparison of pre-and post-training knowledge, state anxiety, and trait anxiety scores

Variable	Pre-Training Median (25th–75th p)	Post-Training Median (25th–75th p)	p
Knowledge Level	6 (4–7)	10 (9–10)	<0.001
State Anxiety Score	35.0 (30.0–41.0)	32.0 (29.0–37.7)	<0.001
Trait Anxiety Score	38.5 (32.0–45.0)	35.0 (29.0–42.0)	<0.001

Data are presented as median (25th–75th percentile)

the training was found to be higher than the other groups (p<0.001). The knowledge level after the training was found to be similar between the education groups (p=0.600). State and trait anxiety scores before and after the training were similar in the education groups (p>0.050).

Prior to the training provided in this study, the baseline knowledge levels of mothers with and without previous BLS training were compared. Participants who had received BLS training previously had a significantly higher mean number of correct answers compared to those without prior training (p<0.001). When the knowledge levels of participants who received and did not receive BLS training were evaluated separately after the training, the increase in knowledge levels was found to be statistically significant (p<0.001).

Both before and after the training knowledge levels were similar between the child number groups (p>0.050).

Table III. Number of correct answers in the questionnaire before and after BLS training

Questions	Pre-Training n (%)	Post-Training n (%)	p
1. What is the first thing you should do when encountering a situation requiring BLS?	28 (28)	94 (94)	<0.001
2. What is the first thing you assess in an infant requiring BLS?	29 (29)	93 (93)	<0.001
3. How do you assess the infant's consciousness?	69 (69)	99 (99)	<0.001
4. By which method is the infant's breathing assessed?	81 (81)	98 (98)	<0.001
5. If you are alone and without a phone in a situation requiring BLS, what should you do?	49 (49)	95 (95)	<0.001
6. If you are alone with a phone in a situation requiring BLS, what should you do?	87 (87)	97 (97)	0.009
7. When providing BLS and there is no suspicion of trauma, how should you open the airway?	61 (61)	93 (93)	<0.001
8. In BLS performed alone, what is the chest compression-to-rescue breath ratio?	15 (15)	96 (96)	<0.001
9. Where should chest compressions be applied during CPR?	74 (74)	100	<0.001
10. What constitutes effective chest compressions in an infant?	69 (69)	98 (98)	<0.001

Data are presented as number (percentage), ***BLS:*** *Basic Life Support,* ***CPR:*** *Cardiopulmonary Resuscitation*

The correlation between the length of stay in the NICU and anxiety levels was evaluated. A positive correlation was found between the length of stay in the NICU and the trait anxiety level both before and after the training. (Rho=0.33, p=0.001) (Rho=0.40, p=0.001), respectively. No significant correlation was found between the length of stay in the NICU and the state anxiety level both before and after the training (p>0.050).

While no correlation was found between the gestational week and the state anxiety after the training (Rho=-0.19, p=0.060), a weak-moderate negative correlation was observed between the trait anxiety after the training (Rho=-0.36, p=0.001).

The answers given by the participants to the knowledge level questionnaire were compared before and after the training. The rate of correct answers to all questions after the training was found to be higher than before the training (p<0.050) (Table III).

DISCUSSION

Preterm infants monitored in NICUs are at a higher risk of requiring BLS, particularly during the early post-discharge period, compared to the general population. One study indicated that families encountering situations requiring BLS often panicked and attempted to transport their children to the hospital rather than performing initial life-saving measures (11). This response reduces the likelihood of timely and effective intervention, adversely impacting outcomes.

In our study, the effects of BLS training on both the knowledge and anxiety levels of mothers of preterm infants were evaluated. The findings demonstrated that BLS training significantly increased knowledge levels while reducing both state and trait anxiety scores.

In the 'Children Save Lives' recommendation approved by WHO in 2015, the starting age for BLS training was shown as 12 (12). Starting BLS training at an early age, repeating and expanding practical skills throughout school life ensures that society has people who can intervene in emergencies, normalizes first aid learning, and increases the desire to intervene when faced with an emergency (13). Seventy-five percent of the mothers in our study reported that they had never received BLS training before, 11% had encountered a situation requiring BLS, and 7% had experienced a BLS event involving their own child. These rates highlight the necessity of education on this topic.

In our study, the proportion of correct answers to BLS knowledge questions ranged from 40% to 70% before training, increasing to 90% to 100% after training. Similarly, a study conducted with newborn parents in Turkey showed that correct answer rates, which ranged between 36.8% and 86.8% before training, increased to 86.2% and 99.2% after training (14). In our study, a statistically significant increase was observed in the number of correct responses for all 10 BLS knowledge questions post-training.

The fact that 25% of the participants had previously received BLS training may have influenced the primary outcome. When we compared participants with and without prior BLS training, there was a significant difference in their pre-training knowledge levels. However, post-training knowledge scores increased significantly for both participants, reaching similar levels. These findings indicate that lay rescuers can apply BLS steps accurately and effectively with appropriate training.

Neither the age of the mothers nor the number of children they had impacted their knowledge levels before or after the training. However, there was a significant difference in knowledge levels based on education levels. Mothers with a university degree had higher pre-training knowledge levels compared to those with primary or secondary education. However, this difference disappeared post-training, suggesting that BLS education can equalize knowledge levels across different educational backgrounds, enabling lay rescuers to apply BLS steps correctly regardless of their education or age.

During the neonatal period, mothers often feel a lack of confidence in caring for their infants. The health and safety of their babies are significant sources of anxiety, particularly for first-time mothers (15). The inability to respond appropriately to emergencies requiring BLS can exacerbate this anxiety (15, 16). In our study, there were no significant differences in state or trait anxiety scores before and after BLS training among groups stratified by the number of children they had.

Mothers who feel more prepared to handle potential emergencies may experience reduced overall anxiety (17). Mothers knowledgeable about BLS can respond to emergencies more calmly and effectively (18). Therefore, providing BLS training during the prenatal or postnatal period can enhance mothers' knowledge and confidence, thereby reducing their anxiety levels.

One study found that mothers of extremely preterm infants were more anxious compared to mothers of moderately preterm infants. This study demonstrated an association between gestational age and state anxiety only (19). In our study, a weak-to-moderate correlation was observed between gestational age and post-training trait anxiety. This finding may be explained by the increased concern among mothers as the degree of prematurity rises, leading to a heightened awareness of the potential need for BLS.

A positive correlation was identified between NICU length of stay and trait anxiety levels both before and after BLS training. This finding suggests that longer NICU stays and increased awareness of BLS may lead to temporary anxieties becoming persistent.

Studies have shown that 10-20% of mothers experience anxiety or depressive disorders during the postpartum period, which can negatively impact the mother, child, and family (20). In our study, BLS training reduced both state and trait anxiety scores among mothers, suggesting that providing such training could alleviate postpartum anxiety and positively affect infant care.

One study linked higher education levels to an increased risk of anxiety (21). However, in our study, no significant relationship was found between education level and state or trait anxiety scores either before or after BLS training. This could be due to the fact that the majority of participants in our study were either high school or university graduates, resulting in minimal variation in educational levels.

Limitations

This study has certain limitations. First, the anxiety levels might have been influenced by the hospital environment during data collection. Second, long-term retention of BLS knowledge was not evaluated. In anticipation of difficulties in reaching participants after discharge, the post-training survey was administered on the day of training or the following day.

Future studies should include follow-up assessments to evaluate long-term knowledge retention and behavioral outcomes.

CONCLUSION

In conclusion, our study demonstrated that BLS training significantly increased knowledge levels and reduced anxiety among mothers of preterm infants. Developing and disseminating appropriate BLS training programs for parents could play a crucial role in reducing mortality and morbidity through timely interventions, thereby improving public health. Additionally, reducing anxiety levels through such training may enhance parental self-efficacy and contribute to improved neonatal care quality.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. Ethical approval was obtained from the Ethics Committee of Clinical Research No. 2 at Ankara Bilkent City Hospital (July 19, 2023/ E2-23-4577).

Contribution of the authors

Study conception and design: ***OS, SK;*** data collection: ***OS;*** analysis and interpretation of results: ***OS, SE, SK;*** draft manuscript preparation: ***OS, SK, SE.*** All authors reviewed the results and approved the final version of the article.

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The authors declare that there is no conflict of interest.

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Original Article

Health literacy levels of adolescents and their parents visiting a pediatric outpatient clinic

Mahmut Talha Uçar[1], Busenur Ergül[2], Esra Çiçek[3], Selman Aktaş[4], Çağatay Nuhoğlu[2]

[1]Department of Public Health Specialist, Hamidiye Faculty of Medicine, University of Health Sciences, İstanbul, Türkiye
[2]Department of Pediatrics, Haydarpaşa Numune Training and Research Hospital, University of Health Sciences, İstanbul, Türkiye
[3]Konya Provincial Health Directorate, Konya, Türkiye
[4]Department of Biostatistics, Hamidiye Faculty of Medicine, University of Health Sciences, İstanbul, Türkiye

ABSTRACT

Objective: This study aimed to assess the health literacy (HL) levels of adolescents and their parents attending the pediatric outpatient clinic of a training and research hospital and to evaluate the hypothesis that HL correlates with serum 25-hydroxyvitamin D3 levels, serum vitamin B12 (cobalamin) levels and sociodemographic characteristics.

Material and Methods: This descriptive cross-sectional study included 302 adolescents aged 14 years and older, along with their parents, who attended the general pediatrics outpatient clinic of Haydarpaşa Numune Training and Research Hospital from November to December 2022. Data were collected using a sociodemographic information form, serum 25-hydroxyvitamin D3 levels, serum vitamin B12 levels of adolescents according to hospital records, the Hacettepe University Health Literacy Scale-Long Form (HU-HL) for parents, and the Adolescent e-Health Literacy Scale (eHEALS) for adolescents. Non-parametric statistical tests were used due to the non-normal distribution of the data.

Results: The mean age of adolescents was 15.47±1.09 years, with 56% identified as female. The mean age of the parents was 44.49±5.02 years, with 84.8% being mothers. Among parents, 21.2% exhibited low HL levels, 57.3% shown moderate levels, and 21.5% displayed high levels. The average total score of eHEALS was 27.78±5.40. Female parents exhibited markedly superior HL scores compared to male parents ($p=0.003$). Serum 25-hydroxyvitamin D3 (25(OH)D3) levels, serum vitamin B12 (cobalamin) levels, as well as body mass index (BMI), exhibited no significant correlation with HL scores. Nonetheless, parents of female adolescents had markedly higher HL scores compared to those of male adolescents ($p=0.013$).

Conclusion: Parents of female adolescents demonstrated significantly higher HL levels than those of male adolescents. These findings underscore the need for targeted interventions to address HL disparities among caregivers and adolescents. Future research should explore longitudinal and causal relationships between HL and biological as well as sociodemographic determinants.

Keywords: Adolescent, health literacy, parents

INTRODUCTION

The concept of health literacy (HL) was first proposed by Simonds in Health Education as Social Policy, which emphasized the importance of HL on national health and the provision of the most basic HL education for students in schools (1). Baker proposed that HL is an important predictor of health status and outcomes (2). Health literacy denotes an individual's ability to access, comprehend, assess, and utilize health-related information and services to sustain optimal health and well-being (3). Health literacy is a complex concept with implications at the individual, family, societal, and systemic levels. The framework encompasses cognitive and functional skills, including reading, comprehending, and analyzing information; interpreting symbols, instructions, and graphical data; assessing health risks and benefits; and making informed decisions (4). Health literacy is an important issue in public health today, especially as patients are taking a greater role in obtaining information about their health. In a study examining the HL level of parents in the management of type 1 diabetes in children and adolescents, it was reported that one in every two parents had problematic, limited and inadequate HL

Correspondence Address:
Mahmut Talha Uçar
e-mail: drtalhaucar@gmail.com

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levels (5). Parental HL is the best-known household facilitator of adolescent HL (6). A comprehensive review of HL among adolescents and young adults in the Eastern Mediterranean region found low-to-moderate levels of HL among adolescents and young adults in the Eastern Mediterranean region (7).

Health literacy is an important factor in disease prevention and control (8). A study assessing the correlation between HL and blood parameters in hypertensive patients revealed that those with high literacy exhibited lower total cholesterol and HDL-C levels compared to those with poor literacy (9). A study investigating HL in hypertensive patients with renal illness was found to correspond with specific blood indicators, including fasting blood glucose and estimated glomerular filtration rate (10). A study investigating the significance of metabolic, hematological, and functional health, along with parental HL in adults with Down syndrome, indicated that the overall health literacy score correlated with hemoglobin and hematocrit levels (11).

Notwithstanding the acknowledged significance of HL, data regarding the concurrent assessment of adolescent and parental HL in Türkiye are limited. This study aimed to assess the HL levels of adolescents and their parents at a pediatric outpatient clinic in a training and research hospital, and to evaluate the hypothesis that HL levels correlate with serum 25-hydroxyvitamin D3 (25(OH)D3) levels, serum vitamin B12 (cobalamin) levels and sociodemographic characteristics.

MATERIALS and METHODS

This cross-sectional study design was used. The study population comprised 302 adolescents aged 14 years and older, accompanied by one parent, who attended the general pediatrics outpatient clinic of Haydarpaşa Numune Training and Research Hospital between November and December 2022. Only literate individuals who gave their voluntary consent were included in the study. Those who were illiterate or failed to provide informed consent were excluded from the study.

Data Collection Tools

Data was collected using three instruments: a sociodemographic information form, the Hacettepe University Health Literacy Scale-Long Form (HU-HL) for parents, and the Adolescent e-Health Literacy Scale (eHEALS) for adolescents. The questionnaires were self-administered by participants under supervision to guarantee precision and accuracy. The researchers measured anthropometric data (height and weight) in the outpatient clinic, while serum 25-hydroxyvitamin D3 (25(OH)D3) levels, serum vitamin B12 (cobalamin) levels were retrieved from hospital records.

