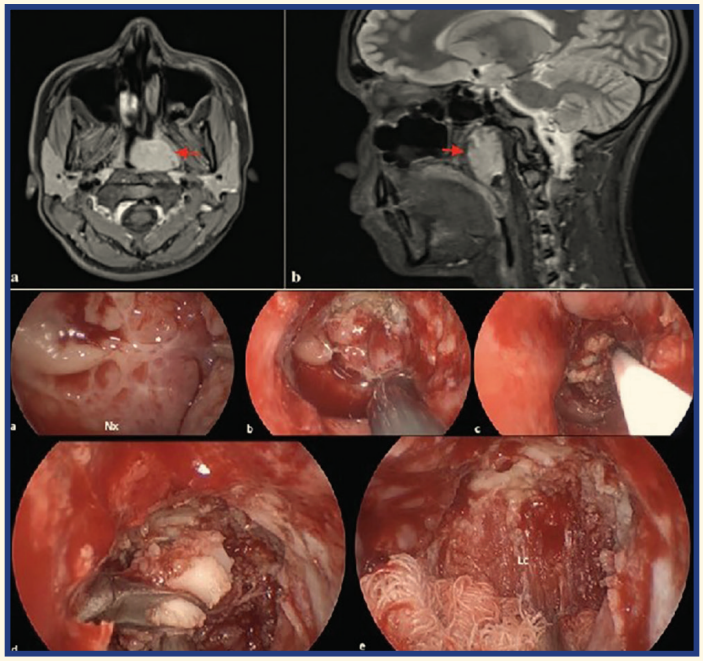
Year: March 2025 Volume: 12 Issue: 1

E-ISSN: 2587-2478

The Journal of Pediatric Research



galenos Publishing House

JPR
The Journal of Pediatric Research

Official Journal of Ege University Children's Hospital

EDITORIAL BOARD

The Journal of Pediatric Research is the official publication of Ege University Faculty of Medicine, Department of Pediatrics and Ege Children's Foundation.

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1
34093 İstanbul, Türkiye
Phone: +90 (530) 177 30 97 / +90 (539) 307 32 03
E-mail: info@galenos.com.tr/yayin@galenos.com.tr
Web: www.galenos.com.tr
Publisher Certificate Number: 14521

Online Publication Date: March 2025
E-ISSN: 2587-2478
International scientific journal published quarterly.

JPR
The Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

EDITORIAL BOARD

JPR
The Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

EDITORIAL BOARD

JPR
The Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

EDITORIAL BOARD

The Journal of Pediatric research is the official publication of Ege University and Ege Children's Foundation

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

The editorial and publication processes of the Journal of Pediatric Research are shaped in accordance with the guidelines of ICMJE, WAME, CSE, COPE, EASE, and NISO. The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

The Journal of Pediatric Research is indexed in **Emerging Sources Citation Index (ESCI), Embase, Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, CABI, Gale/Cengage Learning, Ulakbim TR Dizin, TurkMedline, J-GATE, IdealOnline, Hinari, GOALI, ARDI, OARE, AGORA** and **Türkiye Citation Index**.

The journal is published online.

Owner: Ege University and Ege Children's Foundation

Responsible Manager: Özgür ÇOĞULU

JPR
The Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

SCIENTIFIC ADVISORY BOARD

JPR
The Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

CONTENTS

JPR
The
Journal of Pediatric Research
Official Journal of Ege University Children's Hospital

EDITORIAL

Dear Readers,

We are pleased to present the latest issue of the Journal of Pediatric Research, which highlights significant advancements in pediatric healthcare. This issue encompasses a wide range of topics, from biomarker research in cystic fibrosis to the effectiveness of oral health education, neonatal pain management, and emerging infectious diseases. The diversity of these studies underscores the importance of a multidisciplinary approach to children's health.

This issue features a study investigating fluctuations in serum IGF-1 and IGFBP-3 levels during cystic fibrosis exacerbations and their potential role as clinical biomarkers for disease monitoring. Another article assesses the impact of an educational intervention on parental knowledge and awareness regarding pediatric oral health, demonstrating significant improvements in post-education evaluations. Another study explores the effectiveness of placing a pillow on the abdomen as a simple, non-invasive method to alleviate neonatal pain during lumbar puncture procedures. Researchers also analyze the changing epidemiology of invasive streptococcal infections in the pediatric population before and during the COVID-19 pandemic. One of the studies provides insights into the diagnosis and management of microlithiasis in infants, emphasizing its clinical implications and follow-up strategies. Additionally, a retrospective evaluation examines the prevalence, clinical characteristics, and treatment outcomes of pediatric dental emergencies.

In the case reports section, we present a rare case of hyalinizing clear cell carcinoma of the nasopharynx in a pediatric patient, discussing its diagnostic and therapeutic challenges. Another report highlights a successful pharmacological intervention in a pediatric patient with Kasabach-Merritt syndrome, an uncommon vascular disorder. Additionally, another case describing a self-limiting sternal tumor in a healthy infant contributes to the growing body of literature on benign pediatric chest wall masses. Lastly, in the letter to the editor, an alternative approach to intra-atrial catheterization in pediatric patients requiring central venous access is discussed.

This issue exemplifies the ongoing commitment of pediatric researchers and clinicians to improving child health outcomes through innovation and collaboration. We extend our gratitude to the authors, reviewers, the editorial team, and Galenos Publishing House for their contributions and dedication.

We hope that the research presented in this issue will inspire further advancements in pediatric medicine and encourage interdisciplinary collaboration in this field.

Sincerely,
Assoc. Prof. Dr. Ali Tekin

J Pediatr Res 2025;12(1):1-6
DOI: 10.4274/jpr.galenos.2025.88319

Original Article

Relation of Serum IGF-1 and IGFBP-3 Levels with Acute Exacerbation in Cystic Fibrosis

Ahmet Furkan Eser[1], Ela Erdem Eralp[2], Yasemin Gökdemir[2], Almala Pınar Ergenekon[2], Serap Turan[3], Nadiye Pınar Ay[4], Abdullah Bereket[3], Bülent Karadağ[2]

[1]Acıbadem University, Acıbadem Altunizade Hospital, Clinic of Pediatric Intensive Care, İstanbul, Türkiye
[2]Marmara University Faculty of Medicine, Department of Pediatric Pulmonology, İstanbul, Türkiye
[3]Marmara University Faculty of Medicine, Department of Pediatric Endocrinology, İstanbul, Türkiye
[4]Marmara University Faculty of Medicine, Department of Public Health, İstanbul, Türkiye

ABSTRACT

Aim: Cystic fibrosis (CF) is an autosomal recessive genetic disorder primarily affecting the lungs and it is a leading cause of morbidity and mortality. Progressive lung disease and acute pulmonary exacerbations (PEx) are significant contributors to poor patient outcomes. Early detection and management of PEx are critical in improving prognosis. Biomarkers have gained interest due to their role in diagnosing, monitoring, and evaluating treatment responses in PEx. This study investigated fluctuations in serum levels of insulin-like growth factor-1 (IGF-1) and its IGF binding protein-3 (IGFBP-3) during CF exacerbations in order to assess their potential as clinical biomarkers.