The sociodemographic information form comprised items evaluating participants' age, gender, educational attainment, income-expenditure ratio, and smoking status. Furthermore, the height and weight of adolescents were assessed to compute body mass index (BMI), and serum 25-hydroxyvitamin D3 (25(OH)D3) levels, serum vitamin B12 (cobalamin) levels were retrieved from hospital records. BMI categories were determined based on WHO 2007 growth reference for children and adolescents aged 5–19 years, using BMI-for-age percentiles: underweight (<5th percentile), normal (5th–85th), overweight (85th–95th), and obese (≥95th percentile). Serum 25(OH)D3 levels were categorized as follows: deficiency (<20 ng/mL), inadequacy (20–29 ng/mL), and normal (≥30 ng/mL), based on the Endocrine Society guidelines (12,13).

The Hacettepe University Health Literacy Scale, validated and reliable, was established by Özvarış et al. (14) and comprises 38 questions totaling 71 items, along with an additional self-efficacy section with 16 items. Items are evaluated with a score of 0 or 1, contingent upon accuracy. The overall score varies from 0 to 71, with elevated levels signifying superior health literacy. This study reported Cronbach's alpha values of 0.82 for the subdimension "Health Protection and Promotion," 0.91 for "Access to Treatment and Health Services," and 0.92 for the total scale. The self-efficacy part, evaluated independently had a Cronbach's alpha of 0.84. Health literacy levels were classified as follows: 0–32 (inadequate), 33–52 (moderate), and 53–71 (adequate) (14).

The Adolescent e-Health Literacy Scale, first developed by Norman and Skinner and then modified into Turkish by Coşkun and Bebiş, comprises 10 items. Two items were assessing internet usage and eight were assessing perceived e-health literacy. Responses are evaluated on a 5-point Likert scale (1=strongly disagree to 5=strongly agree), yielding total scores between 8 and 40. Elevated scores indicate enhanced e-health literacy (15). The Cronbach's alpha was 0.78 in the original study and 0.817 in the current sample.

This study did not involve pilot testing for item clarity or cultural adaptation within the sample. Participants were notified prior to the commencement of data collection, and written informed consent was obtained from the volunteers on behalf of themselves and the adolescents.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA) for the Windows operating system. The mean and standard deviation (SD) were calculated for the quantitative data. The data distribution was presented using numerical tables (n) and percentages (%). The distribution normality for each parameter was assessed using the Kolmogorov-Smirnov test. The data acquired from this investigation exhibited a non-normal distribution. The Mann–Whitney U test and the Kruskal–Wallis test were employed to compare the medians of two separate groups and multiple independent groups, respectively. Upon detecting significant differences in the Kruskal–Wallis analysis, pairwise comparisons were performed utilizing the Mann–Whitney U test to ascertain the source of the discrepancy. The statistical significance was accepted as $p<0.050$.

RESULTS

A total of 302 adolescents participated in the study. The mean age was 15.47±1.09 (13-18 years), with 56.0% being female. A significant majority (96.4%) remained enrolled in high school. While 18.2% stated that they smoked at least once, the remaining 81.8% had never smoked. The average height and weight were 166.99±8.58 cm and 62.14±13.92 kg, respectively, yielding a mean BMI of 22.18±4.08. The mean values of serum 25-hydroxyvitamin D3 (25(OH)D3) levels, serum vitamin B12 (cobalamin) levels were 17.60±8.78 ng/mL and 304.10±119.98 pg/mL, respectively. Of the 302 participating parents, 84.8% were female, with an average age of 44.49±5.02 (32-65 years). In terms of educational achievement, 33.1% completed primary school or lower, 25.8% completed secondary school, 31.1% completed high school, and 9.9% obtained a university degree. Regarding income status, 58.9% indicated that their income matched their expenses. A majority of parents (69.9%) classified themselves as housewives. Furthermore, 27.5% of subjects reported smoking daily. The average number of children per parent was 2.59 ±0.97 (Table I).

Table I: Descriptive characteristics of the study participants

Adolescents	
Age*	15.47±1.09 (13-18)
Height† (cm)	166.99±8.58
Weight† (kg)	62.14±13.92
BMI† (kg/m²)	22.18±4.08
25(OH)D3 levels† (ng/mL)	17.60±8.78
Serum vitamin B12 (cobalamin) levels† (pg/mL)	304.10±119.98
Gender‡	
Male	133 (44.0)
Female	169 (56.0)
School attendance‡	
No formal education	9 (3.0)
Secondary school	2 (0.7)
High school	291 (96.4)
Smoking status, ever smoked‡	
No	247 (81.8)
Yes	55 (18.2)
Parents	
Age*	44.49±5.02 (32-65)
Number of children†	2.59±0.97
Gender‡	
Male	46 (15.2)
Female	256 (84.8)
Education level‡	
Primary school or below	100 (33.1)
Secondary school	78 (25.8)
High school	94 (31.1)
University degree	30 (9.9)
Parents smoking‡	
Never	169 (56.0)
Less than daily	50 (16.6)
Daily	83 (27.5)
Employment status‡	
Housewife	211 (69.9)
Worker	20 (6.6)
Tradesmen	14 (4.6)
Self-employed	14 (4.6)
Other	43 (14.2)
Economical situation‡	
Income less than expenditure	99 (32.8)
Income equal to expenditure	178 (58.9)
Income more than expenditure	25 (8.3)

***:** *mean±SD (min–max),* **†:** *mean±SD,* **‡:** *n(%),* **BMI:** *Body Mass Index,* **25(OH)D3:** *Serum 25-hydroxyvitamin D*

Table II: Education level of parents

Education level	**male***	**female***
Primary school or below	12 (26.1)	88 (34.4)
Secondary school	3 (6.5)	75 (29.3)
High school	25 (54.3)	69 (27.0)
University degree	6 (13.0)	24 (9.4)

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

Table III: Health literacy levels of the study participants

Measure	**mean±SD**
Adolescent e-Health Literacy Total Score	27.78±5.40
HU-HL Health Protection and Promotion Subdimension	11.50±3.59
HU-HL Access to Treatment and Health Services Subdimension	30.55±9.04
HU-HL Total Score	42.04±11.85
HU-HL Self-Efficacy Scale Total Score	39.57±5.26

HU-HL: *Hacettepe University Health Literacy*

In our study, 21.2%, 57.3%, and 21.5% of the parents exhibited inadequate, moderate and adequate levels of health literacy, respectively.

Of the mothers surveyed, 34.4% completed primary school or less, 29.3% attained secondary school education, 27.0% finished high school, and 9.4% obtained university degrees (Table II).

The average overall score for eHEALS was 27.78±5.40. The average score for the Health Protection and Promotion subdimension of the HU-HL scale was 11.50±3.59, but the Access to Treatment and Health Services subdimension recorded a mean of 30.55±9.05. The cumulative HU-HL score was 42.05±11.85. The average total score of the Self-Efficacy Scale was 39.57±5.26 (Table III).

In the comparison of scale scores according to adolescent characteristics, female participants exhibited significantly higher scores than their male counterparts in the HU-HL Health Protection and Promotion subdimension (p=0.016), the Access to Treatment and Health Services subdimension (p=0.026), and the overall HU-HL score (p=0.013). No statistically significant differences were detected in the total score of eHEALS, BMI categories, smoking history, educational attainment or serum 25-hydroxyvitamin D3 (25(OH)D3) levels (Table IV).

Table IV: Comparison of adolescents' descriptive characteristics based on HU-HL Scale Scores

Characteristic	Adolescent e-Health Literacy Total Score*	p	HU-HL: Health Protection & Promotion*	p	HU-HL: Access to Treatment & Services*	p	HU-HL Total Score*	p
Gender								
Male	29 (12-40)	0.167†	10 (3-20)	0.016†	28 (6-48)	0.026†	39 (12-67)	0.013†
Female	28 (14-40)		12 (3-20)		33 (5-47)		44 (9-65)	
School Attendance								
No formal education	30 (25-39)	0.345‡	11 (3-17)	0.056‡	22 (14-46)	0.235‡	36 (17-63)	0.132‡
Secondary school	29 (26-32)		5.5 (5-6)		21 (16-26)		26.5 (22-31)	
High school	28 (12-40)		11 (3-20)		31 (5-48)		42 (9-67)	
Ever smoked tobacco								
No	28 (12-40)	0.691†	11 (3-20)	0.675†	30 (5-48)	0.311†	41 (9-67)	0.404†
Yes	28 (14-40)		11 (4-20)		31 (7-47)		43 (16-67)	
BMI Category								
Underweight	29 (16-37)	0.632‡	10 (5-19)	0.074‡	28 (7-48)	0.173‡	39 (16-67)	0.083‡
Normal weight	28 (12-40)		11 (3-20)		31 (6-48)		41 (12-65)	
Overweight	30 (19-37)		12 (3-18)		33 (5-47)		45 (9-65)	
Obese	28 (12-40)		12.5 (8-20)		35.5 (7-47)		49 (16-67)	
(25(OH)D3) levels								
Deficiency	29 (14-40)	0.473‡	11 (3-20)	0.083‡	31 (5-48)	0.922‡	42 (9-67)	0.649‡
Inadequacy	28 (14-38)		12 (5-19)		31 (13-48)		41 (21-65)	
Normal	28 (12-40)		12 (6-19)		28 (8-46)		40 (18-64)	

:** *median (min–max),* **†:** *Mann–Whitney U test,* **‡:** Kruskal Wallis test, ***BMI: *Body Mass Index,* **HU-HL:** *Hacettepe University Health Literacy,* ***25(OH)D3:*** *Serum 25-hydroxyvitamin D*

Table V: Comparison of parental characteristics based on HU-HL Scale Scores

Measure	Fathers of Adolescents*	Mothers of Adolescents*	p†
Adolescent E-Health Literacy Total Score	28 (20-38)	28 (12-40)	0.718
HU-HL Health Protection and Promotion Subdimension	9 (4-19)	11 (3-20)	0.005
HU-HL Access to Treatment and Health Services Subdimension	28 (7-46)	32 (5-48)	0.005
HU-HL Total Score	36.5 (16-64)	43 (9-67)	0.003

:** *median (min–max),†:** *Mann Whitney U test,* **HU-HL:** *Hacettepe University Health Literacy Scale*

In the comparison of parental HL scores, mothers exhibited significantly superior scores compared to fathers in the HU-HL Health Protection and Promotion subdimension (p=0.005), the Access to Treatment and Health Services subdimension (p=0.005), and the overall HU-HL total score (p=0.003). No statistically significant variation was detected in the total score of eHEALS according to parental gender (Table V).

DISCUSSION

This study aimed to assess the HL levels of adolescents and their parents attending the pediatric outpatient clinic of a training and research hospital and to evaluate the hypothesis that HL correlates with serum 25-hydroxyvitamin D3 (25(OH) D3) levels, serum vitamin B12 (cobalamin) levels and sociodemographic characteristics. In our study, it was seen that one in every five parents was in the inadequate health literacy category. In the comparison of scale scores according to adolescent characteristics, female participants exhibited significantly higher scores than their male counterparts in the HU-HL Health Protection and Promotion subdimension, the Access to Treatment and Health Services subdimension, and the overall HU-HL score. In the comparison of parental health literacy scores, mothers exhibited significantly superior scores compared to fathers in the HU-HL Health Protection and Promotion subdimension, the Access to Treatment and Health Services subdimension, and the overall HU-HL total score.

Our study revealed a mean total eHEALS score of 27.78±5.40, indicating a moderate level among adolescents. This finding aligns with multiple research conducted in various locations of Türkiye, indicating a consistent statewide tendency. A study investigating the impact of eHEALS on the health promotion activities of high school students showed a mean eHEALS score of 28.64±4.50, while another study examining its correlation with healthy behaviors in adolescents revealed a mean score of 27.89±6.19 and a third research assessing the eHEALS levels of high school pupils in Türkiye found an average score of 27.52±6.76 (16-18). The results combined indicate a rather steady level of eHEALS across various geographical and socio-cultural situations in Türkiye. Minor disparities in mean scores may result from variations in sample characteristics, access to digital resources, or differences in health education settings.

In our study, mothers exhibited markedly superior HL scores compared to fathers across all HU-HL subdimensions and in the overall score. This finding aligns with prior studies emphasizing the more proactive involvement of mothers in child healthcare and decision-making processes. A study investigating the influence of parental health literacy on paediatric asthma outcomes reported that most participating caregivers were mothers (19). This predominance likely reflects the disproportionate burden of caregiving placed on women in many cultural contexts. Consequently, maternal health literacy may play a decisive role in shaping children's health behaviours and outcomes. Again in a study investigating HL among parents of children sent to a hospital in Iran indicated that 87% parents were mothers (20). Societal norms and conventional caring responsibilities in Türkiye may further exacerbate this inequality. In our sample, 84.8% of respondents were mothers, with a significant proportion being housewives, possibly enhancing their involvement in their adolescents healthcare. Moreover, the educational level of mothers in our sample was typically superior to that of fathers, a feature consistently linked to improved HL outcomes. These findings align with overarching trends in HL research, highlighting the impact of gender roles and socioeconomic factors, especially education, on HL levels.

Regarding the HU-HL subdimensions, our results were generally consistent with prior research conducted in Türkiye. For instance, research involving adolescents and parents indicated comparable or marginally elevated mean ratings in areas such as treatment accessibility and health promotion (21-23). The observed similarities enhance the generalizability of the HU-HL measure and indicate uniform health-related competencies among parents across various contexts.

The distribution of HL levels in our sample—21.2% low, 57.3% moderate, and 21.5% high—mirrors the patterns identified in other studies conducted in outpatient clinics and family health centers (24,25). Although the precise proportions may fluctuate marginally due to measurement instruments and demographic attributes, a steady trend of modest HL seems to endure across Turkish adult populations.

Our study revealed a significant and distinctive finding: parents of female adolescents exhibited markedly higher HL scores compared to parents of male adolescents, especially in the HU-HL subdimensions of Health Protection and Promotion, Access to Treatment and Health Services, as well as in the overall score. A study examining the health literacy levels of parents of adolescents attending a pediatric outpatient clinic at a tertiary adolescent's hospital for routine check-ups or illness revealed that 73.2% parents were mothers, with the majority demonstrating excellent HL (26). A study examining the HL levels of parents with adolescents admitted to a university hospital revealed that the majority of parents (65.0%) were mothers, and those who brought their daughters exhibited higher HL levels, categorized as adequate-excellent (27). Various contextual factors may have influenced this outcome. In our sample, the predominant parents who brought their adolescent to the hospital were mothers (84.8%), and they were more inclined to accompany daughters rather than males. Conversely, fathers (15.2%) more often accompanied sons than daughters. Furthermore, 69.9% of the mothers were housewife, indicating increased accessibility to attend medical appointments and potentially greater engagement in their adolescents healthcare. Previous studies have inadequately addressed the gender-specific approach in evaluating HL levels. This study aims to fill that gap.

The education level of parents may also be an influencing factor. Of the mothers surveyed, 34.4% completed primary school or less, 29.3% attained secondary school education, 27.0% finished high school, and 9.4% obtained university degrees. The reported figures were typically greater than those for fathers in our sample. Prior research indicates that mothers' insufficient or restricted HL can affect adolescent health outcomes, including the likelihood of home accidents (28). These findings suggest that lower maternal educational attainment, as observed in our sample, may be associated with insufficient HL, potentially increasing adolescents' vulnerability to adverse health outcomes.

Limitations of the Study

The exclusion of illiterate individuals in our study may have introduced bias, resulting in a sample skewed towards higher HL levels. This scenario originates from the HU-HL scale. The HU-HL scale is administered through a self-completion method under observation, rather than through face-to-face interaction with illiterate individuals.

CONCLUSION

This study provides novel evidence on the gender-based disparities in health literacy (HL) among adolescents and their parents, highlighting that parents of female adolescents demonstrated significantly higher HL scores than those of male adolescents. Consistent with national trends, adolescents showed moderate e-health literacy levels, and mothers consistently outperformed fathers across all subdimensions of the HU-HL scale. These findings underscore the importance of incorporating gender-sensitive approaches into HL interventions. Future public health strategies should prioritise tailored HL programmes, particularly targeting fathers and caregivers of male adolescents, to reduce gender inequities and promote adolescent health more effectively.

The preliminary findings of the study (in Turkish) were presented as an oral presentation at the 25th National Public Health Congress, held in Antalya, Türkiye, between December 14–17, 2023. Based on the feedback and discussions during the congress, the study was further developed and enhanced with additional statistical analyses, including subgroup comparisons and multivariate modeling. A revised version of the research, focusing on the health literacy levels of adolescents and their parents, was prepared as an original manuscript.

Ethics committee approval

This study complies with the Declaration of Helsinki and was approved by the Scientific Research Ethics Committee of Health Sciences University Hamidiye (Date: 30.09.2022-Approval No: 2022/22).

Contribution of the authors

Study conception and design: ***MTU, BE, ÇN, SA;*** data collection: ***MTU, BE, ÇN;*** analysis and interpretation of results: ***MTU, SA, EÇ;*** draft manuscript preparation: ***MTU, EÇ, BE, ÇN***. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

A 11-year retrospective analysis of intussusception cases in children

Onursal Varlıklı[1], Mustafa Alper Akay[1], Beyza Nur Tağman[1], Berk Sünnetçi[2], Gülşen Ekingen Yıldız[1]

[1]Department of Pediatric Surgery, Kocaeli University, Kocaeli, Türkiye
[2]Department of Radyology, Kocaeli University, Kocaeli, Türkiye

ABSTRACT

Objective: Intussusception is a prevalent etiology of emesis and abdominal discomfort in pediatric patients. This investigation sought to elucidate the correlation between epidemiological factors, clinical progression, diagnostic procedures, therapeutic interventions, and patient outcomes, with particular emphasis on the safety profile of hydrostatic reduction in subjects presenting with intussusception.

Material and Methods: In this retrospective study, we analyzed the data of children who were diagnosed and treated for intussusception in the hospital database and the Picture Archiving and Communication Systems (PACS) from January 2013 to December 2023. Demographic data, symptoms at presentation, mode of diagnosis, treatment modality, and associated complications were also recorded.

Results: Of the 165 patients, 60% were boys and 40% were girls, with a mean age of 35.5 years (1-193 months). Of the patients, 44.2% (n= 73) were presented within 24 hours of symptom onset. All patients had abdominal pain, and 24 (14.5%) had the classic triad of abdominal pain, vomiting, and red stools. Ultrasonography-guided hydrostatic reduction (USHR) and surgery resulted in a cure in 134 (93.3%) and 31 (6.7%) patients, respectively. The overall recurrence rate was 16.3%, with no mortality. There was a statistically significant difference between the length of the invaginated segment (4 cm or more) and USHR (p=0.004).

Conclusion: The USHR of invagination is effective regardless of the duration of symptoms and number of recurrences.

Keywords: Child, intestinal obstruction, intussusception, surgery, ultrasonography

INTRODUCTION

In 1793, the Scottish Surgeon James Hunter published the first description of intussusception. According to his definition, the proximal intestine is telescoped into the distal intestinal segment. The associated mesentery becomes entrapped within an invaginated segment, resulting in venous congestion and edema. If left untreated, this condition progresses to ischemia, subsequently leading to intestinal necrosis, perforation, and peritonitis. Consequently, intussusception in pediatric patients constitutes a medical requiring prompt diagnosis and intervention.

Intussusception is a prevalent cause of abdominal pain and vomiting in pediatric patients. The clinical signs of the condition include persistent episodes of crying, abdominal pain, a palpable abdominal mass, abdominal distension, and viscous bloody stools. The majority of intussusceptions in children are primary and typically occur as ileocolic (85%), ileo-ileocolic (5%), colocolic (2.5%) or jejunojejunal (2.5%) (1,2). In infants and young children, most cases are idiopathic, and the etiology of intussusception is generally attributed to hypertrophic lymphoid tissue in the terminal ileum; however, leading points such as Meckel's diverticulum, polyps, duplication cyst, lymphadenopathy, lymphoma, and foreign body may be identified (3).

Abdominal ultrasonography (US) serves as the primary diagnostic modality for the investigation of intussusception due to its high specificity, sensitivity, and absence of radiation exposure. Kim et al. (4) reported the first successful sonography-guided hydrostatic reduction of intussusception in 1982. Subsequently,

Correspondence Address:
Onursal Varlıklı
e-mail: onursal.varlikli@kocaeli.edu.tr

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ultrasound-guided saline enema reduction techniques have become the initial treatment of choice in numerous institutions, demonstrating favorable outcomes and minimal complications. Imaging-guided hydrostatic reduction has significantly diminished the necessity for surgical intervention. Surgical or laparoscopic reduction is indicated when bowel necrosis or perforation is suspected or when treatment with USHR proves ineffective (3).

This study aimed to elucidate current concepts pertaining to the diagnosis, treatment, complications, and recurrence of intussusception in pediatric patients.

MATERIALS and METHODS

The medical records of 165 patients diagnosed with intussusception who presented to the emergency department of Kocaeli University hospital between 2013 and 2023 and were treated and followed up by pediatric surgery were retrospectively reviewed and analyzed. All children under the age of eighteen were included in the study, and those with incomplete clinical data were excluded. The age, sex, presenting symptoms, clinical findings, time of presentation, diagnosis, and treatment modalities of the patients were evaluated and discussed in the context of the existing literature. A diagnosis of intussusception was established using US and computed tomography (CT). The non-surgical treatment method, USHR, was employed as the primary intervention. USHR was performed in the absence of clinical or imaging findings suggestive of pathological leading points, and in the absence of peritonitis or intestinal necrosis.

The procedure was thoroughly explained to the parents, informed consent was obtained for the hydrostatic reduction procedure, and the patient remains unsedated. Following the diagnosis of intussusception, an enema was administered for routine bowel preparation, and a nasogastric tube was inserted to prevent emesis and aspiration. The children were subsequently positioned in the lithotomy position, with the hips elevated to 30°. An age-appropriate Foley catheter was advanced rectally, the balloon was inflated, and the catheter was retracted and inserted into the entrance of the anal canal through the rectum. Saline, heated to 35–40°C, was then allowed to flow gradually into the colon under the influence of gravity from a height of 100-120 cm above the anus. In pediatric patients, the enema volume was adjusted to ensure that the total volume of saline did not exceed 1000 mL. Reduction of the invaginated segment and potential complications were monitored in real-time using ultrasound by a radiologist. A maximum of three attempts was permitted for this reduction. Each attempt continued as long as the mass demonstrated progressive reduction in size, as observed via ultrasound. If reduction was not achieved after the third attempt, the procedures were terminated, and operative preparation for surgical reduction was initiated. Patients who underwent successful USHR were allowed to evacuate the normal saline enema from their colon. Prior to Foley catheter removal, control ultrasound was performed to confirm complete reduction of the intussusception and exclude complications. Patients were kept under observation for a minimum of 24 hours to monitor for late complications and recurrence. The following day, patients with normal control ultrasound findings were discharged.

Statistical Analysis

The variables were investigated using visual and analytical (Kolmogorov–Smirnov/ Shapiro–Wilk test) methods to determine whether or not they are normally distributed. Descriptive analyses were presented using medians, interquartile range (IQR), minimum, and maximum for the nonnormally distributed and ordinal variables, means and standard deviations for normally distributed variables. The categorical data were analysed as frequency and percentage. Chi-square test was used to compare proportions in different groups. Mann-Whitney U test were used to compare nonnormally distributed parameters. A p value of less than 0.050 was considered to show a statistically significant result.

RESULTS

During the study period, 165 children diagnosed with intussusception were treated. The cohort comprised 99 males and 66 females, with a male-to-female ratio of 1.5:1. The subjects' ages ranged from 1 to 193 months, with a mean age of 35.5 months. The most prevalent age range was between 6 and 12 months.

The duration of symptoms ranged from 2 to 240 h, with a median duration of 32 h. The precise duration of intussusception symptoms is often challenging to ascertain and is contingent upon the recognition of non-specific symptoms, which are frequently poorly articulated in young children. The most prevalent symptoms were colicky abdominal pain (100.0%), vomiting (54.5%), and rectal bleeding (26.0%). The classical clinical triad, characterized by intermittent abdominal pain, stool with a consistency resembling strawberry jelly, and sausage-shaped abdominal masses, was observed in 24 patients (14.5%). Forty-three patients exhibited bloody stools, and the mean age of the patients with bloody stools was 24 months, while the mean age of the patients without bloody stools was 40 months. A total 58.1% (n= 96) patients presented within the first 24 hours after the onset of abdominal pain, while 41.9% (n= 69) presented after 24 hours. Invaginated segments less than 4 cm (62.4%) and segments >4 cm (37.5%) had statistically significant differences in USHR performance (p=0.004). All patients were diagnosed through the use of ultrasound imaging (Figure 1,2)

The invagination types and rates are presented in Table I. Among the 162 patients who underwent ultrasound-guided hydrostatic reduction (USHR), successful reduction was achieved in 137 cases, representing an 84.5% success rate. Additionally, four patients who experienced recurrence were

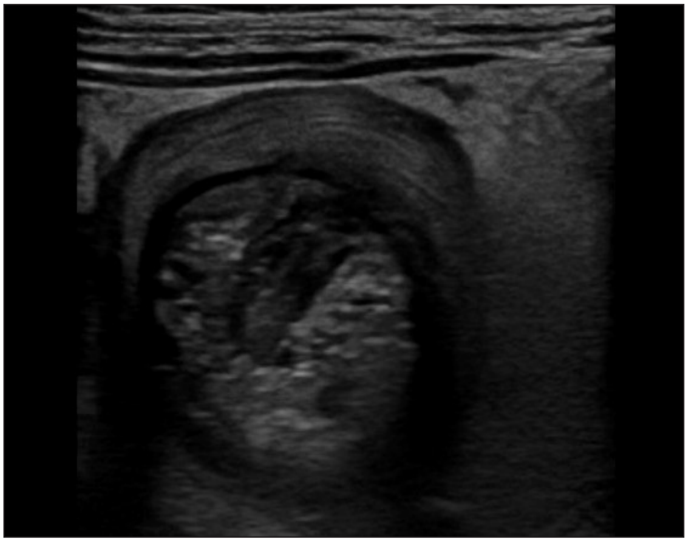

Figure 1: Target sign in ultrasonography imaging

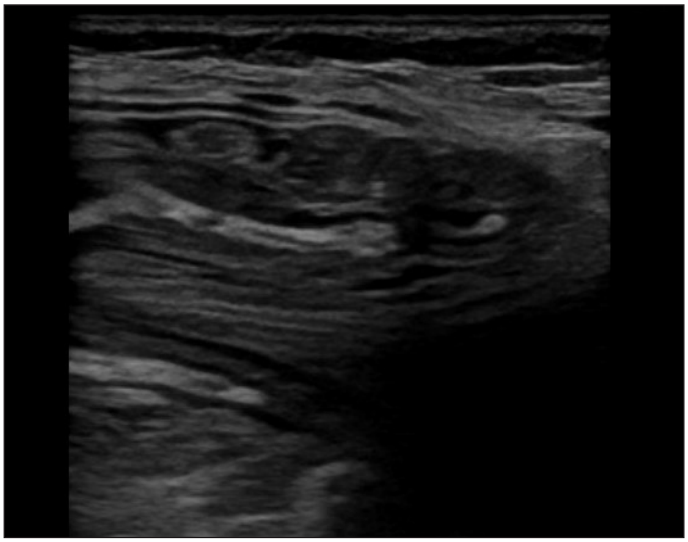

Figure 2: The “sleeve” sign of the intussusception was shown on the longitudinal section