Materials and Methods: A total of 37 CF patients (16 females, 21 males, mean age 96.95±62.56 months), hospitalized for PEx and receiving intravenous antibiotic treatment, were included. Serum levels of IGF-1 and IGFBP-3 were measured at baseline, at the onset of exacerbation, and at the end of the exacerbation. Additionally, for 16 of the patients, serum levels were reassessed one month post-treatment. Forced expiratory volume (FEV1) measurements were performed for those patients who were able to complete the spirometry test.

Results: At baseline, serum IGF-1 and IGFBP-3 levels were significantly lower than those of the normal population ($p<0.001$). Marked decreases in IGF-1 and IGFBP-3 levels were observed at the onset of exacerbation compared to the baseline ($p<0.05$). These levels increased significantly following treatment at the end of the exacerbation ($p<0.05$), although no significant difference was found between the baseline and post-treatment levels. FEV1 values also showed significant differences between the baseline and exacerbation periods ($p<0.05$).

Conclusion: Serum levels of IGF-1 and IGFBP-3 in the CF patients were lower than in healthy age-matched controls, with significant fluctuations corresponding to the progression and treatment of acute exacerbations. These fluctuations offer valuable insight into the diagnosis and monitoring of treatment response. Therefore, IGF-1 and IGFBP-3 levels are potentially useful biomarkers for the clinical management of CF exacerbations.

Keywords: Cystic fibrosis, acute pulmonary exacerbation, IGF-1, IGFBP-3, biomarker

Introduction

Cystic fibrosis (CF) is a genetic disorder caused by *CFTR* gene mutations, leading to impaired chloride ion transport and thickened mucus secretions. While it affects multiple organs, the lungs are the most impacted. Its pathophysiology involves chronic inflammation, recurrent infections, and progressive lung damage, often resulting in respiratory failure (1).

Corresponding Author
Ahmet Furkan Eser, MD, Acıbadem University, Acıbadem Altunizade Hospital, Clinic of Pediatric Intensive Care, İstanbul, Türkiye
E-mail: feser_527@hotmail.com **ORCID:** orcid.org/0000-0001-5824-1868
Received: 19.12.2024 **Accepted:** 02.01.2025 **Epub:** 06.03.2025 **Publication Date:** 17.03.2025

Cite this article as: Eser AF, Eralp EE, Gökdemir Y, et al. Relation of serum IGF-1 and IGFBP-3 levels with acute exacerbation in cystic fibrosis. J Pediatr Res. 2025;12(1):1-6

Pulmonary involvement in CF is a major factor in morbidity and mortality. Acute pulmonary exacerbations (PEx), marked by a sudden worsening of respiratory symptoms, are a significant complication. Often triggered by infections, PEx accelerates lung function decline and causes long-term damage. Early diagnosis and effective management are vital for improving outcomes (2).

The treatment of PEx includes pharmacological options such as antibiotics and anti-inflammatory agents, alongside non-pharmacological methods such as chest physiotherapy. While clinical assessment, respiratory function tests, and imaging are standard for evaluating exacerbations, interest is growing in biomarkers to detect onset, assess severity, and monitor treatment response. Numerous inflammatory and immune-related biomarkers have been studied for their potential roles in managing acute exacerbations (3,4).

Insulin-like growth factor-1 (IGF-1) and its IGF binding protein-3 (IGFBP-3) are potential markers for disease severity and treatment response in CF. CF patients generally have lower serum IGF-1 and IGFBP-3 levels, likely due to nutritional deficiencies and systemic inflammation. Studies indicate that their levels vary during acute exacerbations, reflecting inflammation severity and treatment effectiveness (5-7).

This study investigated the relationships between serum IGF-1 and IGFBP-3 levels and PEx in CF patients. By analyzing their fluctuations during exacerbations and treatment, we aimed to assess their role in diagnosing and monitoring therapy responses.

Materials and Methods

Between January 2016 and June 2017, 37 CF patients aged 0-18 years, followed by the Department of Pediatric Pulmonology, Marmara University Faculty of Medicine, were prospectively included in this study. The participants, hospitalized for PEx and treated with intravenous (IV) antibiotics, were enrolled after obtaining informed consent from their legal guardians. Ethics approval was obtained from the Marmara University Faculty of Medicine, Clinical Research Ethics Committee (date: 06/11/2015, approval no.: 09.2015.291).

As there are no universally accepted criteria for diagnosing CF-related PEx, the diagnoses were based on clinical symptoms and signs. Only hospitalized patients requiring IV antibiotic therapy were included, and those patients treated on an outpatient basis were excluded from this study. Patients without legal guardian consent were excluded. Patients without blood samples at baseline, exacerbation onset, or end of exacerbation, as well as those who withdrew or had baseline samples but no PEx episodes, were also excluded. Serum IGF-1 and IGFBP-3 levels were measured at four-time points: Baseline, exacerbation onset, exacerbation end, and post-treatment. Blood for baseline samples was taken from patients without any active lung infection or recent PEx. Blood samples for exacerbation onset were collected upon hospitalization, and for exacerbation end, on the discharge day after treatment. A total of 37 patients meeting the criteria were included in this study. During the post-treatment follow-up, 21 patients missed their hospital appointments, preventing blood sample collection. Consequently, 37 patients were evaluated over three periods, while 16 patients with follow-up samples were separately assessed across four periods.

For each period, 5 mL of blood was collected in serum separation tubes, centrifuged at 4,000 rpm for 5 minutes, and the serum was stored at -80 °C. IGF-1 and IGFBP-3 levels were measured using the chemiluminescence method on an "immulite 2000" device at the Central Biochemistry Laboratory of Marmara University Faculty of Medicine, Pendik Training and Research Hospital.

Patient data included age at CF diagnosis, age during PEx, gender, height-for-age, weight-for-age, and body mass index (BMI)-for-age z-scores. Spirometry tests were evaluated for those patients capable of performing this procedure.