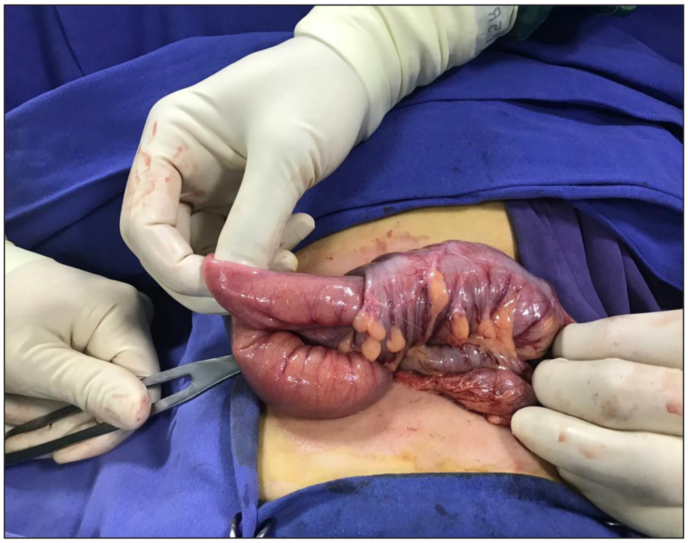

Figure 3: Ileocolic intussusception

Table I: The intussusception types and rates

Intussusceptions	n (%)
Ileocolic	152 (92.2)
Ileoileal	6 (3.6)
Colocolic	5 (3.0)
Ileocolic and ileoileal	2 (1.2)

Table II: The surgically treated intussusception types and rates

Intussusceptions (surgically treated)	n (%)	Manual reduction	Manual reduction and Meckel excision (%4.2)	Resection anastomosis
Ileocolic	26 (66.6)	18	5	3
Ileoileal	10 (25.7)	6	2	2
Ileocolic and Ileoileal	2 (5.2)	2		
Colocolic	1 (2.5)	1		1

successfully managed with subsequent USHR procedures. Notably, no instances of perforation were observed during the procedure in any patient

Hydrostatic reduction demonstrated efficacy in subjects with brief symptom duration; however, the observed difference did not reach statistical significance (p=0.159). A total of 39 (23.6%) patients necessitated open surgery due to partial reduction of invagination/failed reduction, unsuitability for USHR, or recurrence (Figure 3). Recurrence was observed in ten (6.0%) patients. Among these patients, four (15 days-15 months) were managed with repeat USHR and five with open surgery. One patient experienced recurrence following open surgery and was treated accordingly again. A male neonate, aged three days, who had previously undergone surgical intervention for a diaphragmatic hernia, subsequently developed ileoileal intussusception on the second day following the operation. Furthermore, one patient presented with a total of eight ileoileal intussusceptions in conjunction with ileo-colic intussusceptions.

The types and rates of surgically treated intussusceptions are presented in table II. In the present study, the required bowel resection rate was 15.8%. Three of the patients who underwent anastomosis presented with circulatory disturbances, while the others exhibited a leading-point mass, hemangioma, and polyp, respectively. No mortality was observed in this study.

DISCUSSION

Infants predominantly experience small intestinal obstruction due to intussusception, which constitutes the second most common cause of acute abdominal pain in pediatric patients after appendicitis (1,2,5). The incidence of intussusception typically ranges from 15 to 300 cases per 100.000 children annually, with a male-to-female ratio of approximately 1.2–2.1:1 (6-8). Approximately 75-90% of cases are idiopathic, and the presence of lymphoid hyperplasia is reported in the majority of cases (1,5,9). Among the patients in this study, 93.9% presented with idiopathic disease as shown in Figure 1.

In 1.5–12% of intussusception cases, a pathologic leading point is present. Although polyps, tumors, lymphomas, duplication cysts, parasites, hematomas, vascular malformations, inflammatory appendices, and inverted appendiceal roots have been identified as etiological factors, Meckel's diverticulum remains the most prevalent point of origin in infants. The leading points (6.0%) in our series comprised vascular malformation, lymphoma, and Meckel's disease. Additional recognized risk factors for intussusception include nephritic syndrome, Peutz-Jegher syndrome, familial polyposis, Henoch-Schonlein purpura, and cystic fibrosis. Furthermore, intussusception has been documented during the postoperative period and in association with abdominal injuries (1,2). Postoperative ileoileal intussusception was observed in a patient who underwent surgery for diaphragmatic hernia and was subsequently managed with manual reduction.

The majority of pediatric patients present with primary intussusceptions, with the ileocolic type being the most prevalent. Intussusceptions can be categorized as single or multiple based on their quantity. Single intussusceptions are predominantly ileocolic, ileo-ileocolic, or colocolic, while multiple intussusceptions are typically ileoileal or jejunojejunal. In our study, two patients (1.2%) exhibited multiple invaginations. One patient presented with a total of eight ileoileal invaginations in conjunction with ileo-colic invaginations. The highest number of invaginations reported in the literature is 10, which is attributed to secondary trauma (10).

The initial symptom in 80-95% of cases is the acute onset of abdominal pain, typically characterized by cramping for 15-20 minutes, which is severe and progressive in nature (1). Patients may experience complete asymptomatic periods between episodes. In cases of prolonged intussusception, ileus advances, and symptoms of peritonitis may manifest when perforation occurs. In 50-70% of cases, the presence of overt or occult blood in the stool has been documented, exhibiting a characteristic strawberry jelly appearance due to a mixture of blood and mucus. It is crucial to remember that the diagnosis of intussusception is not ruled out if there is no blood in the stool.

The classic clinical triad of Ombredanne syndrome comprises an elongated abdominal mass, feces resembling strawberry jelly, and intermittent abdominal pain. This triad is observed in 7.5–40% of cases, and our incidence aligns with the reported figure of 14.5% in the literature (2,11). Additionally, this condition has been associated with other manifestations, including emesis (60%), diarrhea (30%), lethargy, lacrimation, altered mental status, sepsis, shock, and syncope (1). Delays in diagnosis and treatment reduce the success rate of USHR and increase the probability of bowel resection. However, Wong et al. (12) reported that a mean symptom duration of 2-3 days did not affect the success rate of reduction. Conversely, Chung et al. (13) investigated the risk factors for surgical reduction and determined that prolonged symptom duration (> 24 h) was a risk factor for failed reduction. There was no statistically significant difference between the success of USHR decrease and the duration of symptoms in our study (p=0.159). We posit that the length of the invaginated segment is more significant than the duration of symptoms in determining the success of USHR.

Abdominal radiographs exhibit low sensitivity (29-50%) and are consequently not recommended for the diagnosis of intussusception. Nevertheless, this modality may yield more findings in cases of suspected perforation (6). US serves a crucial role in the diagnosis of intussusception. In pediatric patients, US reduces the cost of screening and radiation exposure, demonstrating a sensitivity of 98%-100% and specificity of 88-100% (1,14). Characteristically "donut," "pseudokidney," or "target sign" are considered diagnostic indicators on ultrasound as shown in Figure 2-3 (1). US additionally contributes to the evaluation of decreased invagination, the presence of a pathologic leading-point mass, and alternative diagnoses (2,15). Due to its high sensitivity and specificity, US should be considered the primary diagnostic tool for radiation protection, while abdominal CT should be employed when a definitive diagnosis cannot be established (1,7).

No standardized guidelines exist for the management of pediatric intussusception. Pediatric patients presenting with a high clinical suspicion of intussusception who are hemodynamically and clinically stable, or who exhibit radiologic evidence of intussusception without signs of intestinal perforation, are optimally managed through nonoperative intervention. In developed countries, nonoperative reduction has become the gold standard in the treatment of intussusception, and the success rate of reduction based on published literature has reached at least 80% and up to 100% (8,16,17). USHR was the primary conservative technique employed at our center to avoid radiation exposure, and our success rate was consistent with the literature (84.5%). Nonoperative treatment methods include fluoroscopic- or ultrasound-guided barium reduction and air or saline reduction. Saline reduction results in less morbidity when perforation occurs compared with barium and water-soluble ionized contrast agent reduction techniques. There is no chance of chemical peritonitis or electrolyte imbalance if intestinal perforation occurs when using saline techniques (7,18).

Dehydration should be treated with intravenous fluid resuscitation prior to reduction. In the majority of cases involving acute primary intussusception, a non-operative reduction should be attempted. However, pediatric patients exhibiting symptoms of peritonitis, shock, sepsis, or the presence of free air on abdominal radiographs are not appropriate candidates for this procedure. The primary benefit of USHR is the elimination of radiation exposure in pediatric patients. This allows for repeated and systematic attempts at reduction. In cases where USHR treatment was initially successful, four patients who experienced recurrence were effectively managed with subsequent USHR procedures. The most significant adverse effect of enema reduction is perforation, which occurs in approximately 1–10% of cases (1,2,7). Infants under six months of age are particularly susceptible to perforation, potentially due to the reduced thickness of their intestinal walls (19). The duration of symptoms in these instances is typically reported to be 36–48 hours or more, and the interval between symptom onset and intervention has been identified as a contributing risk factor (19). The failure of hydrostatic reduction has been associated with several parameters, including young age, rectal bleeding, radiologic evidence of intestinal obstruction, and prolonged symptoms (>72 h) (18, 20). Nevertheless, provided the patient is clinically stable and adequately hydrated, these symptoms do not preclude hydrostatic reduction. To enhance the likelihood of non-operative reduction in numerous patients, it is essential to prevent delayed presentation and to establish an accurate diagnosis promptly.

Following enema administration, the recurrence rate of intussusception ranges from 5% to 20%, irrespective of whether air or liquid reduction techniques are employed (8,21,22). In the present study, the recurrence rate subsequent to USHR (6%) was consistent with previously reported findings. Recurrence rates diminish to approximately 1% when surgical reduction is performed, attributable to the formation of adhesions (23). Nevertheless, the postoperative recurrence rate was observed to be 2.5%.

Surgical intervention is necessitated when reduction with USHR proves unsuccessful and pathological leading point or bowel necrosis is present. The requirement for bowel resection ranges from 25% to 40%, with our rate being lower at 15.8% (24-29). Surgical intervention can be executed via both open and laparoscopic approaches in patients with intussusception.

A more favorable prognosis is generally observed in patients when a reduction occurs within 24 hours of symptom onset. Delayed presentation is associated with decreased reduction rates, an increased necessity for surgical intervention, and associated complications (29). In most regions globally, the mortality rate of intussusception is exceedingly low (<1%). However, mortality rates of up to 9.4% have been reported in Africa (5).

This study's retrospective methodology and absence of a controlled comparison of therapies were its primary limitations.

CONCLUSION

Ultrasound-guided hydrostatic reduction (USHR) should be considered the conservative intervention of choice for the treatment of intussusception due to its cost-effectiveness, efficacy, safety, and elimination of radiation exposure risk. The success rate can be enhanced through the involvement of trained radiologists and the establishment of standardized procedures, including the number and duration of interventions. We propose the adoption of USHR as the standard technique for the management of childhood intussusception.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Kocaeli University (18.01.2024, reference number: KÜ GOKAEK-2024/01.12).

Contribution of the authors

Çalışmanın konsepti ve tasarımı: ***VO, AMA***; veri toplama: ***VO, AMA, TBN, SB***; sonuçların analizi ve yorumlanması: ***O, AMA, TBN, SB, EYG***; taslak makale hazırlığı: ***VO***. Tüm yazarlar sonuçları gözden geçirdi ve makalenin son halini onayladı.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Retinal OCT changes in pediatric epilepsy: Neurodegeneration and antiseizure medication effects

Alper Güneş[1], Kübra Güneş[2]

[1]Department of Ophthalmology, Tokat Gaziosmanpaşa University, Tokat, Türkiye
[2]Department of Pediatrics, Tokat State Hospital, Tokat, Türkiye

ABSTRACT

Objective: This study aimed to evaluate peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell–inner plexiform layer (GCL+IPL) thickness in children with epilepsy using optical coherence tomography (OCT), and to compare these parameters with healthy controls. Additionally, the relationship between retinal structure and epilepsy duration, as well as antiseizure medication (ASM) exposure (notably valproate), was investigated.

Material and Methods: Fifty pediatric epilepsy patients and 50 healthy children aged between 6 and 18 years underwent spectral-domain OCT (Zeiss Cirrus HD-OCT 5000) to measure RNFL, GCL+IPL, and central subfield thickness (CST). Independent-samples t-test and Spearman correlation analysis were used to assess group differences and associations with clinical variables. Retinal thickness values were also compared across ASM subgroups (valproate, levetiracetam, carbamazepine, lamotrigine monotherapy, and polytherapy).

Results: Compared to controls, children with epilepsy had significantly thinner average RNFL (95.0±11.0 µm vs 101.0±9.0 µm; $p = 0.020$) and superior quadrant RNFL (125±15 µm vs 132±14 µm; $p = 0.030$). GCL+IPL thickness was also significantly reduced in the epilepsy group (80.0±5.5 µm vs 85.0±5.0 µm; $p = 0.003$), as was CST (240±22 µm vs 250±20 µm; $p = 0.045$). Longer epilepsy duration correlated negatively with RNFL ($\rho = -0.300$; $p = 0.030$) and GCL+IPL ($\rho = -0.350$; $p = 0.010$). While retinal thickness did not differ significantly across ASM subgroups, the valproate and polytherapy groups had numerically lower values.

Conclusion: Pediatric epilepsy is associated with subtle but significant thinning of RNFL and inner macular layers, suggesting subclinical neurodegenerative effects. The observed correlation with disease duration indicates a possible progressive impact. Although differences between ASM groups were not statistically significant, valproate may contribute to retinal changes. OCT appears to be a valuable noninvasive tool for assessing neuroaxonal integrity in pediatric epilepsy.

Keywords: Epilepsy, optical coherence tomography, pediatrics, retina, valproate

INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent seizures, which may lead to progressive neurodegeneration over time due to repeated excitotoxic and metabolic stress (1,2). Although these effects are primarily observed in the brain, accumulating evidence suggests that the retina may also reflect such neuroaxonal injury (3,4).