Statistical Analysis

Data recording and analysis were performed using "SPSS 20." Descriptive statistics, such as mean, standard deviation, median, frequency, percentage, range, and percentiles (25^{th}, 50^{th}, 75^{th}), were calculated. The Friedman test was used to compare serum IGF-1, IGFBP-3, and FEV1 levels across the baseline, exacerbation onset, end, and post-treatment periods, with $p<0.05$ considered statistically significant. The Wilcoxon test was used to compare the four periods, and p-values were adjusted with the Bonferroni correction. Spearman's correlation coefficients were used to analyze the relationships between serum IGF-1, IGFBP-3, and FEV1. For all tests, except those with Bonferroni correction, $p<0.05$ was considered statistically significant.

Results

This study included 37 CF patients [16 females (43.2%) and 21 males (56.8%)] hospitalized for PEx and treated with antibiotics at the Department of Pediatric Pulmonology, Marmara University Faculty of Medicine.

The mean, standard deviation, median, minimum, maximum, and percentile values for the patients' ages, ages at diagnosis, height-for-age z-scores, weight-for-age z-scores, and BMI-for-age z-scores are presented in Table I. For serum IGF-1 and IGFBP-3 values, which were not normally distributed, descriptive statistics including mean, standard deviation, median, and interquartile range were calculated for the four clinical periods, and these are presented in Table II. Figures 1 and 2 present the minimum, maximum, median, 25th, and 50th percentiles of the IGF-1 and IGFBP-3 levels for three periods as boxplots.

During the serum IGF-1 and IGFBP-3 measurement periods, FEV1% values were recorded for the 20 patients (54.1%) who were able to perform spirometry. In the follow-up period, 9 out of 16 patients were able to perform spirometry (Table II).

The serum IGF-1 and IGFBP-3 levels of 37 patients were compared across baseline, onset of exacerbation, and end of exacerbation, revealing statistically significant differences between periods ($p<0.001$). Pairwise comparisons of the three periods using the Wilcoxon test (Bonferroni correction applied, $p<0.017$) revealed significant differences between

Table I. Descriptive data for age, age at diagnosis, and age-adjusted height, weight, and BMI Z-scores

		Age (months)	Age at diagnosis (months)	Height-for-age Z-score	Weight-for-age Z-score	BMI-for-age Z-score
n		37	37	37	37	37
Mean		96.95	22.35	-0.88	-0.96	-0.71
SD (±)		62.56	47.91	0,93	1.35	1.47
Median		96	3	-1.03	-0.98	-0.78
IQR		95	5	1.21	2.06	2.27
Minimum		2	1	-3.51	-3.54	-3.94
Maximum		207	187	1.14	2.03	1.86
Percentile	**25th**	45	2	-1.42	-2.02	-1.82
	50th	96	3	-1.03	-0.98	-0.78
	75th	139.5	7	-0.20	0.04	0.45

SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index

Table II. Distribution of serum IGF-1, IGFBP-3 levels, and FEV1 measurements across different clinical periods

		n (%)	Mean ± SD	Median (IQR)
IGF-1	Baseline	37 (100)	128.28±89.54	101 (81.20)
	Onset of exacerbation	37 (100)	98.91±76.16	76.40 (62.70)
	End of exacerbation	37 (100)	139±87.52	109 (99.80)
	Post-treatment control	16 (43.2)	125.15±94.10	75.30 (133.53)
IGFBP-3	Baseline	37 (100)	3.49±1.37	3.17 (2.11)
	Onset of exacerbation	37 (100)	2.93±1.51	2.65 (1.51)
	End of exacerbation	37 (100)	3.90±1.52	3.55 (2.53)
	Post-treatment control	16 (43.2)	3.39±1.61	2.73 (2.80)
FEV1	Baseline	20 (54.1)	78.7±21.98	82 (30.5)
	Onset of exacerbation	20 (54.1)	59.5±15.73	59.5 (27.25)
	End of exacerbation	20 (54.1)	74.5±20.34	74 (28.25)
	Post-treatment control	9 (24.3)	76±19.33	82 (32.5)

Serum IGF-1 unit is ng/mL, IGFBP-3 unit is µg/mL and FEV1 values are given as percentages (%)
IGF-1: Insulin-like growth factor-1, IGFBP-3: Insulin-like growth factor binding protein-3, FEV1: Forced expiratory volume, IQR: Interquartile range, SD: Standard deviation

the baseline and exacerbation onset (p<0.001 for IGF-1, and p=0.001 for IGFBP-3). The differences between onset of exacerbation and end of exacerbation values were also found to be significant (p<0.001). When comparing changes between the baseline and post-treatment periods, no statistically significant differences were found (p=0.216 for IGF-1, and p=0.032 for IGFBP-3) (Table II).

In the post-treatment follow-up, the serum IGF-1 and IGFBP-3 levels of 16 patients were compared across the baseline, onset of exacerbation, end of exacerbation, and follow-up periods using the Friedman test, revealing statistically significant differences (p<0.001 for IGF-1, and p=0.002 for IGFBP-3). Pairwise comparisons using the Wilcoxon test (Bonferroni correction, p=0.008) showed no significant differences in serum IGF-1 and IGFBP-3 levels between the baseline and post-treatment periods (IGF-1: p=0.642, and IGFBP-3: p=0.938). The comparison between the onset of exacerbation and post-treatment periods showed significant differences (p=0.004 for IGF-1 and IGFBP-3), while no significant difference was observed between the exacerbation end and post-treatment periods (p=0.278 for IGF-1, and p=0.66 for IGFBP-3).

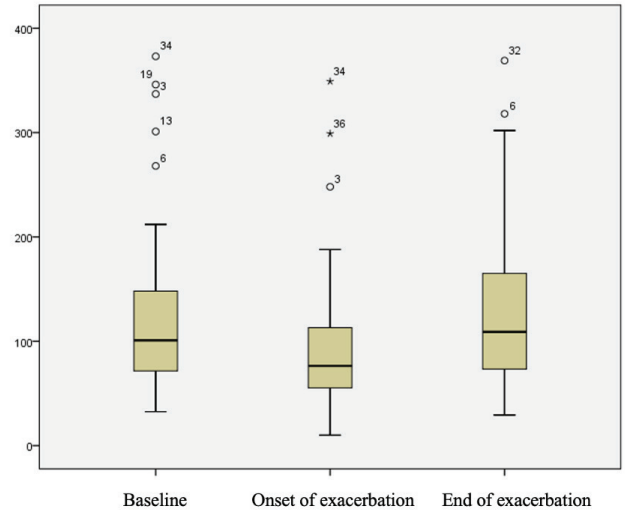


Figure 1. Serum IGF-1 levels at baseline, onset of exacerbation, and end of exacerbation
[x-axis: clinical periods; y-axis: IGF-1 levels (ng/mL)]
IGF-1: Insulin-like growth factor-1