The retina, as an extension of the central nervous system, shares both structural and embryological features with the brain. Optical coherence tomography (OCT) is a noninvasive imaging modality that enables quantitative assessment of retinal neuronal layers, especially the peripapillary retinal nerve fiber layer (RNFL) and the macular ganglion cell–inner plexiform layer (GCL+IPL) (5). Thinning of these layers has been reported in various neurodegenerative and neuroinflammatory disorders, including multiple sclerosis, Alzheimer's disease, and epilepsy (6,7).

Several studies have shown reduced RNFL and GCL thickness in patients with epilepsy, suggesting subclinical retinal involvement (8–11). However, it remains unclear whether these changes are caused by the disease itself or the long-term use of antiseizure medication (ASMs). Valproate, in particular, has been associated with potential retinal toxicity (12,13), whereas agents such as levetiracetam and lamotrigine are considered to have minimal ocular effects. In a pediatric OCT-based study,

Correspondence Address:
Alper Güneş
e-mail: alpergunes@gmail.com

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Durgut et al. (13) demonstrated that levetiracetam monotherapy did not significantly alter RNFL, GCC, or foveal thickness compared to healthy controls, suggesting a favorable retinal safety profile for this drug in children with epilepsy. In pediatric populations, available data are limited and inconsistent, and the relative contribution of epilepsy duration, seizure burden, and ASM exposure to retinal changes remains to be fully clarified (14,15).

However, recent pediatric OCT studies have shown thinning of both RNFL and GCL+IPL layers in children with genetic generalized epilepsy and chronic ASM exposure, particularly in valproate users, further supporting the hypothesis of early subclinical neurodegeneration (16,17).

In this study, we aimed to assess retinal structural changes using spectral-domain OCT in children with epilepsy. We compared RNFL, GCL+IPL, and central subfield thickness measurements between patients and healthy controls, and examined the relationship between these parameters and clinical variables such as disease duration, seizure onset age, and ASM regimen. We hypothesized that children with epilepsy would show measurable retinal thinning and that these changes might be associated with both epilepsy duration and specific treatment exposure.

MATERIALS and METHODS

Study design and participants

This prospective, cross-sectional study included 50 children diagnosed with epilepsy and 50 age- and sex-matched healthy controls, conducted between September 2023 and September 2024. Sample size was calculated based on a moderate effect size (Cohen's d = 0.6) derived from pilot data on RNFL differences, with $\alpha = 0.05$ and 80% power, requiring a minimum of 45 participants per group. Epilepsy patients were consecutively recruited from the Department of Pediatrics at Tokat State Hospital, and ophthalmic assessments were performed at the Department of Ophthalmology, Tokat Gaziosmanpaşa University Faculty of Medicine. Inclusion criteria for the epilepsy group were: age between 6–18 years, clinical diagnosis of epilepsy according to ILAE criteria, and ongoing treatment with one or more antiseizure medication (ASMs). Exclusion criteria included prior use of vigabatrin, any ocular pathology (e.g., glaucoma, optic neuritis), systemic diseases affecting the retina (e.g., diabetes), significant refractive error (±5.0 D sphere or >3.0 D cylinder), previous intraocular surgery or trauma, and any neurological comorbidity other than epilepsy.

Control participants were neurologically healthy children of similar age and sex, with no history of epilepsy or systemic illness. All participants had best corrected visual acuity of 20/25 or better, normal color vision, and no abnormalities on slit-lamp or fundus examination.

Ophthalmic evaluation and OCT imaging

All participants underwent detailed ophthalmological examination including anterior and posterior segment biomicroscopy, non-contact tonometry (mean of three measurements), autorefractometry, and best corrected visual acuity assessment. Only the right eye was included in the analysis unless scan quality required use of the left eye.

Spectral-domain optical coherence tomography (SD-OCT) was performed using the Zeiss Cirrus HD-OCT 5000 device. Peripapillary retinal nerve fiber layer (RNFL) thickness was measured with the Optic Disc Cube 200×200 scan protocol, evaluating average global RNFL and quadrant-specific values (superior, inferior, nasal, temporal). Macular ganglion cell–inner plexiform layer (GCL+IPL) thickness was recorded using the Macular Cube 512×128 protocol with the device's Ganglion Cell Analysis (GCA) software. Additionally, central subfield thickness (CST) was measured as the average retinal thickness in the central 1-mm diameter zone. Only scans with a signal strength of 7 or higher (out of 10) were accepted for analysis. All OCT scans were performed by a certified technician who was blinded to the participants' clinical group (epilepsy vs. control) during image acquisition.

Clinical data and ASM subgrouping

Clinical data collected for each patient included age at seizure onset, duration of epilepsy, and current ASM regimen. Patients were grouped based on treatment as follows: valproate monotherapy, levetiracetam monotherapy, carbamazepine monotherapy, lamotrigine monotherapy, or polytherapy (≥2 ASMs). No patients were receiving vigabatrin. MRI findings were reviewed to exclude patients with visual pathway involvement.

Statistical analysis

Statistical analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean and standard deviation (SD). Normality was assessed with the Shapiro-Wilk test. Group comparisons for OCT parameters were made using independent samples t-tests. Spearman correlation analysis was performed to examine associations between retinal thickness and clinical variables such as epilepsy duration and age at seizure onset. For ASM subgroups, one-way ANOVA was used to compare RNFL and GCL+IPL thicknesses; post-hoc Tukey's test was applied if appropriate. A p-value of <0.050 was considered statistically significant. Bonferroni correction was used for quadrant-wise RNFL comparisons.

RESULTS

A total of 100 participants were included in the study, comprising 50 children with epilepsy and 50 healthy controls. The groups were well matched in terms of age and sex. The mean age was 12.5±3.2 years in the epilepsy group and 12.0±3.4 years in the

Table I: Demographic and clinical characteristics of study participants

Variable	Epilepsy Group	Control Group
Number of patients	50	50
Age (years)*	12.5±3.2	12.0±3.4
Gender (Male/Female)	26 / 24	25 / 25
Age at seizure onset (years)*	7.3±2.5	-
Duration of epilepsy (years)*	5.2±2.0	-

***:** *mean±SD*

Table II: Comparison of peripapillary RNFL thickness between groups

RNFL Region	Epilepsy Group	Control Group	p*
Number of patients	50	50	-
Average RNFL†	95.0±11.0	101.0±9.0	0.020
Superior RNFL†	125±15	132±14	0.030
Inferior RNFL†	126±16	131±15	0.070
Nasal RNFL†	84±12	86±11	0.350
Temporal RNFL†	68±10	70±9	0.400

***:** *Independent samples T test,* **†:** *mean±SD*

control group. The epilepsy group had a mean age at seizure onset of 7.3±2.5 years and a mean disease duration of 5.2±2.0 years (Table I).

Compared to the control group, children with epilepsy showed significantly lower mean RNFL thickness (95.0±11.0 µm vs 101.0±9.0 µm; p = 0.020; mean difference: –6.0 µm, 95% CI: –10.4 to –1.6 µm; Cohen's d =0.62). The most pronounced difference was observed in the superior quadrant (125±15 µm vs 132±14 µm; p =0.030). Differences in inferior, nasal, and temporal quadrants were not statistically significant (Table II).

Children with epilepsy also demonstrated significant thinning in the macular inner retinal layers. The mean GCL+IPL thickness was significantly lower in the epilepsy group (80.0±5.5 µm) compared to controls (85.0±5.0 µm), with a mean difference of –5.0 µm (95% CI:–8.0 to –2.0 µm; p =0.003; Cohen's d = 0.85). Additionally, the central subfield thickness (CST) was mildly reduced in the epilepsy group (240±22 µm vs 250±20 µm; p = 0.045) (Table III).

In the epilepsy group, longer epilepsy duration was significantly associated with reduced RNFL (ρ =–0.30, p =0.030) and GCL+IPL thickness (ρ =–0.35, p =0.010). Additionally, younger age at seizure onset correlated with greater thinning of both RNFL (ρ =+0.28, p =0.040) and GCL+IPL (ρ =+0.32, p =0.020) (Table IV).

When the epilepsy group was analyzed based on current ASM therapy, no statistically significant differences in RNFL or GCL+IPL thickness were found among subgroups (p = 0,426, p = 0.243). However, the valproate and polytherapy subgroups exhibited numerically lower values across both layers (Table V).

Table III: Comparison of macular GCL+IPL and central subfield thickness between groups

Parameter	Epilepsy Group	Control Group	p*
Number of patients	50	50	-
GCL+IPL Thickness†	80.0±5.5	85.0±5.0	0.003
Central Subfield Thickness†	240±22	250±20	0.045

***:** *Independent samples T test,* **†:** *mean±SD*

Table IV: Correlation between clinical variables and retinal layer thickness in the epilepsy group

Clinical Variable	RNFL (ρ)	p*	GCL+IPL (ρ)	p*
Epilepsy duration (years)	–0.30	0.030	–0.35	0.010
Seizure onset age (years)	+0.28	0.040	+0.32	0.020

***:** *Spearman correlation*

Table V: Retinal thickness parameters by antiseizure medication (ASM) subgroups

ASM Group	n	Average RNFL (µm)*	GCL+IPL Thickness (µm)*
Valproate	11	94±10	79±6
Levetiracetam	7	98±9	82±5
Carbamazepine	5	96±11	81±6
Lamotrigine	6	100±8	84±5
Polytherapy	21	92±11	78±7

***:** *mean±SD*

DISCUSSION

In this study, we demonstrated that children with epilepsy exhibit significant thinning of the peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell–inner plexiform layer (GCL+IPL) compared to healthy controls, even in the absence of visual symptoms. These findings may reflect early structural retinal alterations associated with epilepsy, possibly indicating broader neuroaxonal involvement within the central nervous system.

Our results are consistent with previous studies reporting reduced RNFL and inner retinal thickness in epilepsy. Tak et al. (5) showed approximately 7% RNFL thinning in adults with epilepsy, while González de la Aleja et al. (8) found significant superior and inferior RNFL thinning in patients with genetic generalized epilepsy. In our pediatric cohort, average RNFL and GCL+IPL thickness were reduced by approximately 6%, suggesting that retinal involvement is evident even at younger ages and earlier stages of disease.

The superior quadrant RNFL was the most significantly affected region in our cohort. This pattern aligns with prior observations suggesting increased vulnerability of vertical retinal fibers to metabolic stress, inflammation, or mechanical factors such as fluctuating intracranial pressure during seizures (8,9). Similarly, macular GCL+IPL thinning suggests a loss of retinal ganglion cell bodies, analogous to cortical neuronal loss observed in epilepsy-related brain imaging studies (3,4).

We also identified a significant negative correlation between epilepsy duration and both RNFL and GCL+IPL thickness, indicating a cumulative neurodegenerative process. Earlier age at seizure onset was also associated with greater thinning, likely due to longer cumulative disease exposure. These findings support the use of OCT as a potential monitoring tool for tracking neuroaxonal damage over time.

Kaplan et al. (16) also reported that adolescents with genetic generalized epilepsy exhibited inner retinal thinning, even in the absence of visual complaints, supporting the notion of early subclinical involvement.

Importantly, although group comparisons did not reveal statistically significant differences between ASM subgroups, patients receiving valproate or polytherapy showed numerically lower retinal thickness values. This trend is in line with previous reports indicating potential retinotoxic effects of valproate (9,11). Xiong et al. (9) reported that valproate monotherapy was associated with significantly lower RNFL values compared to other ASMs or untreated patients, and meta-analytic data have confirmed RNFL thinning in pediatric patients using valproate, particularly in nasal and inferior quadrants (6). Sahin and Cirakli found that children treated with valproate had lower GCL+IPL and RNFL thickness compared to those receiving levetiracetam, further supporting our findings (17). Although our findings did not reach statistical significance—possibly due to limited subgroup sizes—they suggest that further investigation is warranted. Similarly, a recent pediatric OCT study found that children receiving valproate had significantly lower GCL+IPL and RNFL thickness compared to those on levetiracetam, suggesting a possible drug-specific retinal vulnerability (17).

In contrast, patients receiving levetiracetam or lamotrigine had relatively preserved retinal structure, consistent with their favorable neuro-ophthalmic safety profiles (13). Our data also do not support a strong effect of polytherapy per se, as the observed thinning may be confounded by longer disease duration or valproate inclusion within these regimens.

Chontos et al. (18) recently published a meta-analysis confirming consistent inner retinal thinning in epilepsy, with valproate exposure identified as a significant contributing factor. In another pediatric OCT study, Gultutan et al. (19) observed that retinal blood flow was reduced in children receiving valproate, in parallel with structural thinning. Moreover, a recent pharmacogenomic analysis by Boothman et al. (20) demonstrated that individuals exposed to vigabatrin experienced varying degrees of peripapillary RNFL loss depending on genetic susceptibility, highlighting the potential for personalized risk assessment in ASM-induced retinal toxicity. These findings, together with ours, underscore the importance of considering ASM-specific effects when interpreting OCT data in epilepsy populations.

From a clinical perspective, OCT may serve as a valuable, noninvasive biomarker for detecting early retinal changes in children with epilepsy. Its utility may extend beyond research into monitoring long-term neurotoxic effects of chronic ASM use, particularly in patients requiring long-term therapy or showing signs of cognitive decline. While retinal thinning alone may not impair visual function, it may reflect broader CNS involvement and help identify patients at risk of neurodevelopmental complications. Future studies integrating visual field testing or electrophysiological assessments are needed to clarify the functional consequences of these structural findings.

Our study has several limitations. Its cross-sectional design precludes evaluation of progression over time. The sample size was moderate and not powered to detect subtle inter-drug differences. Although OCT revealed structural alterations, functional visual testing (e.g., visual fields or electroretinography) was not performed. Therefore, the clinical implications of these structural findings in terms of visual function remain uncertain.