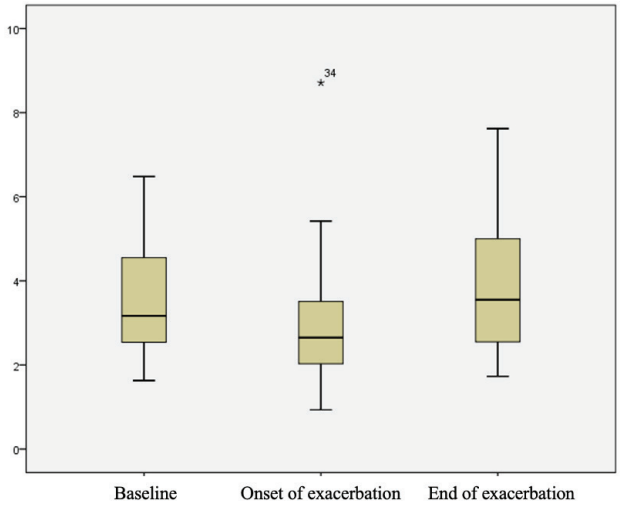


Figure 2. Serum IGFBP-3 levels at baseline, onset of exacerbation, and end of exacerbation
[x-axis: clinical periods; y-axis: IGFBP-3 levels (µg/mL)]
IGFBP-3: Insulin-like growth factor binding protein-3

After comparing IGF-1 and IGFBP-3 levels across the periods, the Spearman's correlation test revealed a significant correlation between IGF-1 and IGFBP-3 levels in all four periods (p<0.001).

The median, interquartile range, mean, and standard deviation of the FEV1 measurements, as shown in Table II, were calculated for the baseline, onset of exacerbation, and end of exacerbation, and Friedman analysis indicated statistically significant differences across these periods (p<0.001).

Significant differences were found in IGF-1, IGFBP-3, and FEV1 values across the periods. IGF-1 and IGFBP-3 levels measured alongside FEV1 were analyzed using Spearman's correlation test, which showed no significant correlation between IGF-1, IGFBP-3, and FEV1 values in any of the four periods.

Discussion

There is no consensus protocol for diagnosing CF-related PEx, and so its diagnosis is often made through clinical assessment. Despite treatment, exacerbations can lead to permanent losses in lung function. This suggests that the current diagnostic and treatment approaches may be insufficient. Therefore, there has been significant research into biomarkers (commonly tested in blood, sputum, or exhaled air) which could help predict, assess severity, evaluate treatment response, and anticipate those conditions which may develop during the post-exacerbation period (3,4,8).

In a review by Shoki et al. (9) it was stated that any biomarkers used in PEx should be clinically applicable, contribute to routine clinical assessments, and provide meaningful information to evaluate treatment efficacy. Additionally, biomarkers should be able to show the current exacerbation status and severity, be easily obtainable from patients, and be suitable to undergo practical laboratory analyses.

Shoki et al. (9), Scott and Toner (10), and Gray et al. (11), highlighted that no clinically applicable biomarker for PEx has been identified to date. Research on biomarkers such as C-reactive protein (CRP), interleukin (IL) 6, IL-8, IL-10, erythrocyte sedimentation rate, tumour necrosis factor alpha, calprotectin, IL-1ra, and lactoferrin reveal that serum CRP levels decrease after treatment, aiding in assessing treatment response. Additionally, serum calprotectin levels at treatment completion can predict the timing of the next exacerbation. A recent study has suggested that the short palate, lung, and nasal epithelium clone 1protein could be a potential biomarker for PEx (12).

In addition, studies have investigated the relationships between IGF-1 and IGFBP-3 with CF and PEx, indicating that CF patients exhibit lower serum levels of these markers, which may be related to growth impairment (5,6). Rogan et al. (13) found that both human and pig CF neonates had lower serum IGF-1 levels than normal. Consistent with this data, the patients included in our study had significantly lower IGF-1 and IGFBP-3 levels compared to the normal population (14).

The IGF-1 and IGFBP-3 levels of our patients were reviewed in relation to their PEx status. IGF-1 is linked to inflammatory and immune responses. Ashare et al. (15) found that reduced IGF-1 levels during sepsis impair bacterial clearance, highlighting its critical role in infection management. Andreassen et al. (16) found a significant correlation between IGF-1 and CRP, highlighting that inflammation suppresses IGF-1 production. Gifford et al. (7) studied IGF-1 changes during PEx in 12 CF patients aged 18 or over. They found that baseline IGF-1 deficiency worsened at PEx onset but improved after treatment. Higher IGF-1 levels were linked to better health in CF patients.

In our study, baseline serum IGF-1 and IGFBP-3 levels showed a statistically significant decrease at the onset of PEx, which is associated with high inflammation ($p<0.001$). IGF-1 levels, with a mean value of 128.28 ng/mL at baseline, decreased by 22.8% to 98.91 ng/mL at the onset of exacerbation. Similarly, IGFBP-3 levels, with a mean value of 3.49 µg/mL at baseline, decreased by 16% to 2.93 µg/mL at the onset of exacerbation.

When the values obtained on the day PEx treatment was completed were compared with the values at the onset of exacerbation, a statistically significant increase was found ($p<0.001$). The average IGF-1 level increased by 28.8%, reaching 139 ng/mL, compared to the values at the onset of exacerbation. Likewise, the average IGFBP-3 level increased by 24.8%, reaching 3.90 µg/mL compared to the onset of exacerbation.

No statistically significant difference was found between baseline and end of exacerbation levels for IGF-1 and IGFBP-3 ($p>0.05$). Although no significant difference was observed, the average and median values of both IGF-1 and IGFBP-3 exceeded the baseline values following treatment, which is noteworthy.

Our study confirmed that there is a decrease in IGF-1 and IGFBP-3 levels during PEx, and these levels rise again after treatment.

In the group of 16 patients from whom post-treatment check-up blood samples were obtained, the analysis showed that the IGF-1 and IGFBP-3 levels in the post-treatment follow-up period were statistically similar to the baseline and end of exacerbation levels ($p>0.05$). Although no significant difference was found, the highest IGF-1 and IGFBP-3 levels in this group were recorded at the end of exacerbation (141.80 ng/mL and 3.81 µg/mL, respectively). IGF-1 and IGFBP-3 levels, which peaked after treatment, showed a slight decrease during the one-month period following discharge; however, this decrease was not statistically significant.