CONCLUSION

This study demonstrated that pediatric epilepsy is associated with subtle but statistically significant thinning of the peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell–inner plexiform layer (GCL+IPL) as measured by spectral-domain optical coherence tomography. These retinal structural alterations may reflect subclinical neuroaxonal damage linked to chronic epileptic activity. The observed negative correlations between disease duration and retinal thickness suggest a cumulative degenerative process, even in the absence of overt visual symptoms. Although no statistically significant differences were observed among antiseizure medication (ASM) subgroups, numerically lower values in the valproate and polytherapy groups raise the possibility of a medication-related effect that warrants further investigation. OCT may serve as a valuable, noninvasive biomarker for monitoring neurodegeneration in pediatric epilepsy. Prospective, longitudinal studies with larger cohorts are needed to validate these findings and determine their potential clinical implications in neurodevelopmental follow-up and therapeutic decision-making.

Ethics committee approval

This study was approved by the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (Decision No: 23-KAEK-195, Date: August 31, 2023).

Contribution of the authors

AG: Conceptualization, ophthalmologic examinations, OCT analysis, data interpretation, manuscript drafting, final approval.
KG: Patient recruitment and follow-up, clinical data collection, coordination of pediatric evaluations, manuscript revision, final approval.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Investigation of the relationship between language skills and behavioral problems in children assessed for language and speech delay

Emel Ömercioğlu[1], Funda Akpınar[1], Gamze Hayran Turmuş[1], Ayşe Mete Yeşil[1], Gözde Şahin[1], Pelin Çelik[1],[2]

[1]Department of Developmental and Behavioral Pediatrics, Ankara Bilkent City Hospital, Ankara, Türkiye
[2]Department of Pediatrics, Ankara Yildirim Beyazit University, Ankara, Türkiye

ABSTRACT

Objective: Delays in language and speech skills can profoundly affect various developmental domains and emotional regulation processes. This study aimed to investigate the relationship between receptive and expressive language skills and behavioral problems in preschool-aged children assessed for language and speech delay.

Material and Methods: The study included 2- to 4-year-old children referred to the Developmental Pediatrics Clinic of Ankara Bilkent City Hospital for language and speech delay, undergoing thorough physical and developmental assessments. The receptive and expressive language development of the children was evaluated using the Test of Early Language Development-Third Edition: Turkish Version. To assess behavioral problems, parents completed the Strengths and Difficulties Questionnaire for 2-4 Year Olds (SDQ 2-4).

Results: The study included 58 children with a mean age of 32.48 ±5.69 months. Notably, 56.9% exhibited total difficulty scores on the SDQ 2-4 that surpassed the cutoff, with an average score of 11.06 ±5.53. The children's receptive language scores showed a negative correlation with conduct issues, hyperactivity/inattention, difficulties in peer relationships, and overall difficulty scores ($p=0.017$, $p=0.029$, $p=0.007$, $p=0.004$, respectively), while no significant associations were found between their expressive language abilities and behavioral problems. Children with typical language skills had a total difficulty score of 7.90 ±2.84, whereas those with expressive delays scored 11.06 ±5.55 and those with both receptive and expressive delays scored 13.40 ±6.06, indicating significant group differences ($p=0.043$).

Conclusion: Preschool-aged children with language and speech delay are frequently seen by primary care providers and pediatric specialists. They often present with behavioral issues, particularly among those from low socioeconomic and sociocultural backgrounds. It can be suggested that addressing behavioral problems alongside language interventions may help mitigate potential long-term effects.

Keywords: Behavioral problem, children, language and speech delay

INTRODUCTION

The process of language acquisition represents a critical milestone, establishing a foundational basis for a range of subsequent developmental achievements. Early language skills exert a substantial influence on lifelong developmental outcomes by contributing to the development of cognitive, social-emotional, and academic competencies (1, 2). Language comprises two components: receptive language, which involves understanding others' language outputs both auditorily and visually, and expressive language, which refers to the ability to convey information, ideas, feelings, and thoughts through the use of words and gestures. Speech is the vocalized form of the language system (3).

Speech and language development delays are the most frequent developmental causes for hospital visits among preschool-aged children. Parents may be more attuned to communication and language problems due to the constraints children experience in their daily functioning. Between 13.4% and 19.1% of toddlers present with delays in language development (4).

Research demonstrates a negative association between preschool behavior problems and language skills, observed both concurrently and longitudinally (1). This relationship is primarily elucidated through the critical role of language in self-

Correspondence Address:
Emel Ömercioğlu
e-mail: emelomercioglu@gmail.com

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regulation and emotional regulation processes. Language and speech delay may adversely affect children's ability to utilize language for the purpose of emotional regulation. Skills related to emotion regulation have been linked to both internalizing and externalizing behaviors among young children (5, 6). A recent meta-analysis demonstrated a moderate distinction in problem behavior ratings between children with language disorders and their typically developing counterparts (4). A multitude of studies have explored the intricate relationships between language skills and both internalizing and externalizing problems during childhood (1, 7). Despite the substantial body of literature on this topic, significant methodological heterogeneity exists among studies, attributable to the diverse assessment and measurement techniques employed for language skills and behavioral issues (1, 4).

Although studies from Türkiye indicate that children with language and speech delay show a higher prevalence of behavioral problems, there remains a lack of research specifically focusing on the link between expressive and receptive language skills and behavioral issues (8-10). Consequently, this study sought to assess children presenting with language and speech delay within this context. It further aimed to explore the relationship between receptive and expressive language skills and behavioral problems, as well as to identify the variables that affect both language competencies and behavioral issues.

MATERIALS and METHODS

Ankara Bilkent City Hospital is one of the largest pediatric institutions in Europe, serving a highly diverse patient population thanks to its strategic central location. The Developmental Pediatrics Clinic at Ankara Bilkent City Hospital offers thorough evaluation, intervention, and ongoing monitoring for children at risk for or exhibiting developmental delays, adhering to a family-centered approach in its care strategies.

Between March and June 2024, children who were evaluated at the Developmental Pediatrics Clinic and referred for language and speech delay between the ages of 2 and 4 years were included in the study. Comprehensive clinical evaluations and observations were conducted by specialists in developmental pediatrics. The study excluded children presenting with global developmental delay, severe cognitive impairment, neurodevelopmental disorders, or genetic syndromes. None of the patients were receiving specialized education in any developmental domain, and this marked their first visit to the clinic. The family sociodemographic characteristics of 58 children who met all these criteria, as well as their daily screen time, background screen exposure, and reading frequency, were collected through questionnaires administered to their parents. The Hollingshead-Redlich Scale was used to determine the socioeconomic and sociocultural levels of families. This scale is based on the educational and occupational status of the parents. Parents completed the Strengths and Difficulties Questionnaire (SDQ) to evaluate their children's behavioral issues. Each child underwent the Test of Early Language Development-Third Edition: Turkish Version (TEDIL), a comprehensive assessment of receptive and expressive language skills, administered by a qualified speech-language therapist.

Test of Early Language Development-Third Edition: Turkish Version (TEDIL)

Language development was evaluated using the TEDIL, the Turkish version of the Test of Early Language Development (TELD-3), which was developed by Hresko et al. (11) in 1999. The TEDIL is a widely utilized language assessment tool for children aged 0 to 7 years, designed to evaluate receptive and expressive language skills. The test was adapted to our cultural context by Güven and Topbaş, and it has been established as a valid and reliable language assessment tool (12). The TEDIL provides norm-referenced scores, including standard scores, percentiles, and age-equivalent values, for receptive and expressive language skills. Standard scores ranging from 90 to 110 are accepted as within the average range. Based on the composite score results obtained from the assessment, the level of language development is classified as very poor; weak/poor; below average; average; above average; good; and very good.

Strengths and Difficulties Questionnaire for 2–4 Year Olds (SDQ 2–4). The Strengths and Difficulties Questionnaire, developed by British psychiatrist Robert Goodman in 1997, serves as a screening tool for childhood psychopathologies. The SDQ is characterized by its ease of application and widespread use globally. It comprises 25 items that assess both positive and negative behavioral characteristics and is organized into five subcategories: emotional symptoms, hyperactivity/inattention, conduct problems, peer relationship difficulties, and prosocial behavior. The 'Total Difficulty Score' is derived by summing the scores from the first four categories (13). A reliability-validity study and psychometric evaluations of the SDQ for children aged 2–4 years were conducted by Dursun and colleagues. They established a cut-off value of 10 for the Total Difficulties Scale, which demonstrated 80% sensitivity and 88% specificity (14).

Statistical analysis

Statistical analyses were conducted using IBM Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). The normality of continuous variables was assessed using the Shapiro–Wilk test, histograms, and boxplots. Numerical variables were summarized as means, standard deviations (SD), and/or medians (min-max), while categorical variables were reported as frequencies and percentages. Differences between groups in continuous variables were assessed using either an independent samples t-test or a Mann-Whitney U test, as appropriate. The Pearson chi-square test was employed to evaluate differences among categorical variables. The relationships among continuous variables were assessed using both bivariate Pearson and Spearman correlation coefficients. To compare more than two independent groups, the Kruskal–Wallis test was used as a nonparametric method. Furthermore, a meta-analysis in the literature indicated a moderate effect size (g=0.43; 95% confidence interval:0.34 to 0.53; p<0.001) in the ratings of problem behaviors between children with language disorders and their typically developing peers. Assuming that the receptive or expressive language skills of children with language delays have a moderate effect size (0.40) on the total difficulties scale scores of the SDQ 2–4, a sample size of 58 was calculated, achieving 95% power with a 5% type I error rate. A p-value of less than 0.050 was regarded as statistically significant.

RESULTS

The study involved 58 children with an average age of 32.48 ±5.69 months, of which 63.8% were male. Among the participants, 12% had a history of prematurity. Additionally, 43% of the mothers and 67% of the fathers had an education level below high school (Table I). The average daily screen time for the children was 2.19±2.20 hours, with 44.83% adhering to the guidelines set by the American Academy of Pediatrics regarding screen time (Table II).

The participants' average receptive language scores were 95.51 ±11.45, whereas their average expressive language scores were 82.05±11.45. Table II presents a detailed classification of receptive and expressive language skills. Among the children referred for language and speech delay, 11 (19%) demonstrated typical development in both receptive and expressive language. In contrast, 32 (55.2%) exhibited delays in both receptive and expressive language development, while 15 (25.9%) had delays solely in expressive language. Notably, no children were identified with impaired receptive language skills alongside normal expressive language capabilities. Furthermore, 56.90% of the children had total difficulty scores on the SDQ 2-4 that surpassed the established cutoff value, with an average score of 11.06±5.53.

The relationships between sociodemographic variables, language abilities, and behavioral problems were thoroughly investigated. Specifically, children of mothers with a high school education or higher exhibit significantly higher receptive and expressive language scores than those whose mothers possess less than a high school education (receptive language: 99.2±11.9 vs. 90.6±8.9, p=0.002; expressive language: 85.6 ±11.9 vs. 77.3±9.0, p=0.004). Likewise, children of fathers with higher educational attainment had significantly higher receptive and expressive language scores than those with less educated fathers (receptive language: 100.4±13.1 vs. 93.1±9.9, p=0.041; expressive language: 86.8±9.9 vs. 79.7±11.6, p=0.019). Total difficulty scores on the SDQ 2-4 were significantly higher in children of mothers with less than a high school education compared to those of mothers with education above high school (13 [6–25] vs. 9 [1–23], p = 0.030). No significant difference was found between fathers' education levels and children's total difficulty scores (10 [1–25] vs. 10 [3–18], p=0.584). The socioeconomic and sociocultural level of families, as determined by the Hollingshead-Redlich Scale, demonstrated a negative correlation with receptive and expressive language skills (receptive language: r =–0.359, p = 0.002; expressive language: r=–0.292, p=0.009), while no significant association was observed with behavioral problems (r=0.235, p=0.076). Daily screen time among children exhibited a significant negative correlation with both receptive and expressive language scores (receptive language: r=–0.332, p=0.011; expressive language: r=–0.334, p=0.010), whereas increased screen time was associated with a notable rise in hyperactivity and inattention problems (receptive language: r =–0.332, p=0.011; expressive language: r=–0.334, p=0.010) (r=0.326, p=0.013). An increase in the frequency of daily

Table I: Sociodemographic characteristics of the children with language delay

Variable	Values
Age (months)*	32.48±5.69
Sex (male)†	37 (63.8)
Gestational age‡	38 (31-42)
<37 weeks †	7 (12.06)
Birth weight (grams)‡	3200 (1220-4200)
Maternal age*	31.48±5.69
Maternal education level †	
Illiterate/unschooled	0
Primary school	11 (18.96)
High school	14 (24.13)
University	33 (56.90)
Employed mothers †	13 (22.41)
No maternal chronic disease †	48 (82.76)
Paternal age*	35.20±6.37
Paternal education level †	
Illiterate/unschooled	0
Primary school	13 (22.41)
High school	26 (44.83)
University	19 (32.76)
Employed fathers †	58 (100)
No paternal chronic disease †	51 (87.93)
Child's birth order‡	2 (1-4)
Number of members in the family‡	4 (3-7)
Number of siblings‡	2 (1-4)
Hollingshead-Redlich Scale †	
I	0
II	15 (25.86)
III	19 (32.76)
IV	24 (41.38)
V	0

**: mean±SD, †: n(%), ‡: median (min-max)*

Table II: Communicative environmental factors, TEDIL scores, and behavioral problem scores in children with language delay

Variable	Values
Screen time (hours)*	2.19 ±2.20
Meeting screen time guidelines†	26 (44.83)
Background television exposure (hour)*	3.75±4.04
Daily reading to child (week/day)‡	3 (0-7)
Preschool attendance (yes)†	8 (13.80)
Having a family member with language delay (yes)†	13 (22.41)
TEDIL scores/Receptive language†	
Very good	0 (0)
Good	2 (3.45)
Above average	4 (6.90)
Average	37 (63.80)
Below average	13 (22.41)
Weak/poor	1 (1.72)
Very poor	1 (1.72)
TEDIL scores/Expressive language†	
Very good	0 (0)
Good	0 (0)
Above average	1 (1.72)
Average	10 (17.24)
Below average	24 (41.38)
Weak/poor	14 (24.14)
Very poor	9 (15.52)
SDQ/Total difficulties score*	11.06±5.53
<10†	25 (43.10)
≥10†	33 (56.90)

:** *mean ± SD,* **†:** *n(%),* **‡:** *median (min-max),* ***TEDIL: *Test of Early Language Development-Third Edition: Turkish Version,* ***SDQ:*** *Strengths and Difficulties Questionnaire*

reading to children was associated with a significant reduction in all behavioral problems, including emotional symptoms, hyperactivity/inattention, conduct problems, peer relationship difficulties, and total difficulty scores (r=–0.266, p=0.043; r= –0.421, p=0.001; r=–0.348, p=0.007; r =–0.348, p=0.007; r = –0.502, p < 0.001; respectively). The frequency of book reading did not demonstrate a significant relationship with language skills.