When looking at the percentage changes in IGF-1 and IGFBP-3, it was observed that the change in IGF-1 was higher than that of IGFBP-3. However, it was also shown that IGF-1 and IGFBP-3 levels correlated with each other across the four different clinical periods.

Study Limitations

The FEV1 measurements in our patients showed a 24.3% decrease in their average value at the onset of exacerbation when compared to the baseline period. At the end of exacerbation, with treatment, the average value showed a 20% increase. These observed decreases and increases were statistically significant.

Although it was shown that IGF-1, IGFBP-3, and FEV1 decreased with the onset of exacerbation compared to the baseline and then increased with treatment, the correlation tests revealed that IGF-1 and IGFBP-3 did not show a correlation with FEV1.

Conclusion

Our findings suggest that serum IGF-1 and IGFBP-3 levels are valuable in diagnosing exacerbations and assessing treatment responses. These markers, requiring only small blood samples and being easier to handle in laboratories compared to many other biomarkers, show promise for use during PEx in CF patients. Further clinical studies are needed in order to explore this in greater depth.

Ethics

Ethics Committee Approval: Ethics approval was obtained from the Marmara University Faculty of Medicine, Clinical Research Ethics Committee (date: 06/11/2015, approval no.: 09.2015.291).

Informed Consent: They were included in the study after obtaining informed consent from their legal guardians.

Footnotes

Authorship Contributions

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

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

Financial Disclosure: The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. O'Sullivan BP, Freedman SD. Cystic fibrosis. The Lancet. 2009; 373:1891-904.
2. Waters V, Ratjen F. Pulmonary exacerbations in children with cystic fibrosis. Ann Am Thorac Soc. 2015; 12 Suppl 2:200-6.
3. Maryam A, Christopher W, Iram H, Robert DG, Malcolm B. Definitions of pulmonary exacerbation in people with cystic fibrosis: a scoping review. BMJ Open Respiratory Research. 2024; 11:e002456.
4. Cogen JD, Quon BS. Update on the diagnosis and management of cystic fibrosis pulmonary exacerbations. Journal of Cystic Fibrosis. 2024; 23:603-11.
5. Laursen EM, Juul A, Lanng S, et al. Diminished concentrations of insulin-like growth factor I in cystic fibrosis. Arch Dis Child. 1995; 72:494-7.
6. Ozen M, Cokugras H, Ozen N, Camcioglu Y, Akcakaya N. Relation between serum insulin-like growth factor-I and insulin-like growth factor-binding protein-3 levels, clinical status and growth parameters in prepubertal cystic fibrosis patients. Pediatrics International. 2004; 46:429-35.
7. Gifford A, Nymon A, Ashare A. Serum insulin-like growth factor-1 (IGF-1) during CF pulmonary exacerbation: Trends and biomarker correlations. Pediatr Pulmonol. 2014; 49:335-41.
8. Ishak A, Stick SM, Turkovic L, et al. BAL inflammatory markers can predict pulmonary exacerbations in children with cystic fibrosis. Chest. 2020; 158:2314-22.
9. Shoki AH, Mayer-Hamblett N, Wilcox PG, Sin DD, Quon BS. Systematic review of blood biomarkers in cystic fibrosis pulmonary exacerbations. Chest. 2013; 144:1659-70.
10. Scott LK, Toner R. Clinically promising biomarkers in cystic fibrosis pulmonary exacerbations. Lung. 2017; 195:397-401.
11. Gray RD, Downey D, Taggart CC. Biomarkers to monitor exacerbations in cystic fibrosis. Expert Rev Respir Med. 2017; 11:255-7.
12. Ben-Meir E, Perrem L, Shaw M, Ratjen F, Grasemann H. SPLUNC1 as a biomarker of pulmonary exacerbations in children with cystic fibrosis. J Cyst Fibros. 2024; 23:288-92.
13. Rogan MP, Reznikov LR, Pezzulo AA, et al. Pigs and humans with cystic fibrosis have reduced insulin-like growth factor 1 (IGF1) levels at birth. PNAS. 2010; 107:20571-5.
14. Bereket A, Turan S, Omar A, et al. Serum IGF-I and IGFBP-3 levels of Turkish children during childhood and adolescence: establishment of reference ranges with emphasis on puberty. Horm Res Paediatr. 2006; 65:96-105.
15. Ashare A, Nymon AB, Doerschug KC, et al. Insulin-like growth factor-1 improves survival in sepsis via enhanced hepatic bacterial clearance. Am J Respir Crit Care Med. 2008; 178:149-57.
16. Andreassen M, Raymond I, Hildebrandt P, et al. Associations between plasma insulin-like growth factor-I and the markers of inflammation interleukin 6, C-reactive protein and YKL-40 in an elderly background population. Inflamm Res. 2010; 59:503-10.

J Pediatr Res 2025;12(1):7-13
DOI: 10.4274/jpr.galenos.2025.54765

Original Article

Evaluation of the Effectiveness of Parental Oral Health Education

Ceren Sağlam[1], Neda Mojarrab[2], Elif Merve Ahlat[2], Buğse Şakı Çınarcık[2], Nazan Ersin[1], Fahinur Ertuğrul[1], Dilşah Çoğulu[1]

[1]Ege University Faculty of Dentistry, Department of Pediatric Dentistry, İzmir, Türkiye
[2]Private Dentist, İzmir, Türkiye

ABSTRACT

Aim: Oral and dental health problems are significant global public health challenges. Maintaining optimal oral health requires the adoption of proper oral hygiene practices, regulating cariogenic food intake, and routine dental check-ups. Parents play a crucial role in enhancing their children's knowledge, attitudes, and practices related to oral health, making their involvement critical in promoting healthy behaviors. This study aimed to assess parents' knowledge of oral health and to evaluate the effectiveness of parental oral health education.

Materials and Methods: This study involved the parents of 227 children, aged 7-13 years, who attended the Department of Pediatric Dentistry at Ege University Faculty of Dentistry for routine dental examinations. After ethical approval, a pre-test consisting of 20 questions was administered to the participants in order to assess their baseline knowledge of oral health. Following the completion of the educational session, a post-test with the same questions was administered to all participants. Additionally, the parents were asked to complete a satisfaction survey in order to assess their perception of the educational intervention. The total scores of the pre- and post-tests were assessed based on the number of correct responses. Statistical analysis was performed using the SPSS 25.0 program, by chi-square test, t-test, and Fisher's exact test.

Results: The mean age of the parents included in this study was 38.72±13.46 years. Of the 227 parents, 54% were female and 46% were male. No significant differences were observed in the distribution of parents' gender, age, and education levels ($p>0.05$). The mean total score in the pre-test was 7.13±1.91, which increased to 12.21±2.08 in the post-test, indicating a significant improvement in knowledge following the educational intervention. Notably, 56% of the parents demonstrated an increase in their total score in the post-test compared to the pre-test. According to the satisfaction survey, 74% of parents expressed satisfaction with the educational session provided.

Conclusion: These findings indicate that providing parents with structured educational programs on oral and dental health can greatly improve their knowledge and facilitate the development of improved oral health practices among children. Expanding these programs throughout the population could significantly enhance children's oral health in the long term.

Keywords: Oral health education, pediatric dentistry, oral hygiene, parental involvement, preventive dentistry

Introduction

Oral health is a critical component of overall health, with its maintenance from an early age being essential (1). Effective oral health management relies on factors such as establishing proper oral hygiene practices, reducing the intake of cariogenic foods, and ensuring routine dental check-ups (2-4).

Oral health education is a fundamental aspect of preventive dentistry, playing a pivotal role in reducing the incidence of dental diseases through early intervention and

Corresponding Author
Dilşah Çoğulu, Ege University Faculty of Dentistry, Department of Pediatric Dentistry, İzmir, Türkiye
E-mail: dilsah.cogulu@ege.edu.tr **ORCID:** orcid.org/0000-0002-3156-9801
Received: 27.11.2024 **Accepted:** 27.01.2025 **Epub:** 06.03.2025 **Publication Date:** 17.03.2025

Cite this article as: Sağlam C, Mojarrab N, Ahlat EM, et al. Evaluation of the effectiveness of parental oral health education. J Pediatr Res. 2025;12(1):7-13

proactive care (5). By providing individuals with essential knowledge regarding effective oral hygiene practices, such as proper brushing and dental flossing techniques, the role of diet in oral health, and the importance of regular dental visits, education facilitates informed decision-making and enables individuals to take responsibility for their oral health. This approach not only reduces the prevalence of dental caries and periodontal diseases but also lowers the need for more complex and costly dental treatments in the future (5-7). Furthermore, oral health education promotes a preventive health paradigm, highlighting the interrelationship between oral health and general health outcomes. Incorporating comprehensive oral health education into preventive dentistry models contributes to long-term oral health maintenance, fostering healthier communities and enhancing the overall well-being of individuals, thereby supporting the sustainability of dental care systems (7,8).

Children acquire a substantial portion of their daily life skills and knowledge from their parents, relying on them to develop habits during early childhood (9). Parents play a crucial role in enhancing their children's knowledge, attitudes, and practices related to oral health, making their involvement critical in promoting healthy behaviors (10,11). It has been reported that mothers' oral care routines positively impacted their children's oral health practices (12). Similarly, another piece of research indicated that inadequate parental knowledge and negative attitudes toward oral health are associated with higher caries rates in infants and young children, highlighting the critical importance of the caregivers' knowledge levels (13).

Parental supervision and guidance are thus essential for establishing and maintaining good oral health habits in children. However, evidence suggests that parents often lack sufficient knowledge regarding their children's oral and dental health (14,15). Effective parental education programs can bridge gaps in knowledge, address misconceptions, and empower caregivers to model and promote positive oral health behaviors, ultimately enhancing the overall oral health status of the future generation. This study aimed to examine the knowledge levels of parents regarding their children's oral health and to evaluate the effectiveness of parental oral health education.

Materials and Methods

This study involved the parents of 227 children, aged 7-13 years, who attended the Department of Pedodontics at Ege University Faculty of Dentistry for routine dental examinations. A total of 227 participants were enrolled, comprising 122 females aged 24-43 years and 105 males aged 28-46 years. Ethical approval for this study was obtained from the Ethics Committee of Medical Research at the Ege University Faculty of Medicine (approval no.: 23-6.1T/59, date: June 22, 2023). Informed consent was obtained from the parents who voluntarily participated in this study. This study utilized a single-group pre-test/post-test design. Before initiating the educational intervention, the participants were informed about the confidentiality of their responses to the pre-test and post-test administered as part of this research. The measurement tools used in this study were designed by two experts and consisted of forms with 20 questions (yes/no) to assess the parents' knowledge about children's oral and dental health. Both the pre-test and post-test included the same topics, such as children's dental development, oral hygiene habits, diet, fluoride usage, and dental visits. Following the completion of the pre-test, the participants attended an educational session designed to provide comprehensive information on the oral and dental health of children. The session was conducted via a 30-slide PowerPoint presentation. After the educational session concluded, a post-test comprising the same set of questions was conducted with all of the participants. Additionally, the parents were asked to complete a satisfaction survey to assess their perception of the educational intervention. The total scores of the pre- and post-tests were assessed based on the number of correct responses.

Statistical Analysis

Statistical analyses were conducted using SPSS version 25.0. Descriptive statistics were used to analyze the demographic characteristics and baseline knowledge levels of the participants. The effectiveness of the educational intervention was evaluated using the Paired Samples t-test, while the chi-square test and Fisher's exact test were employed to analyze categorical data.

Results

The mean age of the participants was 38.72±13.46 years. Among the 227 parents included in this study, 54% were female, and 46% were male. Detailed demographic characteristics of the participants are presented in Table I. No significant differences were observed in the distribution of the parents' gender, age, or education levels ($p>0.05$).

The distribution of responses to the pre-test and post-test questions is summarized in Table II. In the post-test conducted after the educational intervention, the

proportion of the correct responses significantly increased for the questions numbered 5, 14, 15, 16, 18, and 19 compared to the pre-test ($p<0.05$). Additionally, those participants with higher education levels were more likely to answer these six questions correctly in the pre-test ($p<0.05$).

In the pre-test, only 3.5% of the parents (n=8) answered all of the questions correctly. This proportion increased to 25% (n=56) in the post-test. The mean total score, determined by summing the number of correct responses, was 7.13±1.91 in the pre-test and 12.21±2.08 in the post-test. No statistically significant associations were found between gender, age, or educational levels and the pre/post-test scores ($p>0.05$). 56% of the participants demonstrated an improvement in their total scores following the educational intervention. Results from the satisfaction survey indicated that 74% of the parents were satisfied with the educational intervention.