The children's receptive language scores were negatively correlated with conduct problems, hyperactivity/inattention, peer relationship difficulties, and total difficulty scores (r= –0.313, p=0.017; r=–0.287, p=0.029; r=–0.350, p=0.007; r=–0.373, p=0.004; respectively), while no significant relationships were observed between their expressive language skills and behavioral problems. On the other hand, children with typical language skills had a total difficulty score of 7.90±2.84 on the SDQ 2-4, while those with only expressive language delays scored 11.06±5.55, and those with both receptive and expressive delays scored 13.40±6.06, revealing a statistically significant difference among the groups (p=0.043). Moreover, the findings indicated that within these three groups, the proportions of children with total difficulty scores exceeding 10 on the SDQ were 27.7%, 59.38%, and 73.33%, respectively. The pairwise comparison results indicated a statistically significant difference between children with typical language skills and those with both receptive and expressive language delays (p=0.013). It is notable that the total difficulty scores for children with expressive language delays exceeded the set cutoff values, even though the difference in behavioral problems between those with isolated expressive language delays and those with typical language development did not reach statistical significance (p=0.074).

DISCUSSION

Research indicates that children with diminished receptive language competencies may encounter significant challenges in comprehending communication during social interactions. This impairment can lead to a decline in positive peer engagement and may precipitate behavioral issues, including social withdrawal or disruptive conduct (15, 16). Expressive language is crucial for positive interactions and frequent exchanges about needs, desires, and emotions. Deficits in this skills can significantly increase the risk of internalizing behavioral problems, such as social withdrawal (1, 15). Alternatively, when poorer language skills hinder the use of verbal strategies for communication, they may potentially result in maladaptive behavioral expressions, such as temper tantrums and aggressive behaviors (6, 17).

While most studies link language and speech difficulties to behavioral issues, one study presented contrasting findings. After controlling for cognitive abilities, it reported that language delays did not predict behavioral problems, either concurrently or longitudinally (18). In our study, a negative correlation was observed between children's receptive language skills and conduct problems, hyperactivity/inattention, peer relationship difficulties, and overall difficulty scores. In contrast, expressive language skills did not exhibit significant correlations with behavioral issues. The observed relationships with receptive language skills align with and reinforce the findings established in the existing literature (1, 2). In contrast, the finding that 59.38% of children with only expressive language delays and 73.33% of those with both receptive and expressive delays exceeded the SDQ cutoff for total difficulty scores indicates that expressive language delays may indeed present a substantial risk for behavioral problems. The absence of a significant correlation may be attributed to the limited sample size or implies that behavioral problems might manifest independently of the severity of expressive language delays.

Language and speech delay during early childhood often represent critical concerns for families. A study investigating the diagnostic processes for children with speech delays revealed that 19% of the participants demonstrated typical language development, indicating a prevalence rate comparable to that found in our research (19). It is well established that low parental education and low socioeconomic status serve as potential risk factors for children's language development as well as for their overall developmental outcomes (20, 21). Mothers with higher educational attainment are more likely to facilitate their children's engagement with enriching learning experiences and to furnish a diverse array of educational resources at home, thereby significantly advancing their developmental outcome. An investigation into the factors influencing child development in low- to middle-income countries identified a notable association between the educational levels of both mothers and fathers and the language proficiency scores of their children (22). Poverty and socioeconomic adversity negatively impact children's physiological systems and brain development while also influencing their overall development through maternal sensitivity and the learning opportunities that parents create in home and social contexts (2, 22). Our research underscores the existing literature by elucidating the relationship between parental education, family socioeconomic status, and their significant influence on children's receptive and expressive language competencies.

Research suggests that excessive screen time during early childhood is associated with detrimental effects on children's receptive and expressive language skills, as well as their academic competencies in subsequent developmental stages (23). In this study, aligning with existing literature, we found that screen time was negatively associated with both receptive and expressive language skills. It is posited that this condition arises from both diminished parent-child interactions during television viewing and compromised family functioning in households marked by elevated media usage (24). Screen time is associated with poor mental health outcomes by displacing essential activities such as physical exercise, sleep, social interactions, and learning opportunities while simultaneously increasing arousal levels due to fast-paced and intense audiovisual effects, which may hinder self-regulation strategies and elevate the risk of behavioral issues (25). The finding that screen time is linked to hyperactivity and inattention problems in children aligns with the literature emphasizing a stronger connection between language delays and externalizing issues (26). A further notable finding is that children with speech delays had an average daily screen time of 2.19 hours (±2.20), with only 44.83% of the participants complying with the screen time guidelines established by the American Academy of Pediatrics (24).

Notwithstanding the extensive exploration of the relationships between language skills and behavioral problems in the literature, the methodological heterogeneity among studies highlights the continued necessity for further research in this domain. The majority of studies have focused on children with developmental language disorders or typically developing children. Families frequently voice concerns regarding their children's language and speech development; thus, our study's examination of children with language and speech delay, alongside those with typical language development, provides a distinctive and comprehensive perspective on this critical issue. A key strength of this study lies in its thorough examination of children presenting with language and speech delay complaints from a developmental pediatrics perspective, supported by comprehensive developmental assessments. The exclusion of children with neurodevelopmental disorders or significant cognitive delays, accomplished through the use of current developmental assessment tools, has effectively mitigated potential confounding factors. Furthermore, we posit that our study contributes to the literature as it represents one of the first investigations on this topic conducted in a developing country such as Turkiye.

Limitations

The limitations of our study are primarily related to the small sample size and its cross-sectional design. This limitation constrained the depth of data analysis and limits to generalisability of our findings. Future studies with a larger sample size and longitudinal design would facilitate a more comprehensive examination of the behavioral issues associated with children experiencing speech delays.

CONCLUSION

Preschool-aged children with language and speech delay represent a patient demographic that primary care providers, as well as pediatricians and pediatric subspecialists, often encounter in clinical practice. Children with delays in language and speech development frequently accompany behavioral issues, and it is particularly noteworthy that those from families with low socioeconomic and sociocultural backgrounds are at heightened risk. To potentially reduce the risk of long-term behavioral challenges that may extend into adulthood, it is important to address behavioral problems alongside language interventions.

Ethics committee approval

This study approved by Ankara Bilkent City Hospital Ethics Committee (date: 29.05.2024, number: TABED 2-24-192).

Contribution of the authors

Study conception and design: ***EÖ, F.A., G.H.T., A.M.Y., G.Ş., P.Ç***; Data collection: ***F.A., G.H.T., A.M.Y., G.Ş***; Analysis and interpretation of results: ***EÖ, P.Ç***; Draft manuscript preparation: ***EÖ, P.Ç***. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Original Article

Clinical characteristics and outcomes of pediatric code blue activations in a tertiary care hospital: A retrospective cohort study

Funda Kurt[1], Devrim Tanıl Kurt[2]

[1]Department of Pediatric Emergency, Ankara Bilkent City Hospital, University of Health Sciences, Ankara, Türkiye
[2]Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

ABSTRACT

Objective: The code blue system is an in-hospital early warning and emergency response mechanism designed to ensure rapid and effective intervention in critically deteriorating patients. This study aimed to evaluate the code blue activations implemented in our tertiary pediatric hospital.

Material and Methods: Demographic and clinical data of code blue events recorded between October 2019 and December 2020 at a tertiary pediatric hospital were retrospectively analyzed.

Results: The median age of patients was 146.0 months (IQR: 67.0–183.0), with 23 (39.0%) being male. Underlying chronic conditions were present in 27 patients (45.8%), most commonly neurological (n=9, 33.3%), followed by metabolic/genetic (n=6, 22.2%) and hematologic/oncologic disorders (n=6, 22.2%). Cardiopulmonary resuscitation (CPR) was performed in 10 patients, with a mean duration of 41.25±18.87 minutes (range: 25–60). The return of spontaneous circulation (ROSC) rate among those who received CPR was 90%. There were 4 in-hospital deaths (6.8%) following arrest. Comparison of admitted vs. non-admitted patients revealed that 13 (76.5%) of the admitted group were male ($p<0.001$), and their median age was significantly lower [67.0 (6.0–184.0) vs. 154.0 (99.5–184.0), $p=0.013$]. Among admitted patients, 10 (58.8%) were under 73 months of age, and 15 (88.2%) had chronic comorbidities ($p<0.001$). Code blue calls from pediatric wards resulted in hospital admission in 11 cases (84.6%), whereas 22 calls (52.4%) from phlebotomy units did not require admission ($p<0.001$).

Conclusion: The high frequency of sudden clinical deterioration among pediatric patients particularly in early childhood and those with chronic conditions emphasizes the critical need for timely and structured in-hospital emergency response. Strengthening code blue teams through early warning systems, continuous training, and structured protocols is essential for improving outcomes and reducing preventable adverse events.

Keywords: Code blue, cardiopulmonary resuscitation, mortality, rapid response team, pediatric, survival

INTRODUCTION

In-hospital cardiopulmonary arrest represents one of the most critical emergencies in pediatric medicine, requiring rapid, well-coordinated, and evidence-based intervention. Pediatric patients, due to their inherently limited physiological reserves and increased susceptibility to sudden clinical deterioration, are particularly vulnerable in such scenarios. Timely initiation of CPR and advanced life support by trained healthcare professionals has been consistently associated with improved survival rates and more favorable neurological outcomes in this population (1,2).

To optimize response in these life-threatening situations, many healthcare systems have implemented structured Code Blue protocols. Code Blue refers to a standardized in-hospital emergency response system that ensures the immediate mobilization of a multidisciplinary resuscitation team upon the recognition of cardiopulmonary arrest. While most commonly activated for cardiopulmonary arrest, in some institutions or under clinician judgment, critical events such as seizures or syncope may also prompt a Code Blue, depending on local protocols. The effectiveness of such systems hinges upon minimizing the time from arrest recognition to the initiation of life-saving interventions. In high-acuity environments such as tertiary referral hospitals, pediatric Code Blue systems are

Correspondence Address:
Funda Kurt
e-mail: drfundakurt@gmail.com

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particularly critical for standardizing care processes, reducing variability in response times, and enhancing overall patient safety (3,4).

Although Code Blue systems have become increasingly prevalent worldwide, the existing body of literature predominantly reflects data derived from adult populations in high-income countries. Pediatric-specific data remain limited, and contextual evidence from low and middle-income settings is especially scarce (5). Furthermore, the unique pathophysiology of pediatric arrest frequently secondary to progressive respiratory or circulatory failure necessitates dedicated evaluation of the timeliness and appropriateness of Code Blue responses in children.

In Türkiye, the Ministry of Health has formally mandated the establishment of Code Blue systems in all healthcare institutions, as outlined in regulations published in 2009 and 2011 (6,7). The national emergency activation line (2222) was designated to standardize call procedures, and institutional policies were developed to promote consistent implementation. However, despite these national efforts, real-world data regarding pediatric Code Blue activations, response characteristics, and clinical outcomes remain largely unexplored.

This study aimed to address this knowledge gap by retrospectively evaluating pediatric Code Blue activations at Ankara Bilkent City Hospital, one of the largest tertiary care centers in Türkiye. By examining cases reported between August 2019 and March 2021 in patients aged 1 month to 18 years, the study seeks to characterize the demographic and clinical profiles of the patients, analyze the response and resuscitation processes, and assess short-term clinical outcomes. The findings are expected to inform quality improvement initiatives and contribute to the optimization of in-hospital emergency response systems for pediatric populations.

MATERIALS and METHODS

Study Design and Setting

This study was designed as a retrospective, observational cohort analysis and conducted at Ankara Bilkent City Hospital, a high-capacity tertiary care institution serving as a major pediatric referral center in Türkiye. The study population comprised all pediatric patients aged between 1 month and 18 years for whom a Code Blue activation was initiated between August 2019 and March 2021.

Institutional Code Blue System

The Code Blue protocol at Ankara Bilkent City Hospital is governed by standardized institutional guidelines that clearly delineate the roles, responsibilities, and scope of practice of the emergency response team. Each team is composed of at least one physician and either an anesthesia technician or an emergency medical technician, and provides round-the-clock (24/7) coverage across all inpatient units, excluding emergency departments, intensive care units (ICUs), and operating theatres, where Code Blue activation is not permitted under hospital policy.

Code Blue alerts are triggered via internal landline telephones by dialing “2222-5”, and the termination of the alert is carried out by dialing “2222-99” after the team arrives on-site and completes the required interventions. Upon activation, the resuscitation team is expected to reach the designated location within three minutes, carrying a fully equipped emergency intervention kit.

The scope of responsibility for Code Blue responders includes:

- immediate assessment of the patient’s clinical status,
- initiation of cardiopulmonary resuscitation (CPR),
- delivery of advanced life support (ALS) as indicated, and
- safe transfer of the patient to the appropriate level of care if stabilization is achieved.

All procedures and clinical interventions performed during Code Blue events are meticulously documented in the AD.FR.001 Code Blue Intervention Form, an institutional template for standardized data collection.

Operational tools, including DECT phones and access control cards, are rotated among team members between shifts to ensure seamless continuity. Daily inventory checks and handovers of emergency medications and supplies in the resuscitation kits are performed and recorded using the İY.FR.040 Emergency Medication and Supply Tracking and Handover Form. The anesthesia technician is responsible for maintaining appropriate stock levels, verifying expiration dates, and replenishing depleted materials in accordance with hospital protocols.

Data Collection

Data for the current study were retrospectively obtained from two primary sources:

1. The AD.FR.001 Code Blue Intervention Forms, completed contemporaneously by Code Blue responders; and
2. The institution’s electronic medical record (EMR) system, from which demographic data, clinical characteristics, resuscitation details, and patient outcomes were extracted.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 29.0.2.0 (IBM Corp., Armonk, NY, USA). Frequency distributions were presented as numbers and percentages, and continuous variables were expressed as medians with interquartile ranges (IQR). The Kolmogorov–Smirnov test was used to assess the normality of data distribution.

For statistical evaluation, the Mann–Whitney U test was used for non-normally distributed data, and the Chi-square test was applied for categorical variables. For comparisons involving more than two groups, the Kruskal–Wallis test was used. A p-value of <0.05 was considered statistically significant.

RESULTS

During the study period, a total of 169202 visits to the pediatric emergency department and 169894 visits to pediatric outpatient clinics were recorded. A cohort of 59 pediatric patients with documented in-hospital code blue activations was retrospectively evaluated.

The median age of the patients was 146.0 months (interquartile range [IQR]: 67.0–183.0), and 23 (39.0%) were male. Nine patients (15.3%) were under the age of 25 months. An underlying chronic medical condition was present in 27 patients (45.8%), most commonly neurological disorders (n =9, 33.3%), followed by metabolic/genetic diseases (n =6, 22.2%) and hematologic/oncologic conditions (n =6, 22.2%) (Table I).

The majority of code blue activations (n =49, 83.1%) occurred during regular working hours (08:00–16:00). The most frequent locations of code blue events were the phlebotomy unit (n =22, 37.3%), pediatric inpatient wards (n =13, 22.0%), and hospital corridors (n =10, 16.9%). Syncope (n =37, 62.7%) was the leading cause of activation, followed by seizure activity (n = 9, 15.3%) and respiratory arrest (n =7, 11.9%). The mean response time of the code blue team was 1.53±0.6 minutes (range: 1.0–3.0) (Table II).

On-site emergency intervention was performed in 33 patients (55.9%), with intravenous access (n=26, 44.1%) and supplemental oxygen administration (n=16, 27.1%) being the most common procedures. A total of seven patients required resuscitative efforts in the pediatric intensive care unit (PICU), including three patients with respiratory arrest and 2 with cardiopulmonary arrest in the pediatric wards, and two patients who developed respiratory arrest during imaging procedures. All three patients with respiratory arrest on the ward achieved ROSC, although one subsequently died after one day in the PICU. Among the patients who experienced cardiopulmonary arrest, one failed to achieve ROSC despite resuscitative

Tablo I: Demographic characteristics of the patients

Age (months)*	146.0 (67.0-183.0)
1- 24 †	9 (15.3)
25- 72 †	6 (10.2)
73- 132 †	12 (20.3)
133-216 †	32 (54.2)
Gender †	
Female	36 (61.0)
Male	23 (39.0)
Presence of underlying disease †	
Yes	27 (45.8)
No	32 (54.2)
Type of underlying disease †	
Neurological disease	9 (33.3)
Metabolic/genetic disease	6 (22.2)
Hematologic/oncologic disease	6 (22.2)
History of major surgery	5 (18.6)
Respiratory disease	1 (3.7)

***:** *median (IQR),* **†:** *n (%)*

Tablo II: Characteristics of pediatric in-hospital code blue activations

Code Blue Activation Time*	
8:00 am to 4:00 pm	49 (83.1)
4:01pm to 11:59 pm	5 (8.5)
12 midnight to 07:59 am	5 (8.5)
Location of Code Blue Activation*	
Blood Collection Unit	22 (37.3)
Inpatient Ward	13 (22.0)
Hospital Corridor	10 (16.9)
Radiology Department	7 (11.9)
Outpatient Department	7 (11.9)
Reason for Code Blue Activation*	
Syncope	37 (62.7)
Convulsion	9 (15.3)
Respiratory Arrest	7 (11.9)
Cardiopulmonary Arrest	3 (5.1)
Respiratory Distress	3 (5.1)
Response Time of the Code Blue Team†	1.53±0.6 (1.0-3.0)
On-site Emergency Intervention*	
Yes	33 (55.9)
No	26 (44.1)

***:** *n (%),* **†:** *mean ± SD (min-max)*

Table III: Management and outcomes of pediatric in-hospital code blue events

Location of Intervention*	
Pediatric emergency department	36 (61.0)
PICU	10 (16.9)
Pediatric ward	7 (11.9)
On-site	6 (10.2)
On-site Interventions*,†	
Intravenous access	26 (44.1)
Oxygen administration	16 (27.1)
Endotracheal intubation	10 (16.9)
Cardiopulmonary resuscitation	10 (16.9)
Drug administration	8 (13.6)
Bag-mask ventilation	5 (8.5)
Defibrillation	0 (0.0)
Outcome of cardiopulmonary resuscitation*	
ROSC	9 (90.0)
Death	1 (10.0)
Duration of Cardiopulmonary Resuscitation (minutes)‡	41.25±18.87 (25- 60)
Hospitalization unit*	
Pediatric ward	9 (15.3)
PICU	8 (13.6)
Outcome*	
Discharged	55 (93.2)
Death	4 (6.8)
Observation in emergency department (hours)§	2.0 (2.0-4.0)
Length of inpatient stay (days)§	7.5 (4.0- 5.8)
Length of PICU stay (days)§	4.0 (1.0- 0.0)

***:** *n(%),* **†:** *Multiple interventions were performed in some patients,* **‡:** *mean±SD (min-max),* **§:** *median (IQR),* **PICU:** *Pediatric Intensive Care Unit,* **ROSC:** *Return of Spontaneous Circulation*

Table IV: Comparison of hospitalized and non-hospitalized pediatric code blue cases

	Hospitalized	Non-Hospitalized	p
Gender*			<0.001[‡]
Female	4 (23.5)	32 (76.2)	
Male	13 (76.5)	10 (23.8)	
Age (months)[†]	67.0 (6.0- 184.0)	154.0 (99.5- 184.0)	0.013[§]
1- 24*	7 (41.2)	2 (4.8)	0.001[‡]
25-72*	3 (17.6)	3 (7.1)	
73- 132*	0 (0.0)	12 (28.6)	
133- 216*	7 (41.2)	25 (59.5)	
Presence of underlying disease*			<0.001[‡]
Yes	15 (88.2)	12 (28.6)	
No	2 (28.6)	30 (71.4)	
Location of code blue activation*			<0.001[‡]
Blood collection unit	0 (0.0)	22 (52.4)	
Inpatient ward	11 (84.6)	2 (4.8)	
Hospital corridor	1 (5.9)	9 (21.4)	
Radiology department	5 (29.4)	2 (4.8)	
Outpatient department	0 (0.0)	7 (16.7)	
Reasons for issuing code blue*			<0.001[‡]
Syncope	3 (17.6)	34 (81.0)	
Convulsion	2 (11.8)	7 (16.7)	
Respiratory arrest	7 (41.2)	0 (0.0)	
Cardiopulmonary arrest	2 (11.8)	1 (2.4)	
Respiratory distress	3 (17.6)	0 (0.0)	

***:** *n(%),* **†:** *median (IQR),* **‡:** *chi-squared test,* **§:** *Mann-Whitney U test*

efforts on the ward. Ten patients underwent cardiopulmonary resuscitation (CPR), with a mean duration of 41.25±18.87 minutes (range: 25–60). The ROSC rate in this subgroup was 90%. Nine patients (15.3%) were admitted to pediatric inpatient wards and eight (13.6%) to the PICU. Four patients (6.8%) died following in-hospital arrest. Of the 36 patients who received initial intervention in the pediatric emergency department, 19 (52.8%) were discharged after observation. The median length of stay was 2.0 days (IQR: 2.0–4.0) for the pediatric emergency department, 7.5 days (IQR: 4.0–15.8) for pediatric wards, and 4.0 days (IQR: 1.0–10.0) for the PICU (Table III).

When hospitalization status was analyzed, male sex was significantly more prevalent among hospitalized patients (76.5% vs. 23.5%; p<0.001). The median age was significantly lower in hospitalized patients [67.0 months (IQR: 6.0–184.0)] compared to those not admitted [154.0 months (IQR: 99.5–184.0); p= 0.013]. Furthermore, 41.2% of hospitalized patients were under 25 months of age, and 58.8% were under 73 months. A chronic underlying condition was present in 88.2% of hospitalized patients (p<0.001) (Table IV).

The site of code blue activation was significantly associated with hospitalization status. Among patients with code blue activations originating from pediatric wards, 84.6% required admission, whereas 52.4% of those from the phlebotomy unit were not hospitalized (p<0.001).

Analysis based on the cause of activation revealed that 81.0% of patients with syncope were discharged, while 41.2% of hospitalized patients presented with respiratory arrest (Table IV).

DISCUSSION

This study provides a comprehensive analysis of pediatric in-hospital code blue activations within a tertiary care institution, with a particular focus on patient demographics, underlying etiologies, temporal and spatial distribution patterns, implemented interventions, and subsequent clinical outcomes. The findings contribute valuable real-world data that support benchmarking against national and international standards, with potential implications for refining institutional patient safety strategies and emergency response protocols.

A key observation was the predominance of code blue activations during routine working hours (83.1%), predominantly occurring in procedural or high-traffic areas such as phlebotomy units and hospital corridors. This distribution is consistent with prior reports indicating temporal clustering of pediatric emergencies during peak operational periods, likely reflecting the heightened frequency of procedures and care transitions during these intervals (3,4,8).

Syncope emerged as the leading cause of code blue activation (62.7%), with the majority of such cases being discharged from the emergency department. In contrast, respiratory arrest demonstrated a strong association with PICU admission, reinforcing the well-established role of respiratory compromise as a key determinant of clinical severity and poor outcomes in hospitalized children (2,5,9).

Furthermore, younger age, male sex, and the presence of chronic comorbidities were significantly associated with postactivation hospital admission. Children with complex chronic conditions particularly neurological, genetic/metabolic, and hematologic/oncologic disorders were disproportionately represented among admitted cases. These findings are aligned with existing literature, which highlights the increased vulnerability of medically complex pediatric populations to acute clinical decompensation and the corresponding need for intensive monitoring and escalation of care (10–13).

Hospitalized patients had a significantly lower median age compared to non-admitted counterparts, supporting the notion that younger children, especially infants, possess limited physiological reserves and are more susceptible to rapid deterioration during acute events (14). Moreover, early clinical signs of decline in this age group may be subtle and easily overlooked by non-specialized personnel, underscoring the importance of standardized early warning tools such as the Pediatric Early Warning Score (PEWS) to support timely recognition and intervention (15,16).

The code blue team demonstrated a mean response time of 1.53 minutes, aligning with both national benchmarks and international best practice recommendations (1,9). Timely response remains a critical determinant of survival and neurological outcomes in pediatric resuscitation efforts. Notably, the ROSC was achieved in 90% of patients receiving CPR surpassing rates reported in several other series while the overall in-hospital mortality following arrest was 6.8%, in concordance with recent epidemiological data from North America and Europe (5,9,17).

A salient structural finding was the correlation between the location of activation and subsequent hospital admission. Code blue events occurring in inpatient wards were more frequently associated with hospital admission, likely reflecting the higher baseline acuity of these patients. In contrast, many activations in procedural areas such as phlebotomy units were transient and did not necessitate prolonged care. This spatial pattern underscores the potential value of implementing unit-specific training and early recognition protocols tailored to the clinical risk profile of different hospital zones (18).

While this study was conducted in a facility with an established code blue team, the broader integration of Pediatric Rapid Response Teams (PRRTs) and structured early escalation systems has been shown to significantly reduce the incidence of in-hospital cardiac arrest and improve early detection of clinical deterioration (19,20). The incorporation of such proactive and multidisciplinary response frameworks may further mitigate preventable arrests and contribute to the development of a robust and safety-oriented institutional culture.

This study has several limitations. Firstly, due to its retrospective design, the quality of the data relied heavily on the accuracy and completeness of existing medical records, and certain clinical details may have been missing or inconsistently documented. Additionally, as a single-center study, the generalizability of the findings is limited; variations in hospital infrastructure and code blue protocols across institutions may influence outcomes. The assessment of code blue events may also have been affected by subjective reports or incomplete documentation from the responding personnel. Lastly, due to the lack of long-term follow-up data, it was not possible to evaluate the sustained impact of interventions. Therefore, future multicenter prospective studies are recommended to validate and expand upon these findings.

In conclusion, sudden clinical deterioration is frequently observed in pediatric patients, particularly among younger age groups and those with underlying chronic conditions, necessitating prompt and effective intervention. Timely and competent administration of CPR by the Code Blue team is crucial for improving survival outcomes and minimizing long-term morbidity. Therefore, ensuring that healthcare personnel receive regular, up-to-date training and comply with national safety standards set forth by the Ministry of Health is essential to enhance the overall quality and effectiveness of emergency response in pediatric care settings.

Ethics committee approval

This study was approved by the Ankara Bilkent City Hospital Clinical Research Ethics Committee (Decision No: E2-21-99; Approval Date: 10.02.2021).

Contribution of the authors

Study conception and design: ***FK, DTK***; data collection: ***DTK***; analysis and interpretation of results: ***FK***; draft manuscript preparation: ***FK***.

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Conflict of interest

The authors declare that there is no conflict of interest.

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