Table I. Demographic characteristics of parents

		n	%	p
Gender	Female	122	54	0.08
	Male	105	46	
Age (years)	<25	18	8	0.06
	25-40	101	44.5	
	>40	108	47.5	
Education level	Illiterate	25	11	0.06
	Primary/secondary school	54	24	
	High School	116	51	
	University or higher	32	14	

p<0.05 statistically significant

Table II. Distribution of responses in pre-test and post-test among parents

	Pre-test		Post-test		p
Questions	**Yes (%)**	**No (%)**	**Yes (%)**	**No (%)**	
1. Children's first primary tooth erupts around 6 months of age.	16	84	24	76	>0.05
2. A child's first dental visit should occur as soon as the first primary tooth appears.	11	89	16	84	>0.05
3. The first permanent tooth usually erupts around the age of 6 years.	33	67	39	61	>0.05
4. Children should brush their teeth regularly.	52	48	56	44	>0.05
5. Parents should supervise children's toothbrushing until about the age of 7-8 years.	14	86	68	32	**0.02***
6. Teeth should be brushed with non-fluoride toothpaste in children.	54	46	41	59	>0.05
7. Children should brush their teeth at least twice a day.	24	76	28	72	>0.05
8. Each toothbrushing session should last for 2 minutes.	21	79	29	71	>0.05
9. Children should not avoid using dental floss.	19	81	22	78	>0.05
10. Preventive applications like fissure sealants and fluoride varnishes are beneficial for children's dental health.	49	51	53	47	>0.05
11. Treatment of the primary teeth is not necessary.	66	34	61	39	>0.05
12. Habits such as mouth breathing during sleep, thumb sucking, and the prolonged use of pacifiers or bottles can impact jaw and tooth development.	43	57	49	51	>0.05
13. Immediate care is required in cases of dental trauma in children.	37	63	42	58	>0.05
14. The first sign of dental caries is the appearance of white spots on teeth.	19	81	56	44	**0.01***
15. Sweet foods and drinks should be consumed at times apart from main meals.	71	29	38	62	**0.02***
16. Teeth should be cleaned after taking syrups or other medications.	28	72	73	27	**0.01***
17. Natural foods such as molasses and honey can contribute to dental caries.	81	19	77	23	>0.05
18. The first primary teeth should be cleaned after every meal once they erupt.	24	76	81	19	**0.01***
19. Dental caries do not occur due to breastfeeding.	82	18	33	67	**0.03***
20. Regular dental check-ups every 6 months are essential for children.	62	38	70	30	>0.05

*p<0.05 Statistically significant

Discussion

Oral and dental health issues represent a significant and widespread public health challenge globally (1). In many countries, including our own, the rising prevalence of oral health problems underscores the urgent need for the development and implementation of protective and preventive strategies. A critical factor influencing the oral health of a population is oral health literacy, which plays a central role in shaping health behaviors and outcomes (2-4). For instance, a study conducted in Tehran explored the relationship between parents' oral health literacy and the caries indices of both the parents and their children. The findings of that study emphasized the direct correlation between increased oral health literacy in parents and improvements in both their own oral health and that of their children, including reductions in caries indices and enhanced oral health behaviors (13).

This evidence underscores the crucial role of improving oral health literacy, particularly among parents, in enhancing oral health outcomes for both individuals and their families. This improvement not only fosters better decision-making but also strengthens the foundation for healthier communities. The importance of targeted educational interventions cannot be overstated as increasing both awareness and understanding of oral health can lead to substantial long-term health benefits, and so reduce the prevalence and burden of oral diseases across populations (5-7).

Education plays a pivotal role in promoting oral and dental health and preventing associated issues. Parents, as primary role models in the early development of children, significantly influence the establishment of healthy habits, including those related to oral hygiene. Thus, parents need to possess accurate and comprehensive knowledge of oral health to ensure that they can pass this knowledge on to their children. Increasing parents' awareness of the importance of oral health is particularly effective in preventing dental problems in children. Furthermore, involving parents in preventive dental programs, especially those targeting dental caries, can lead to improved oral health outcomes at the community level (7,8).

Educational programs focused on oral health play a critical role in fostering long-term positive health behaviors in both parents and their children. By equipping parents with the knowledge and skills necessary to educate their children about good oral hygiene practices, these programs ensure that foundational habits are established early. Furthermore, they empower parents to actively monitor their children's oral health practices and provide ongoing reinforcement, which is essential for maintaining healthy habits over time. As highlighted by Mutluay et al. (16), these programs offer a dual benefit: they not only serve as a conduit for disseminating vital oral health information directly to children but also encourage sustained engagement with oral health behaviors beyond the immediate educational session. This ongoing involvement of the parents helps solidify the integration of these practices into daily routines, ultimately improving long-term oral health outcomes. Moreover, by fostering a collaborative approach where both parents and children are actively engaged in learning and practicing proper oral hygiene, such educational initiatives contribute to a more holistic approach to health promotion, emphasizing the importance of prevention and self-care in oral health management. These programs, therefore, represent a key strategy in reducing oral health disparities, especially when combined with other community-level interventions which target both individual and systemic barriers to oral health education (16).

This study was designed to assess the level of parental knowledge regarding their children's oral health and to evaluate the effectiveness of an oral health education program. This study involved the parents of 227 children, aged 7-13 years, who attended a university dental clinic for routine dental examinations. The initial phase of this study involved assessing the parents' baseline knowledge via a pre-test, followed by a targeted educational session covering key topics such as oral hygiene, diet, fluoride usage, dental development, and the importance of regular dental visits. The post-test results revealed a statistically significant improvement in the number of correct responses ($p<0.05$), confirming that educational interventions can substantially enhance parents' understanding of essential oral health practices. The findings emphasize the critical need to identify knowledge gaps regarding oral and dental health and to develop targeted educational programs which address these deficiencies. Such interventions are essential in preventing oral health issues, benefiting not only parents but also their children.

Research indicates that parents should assist their children with tooth brushing until the age of 7-8 years, as children below this age are often unable to perform this task effectively on their own (17,18). In the present study, the percentage of correct responses regarding this practice increased significantly, from 14% in the pre-test to 68% in the post-test.

Research has demonstrated that primary teeth should be cleaned promptly upon eruption, as early implementation of oral hygiene practices is critical for the prevention of dental complications (19). Early childhood caries have also been associated with breastfeeding, particularly in cases where proper oral hygiene practices are not adequately maintained (19,20). In the present study, the percentage of parents who reported cleaning their children's teeth after every meal increased from 24% in the pre-test to 81% in the post-test, illustrating the substantial positive impact of education on behavioral change.

In the present study, it is noteworthy that the percentage of correct responses regarding the usage of fluoride toothpaste in children increased from 46% in the pre-test to 59% in the post-test. According to clinical guidelines, fluoride toothpaste must be used in children to effectively prevent early childhood caries and promote optimal oral health (21,22). However, despite the provision of targeted education, the increase in knowledge on this matter was relatively modest. The limited improvement observed may be attributed to widespread misinformation and misconceptions regarding fluoride usage, exacerbated by misleading claims frequently disseminated by social media influencers. These sources often share conflicting or oversimplified information, which can weaken the effectiveness of educational efforts and reinforce misconceptions about the safety and benefits of fluoride. A focused approach is needed to counter unreliable information and promote evidence-based guidelines effectively. Addressing this issue requires a multifaceted approach which includes integrating evidence-based messaging into social media channels, leveraging the influence of credible healthcare professionals online, and actively debunking common myths about fluoride. By adopting these targeted strategies, public health initiatives can effectively combat misinformation, enhance knowledge, and promote informed decision-making regarding fluoride use and oral health practices. This underscores the importance of utilizing social media not only as a platform to identify misinformation but also as a powerful tool to disseminate accurate, evidence-based information to a broader audience.

The association between the frequency of sugary food intake and the development of dental caries is well-established in contemporary dental research. Excessive consumption of sugar, particularly in frequent or prolonged exposure, provides an ideal environment for harmful bacteria in the mouth to produce acids which demineralize tooth enamel. This process significantly increases the risk of caries formation, especially when oral hygiene practices are inadequate. Cariogenic food negatively affects oral health not only by directly damaging enamel but also by altering the oral microbiota, which further accelerates the development of dental caries. Given this understanding, it is essential to emphasize dietary modifications as a fundamental component of caries prevention strategies, particularly in educational programs targeting both children and their caregivers (23,24). In the present study, the percentage of parents who understood the importance of consuming cariogenic foods and drinks during main meals rather than as snacks increased from 29% in the pre-test to 62% in the post-test, further emphasizing the effectiveness of education in altering dietary habits.

In the present study, according to the satisfaction survey, 74% of the parents expressed satisfaction with the educational session provided. The observed satisfaction rate is favorable; however, it is believed that the level of satisfaction with the educational program could have been higher had the knowledge assessments not been administered to the families. The application of such tests may have influenced the participants' perceptions of the program, potentially leading to a less favorable evaluation due to test-related stress or discomfort. Consequently, future educational initiatives might benefit from focusing on the delivery of content without incorporating formal assessments, which could enhance overall satisfaction and engagement.

Providing oral and dental health education to parents not only enhances their knowledge but also ensures the transmission of improved oral health practices to their children. This is essential for the long-term prevention of dental issues. However, to fully understand the lasting impact of these interventions, further longitudinal studies are required in order to assess how parental education affects the incidence of oral health problems in children over time. Pediatricians also play a pivotal role in promoting and maintaining oral health in children, serving as a vital link between general health care and dental care.

Study Limitations

There are several limitations of this study. Firstly, the data was limited to the variables measured by the pre-designed forms and relied on the subjective responses of parents. Additionally, since the study participants were drawn from those seeking treatment at a university clinic, the findings may not be fully representative of the broader population. Future research could benefit from a more diverse sample in order to enhance the generalizability

of the results and provide a clearer understanding of the impact of educational interventions across different demographic groups.

Conclusion

Oral and dental health education is most effective when provided by qualified professionals. In order to enhance their effectiveness and accessibility, these programs should be systematically planned and expanded. We recommend implementing nationwide programs to improve parents' understanding of oral health, focusing on turning this knowledge into lasting behavioral changes. Regularly scheduled educational sessions would reinforce healthy practices and address evolving oral health challenges as children develop. Professionally administered, continuous interventions are vital in preventing early oral health issues, ultimately fostering improved long-term health outcomes for future generations.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Ethics Committee of Medical Research at the Ege University Faculty of Medicine (approval no.: 23-6.1T/59, date: June 22, 2023).

Informed Consent: Informed consent was obtained from the parents who voluntarily participated in this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Concept: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Design: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Data Collection or Processing: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Analysis or Interpretation: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Literature Search: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç., Writing: C.S., N.M., E.M.A., B.Ş.Ç., N.E., F.E., D.Ç.

Conflict of Interest: One author of this article, Dilşah Çoğulu, is a member of the Editorial Board of The Journal of Pediatric Research. However, she did not involved in any stage of the editorial decision of the manuscript. The other authors declared no conflict of interest.

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

References

1. Bennett MG. Impact of research paradigms on low-income female caregivers and their children: an oral health literacy discourse. Can J Dent Hyg. 2024; 58:106-110.
2. Poudel P, Griffiths R, Wong VW, et al. Oral health knowledge, attitudes and care practices of people with diabetes: a systematic review. BMC Public Health. 2018; 18:577.
3. Kumar S. Evidence-based update on diagnosis and management of gingivitis and periodontitis. Dent Clin North Am. 2019; 63:69-81.
4. Mattheus D, Shannon M, Gandhi K, Lim E. Oral health knowledge and practices of pediatric and family nurse practitioners. J Pediatr Health Care. 2018; 32:356-362.
5. Geetha Priya PR, Asokan S, Janani RG, Kandaswamy D. Effectiveness of school dental health education on the oral health status and knowledge of children: A systematic review. Indian J Dent Res. 2019; 30:437-449.
6. de Paiva Buischi Y, de Campos Kajimoto N, Funari SL, Kimathi M, Loomer PM. Improving oral health of adolescent girls in Kenya through education - An observational study. Int J Dent Hyg. 2023; 21:575-581.
7. Yi Mohammadi JJ, Franks K, Hines S. Effectiveness of professional oral health care intervention on the oral health of residents with dementia in residential aged care facilities: a systematic review protocol. JBI Database System Rev Implement Rep. 2015; 13:110-122.
8. Lamster IB, Myers-Wright N. Oral health care in the future: expansion of the scope of dental practice to improve health. J Dent Educ. 2017; 81:eS83-eS90.
9. Bektas G, Boelsma F, Wesdorp CL, Seidell JC, Baur VE, Dijkstra SC. Supporting parents and healthy behaviours through parent-child meetings - a qualitative study in the Netherlands. BMC Public Health. 2021; 21:1169.
10. Kaushik M, Sood S. A systematic review of parents' knowledge of children's oral health. Cureus. 2023; 15:e41485.
11. Angarita-Díaz MDP, Durán-Arismendy E, Cabrera-Arango C, et al. Enhancing knowledge, attitudes, and practices related to dental caries in mothers and caregivers of children through a neuroeducational strategy. BMC Oral Health. 2024; 24:60.
12. Petrauskienė S, Narbutaitė J, Petrauskienė A, Virtanen JI. Oral health behavior, attitude towards, and knowledge of dental caries among mothers of 0- to 3-year-old children living in Kaunas, Lithuania. Clin Exp Dent Res. 2020; 6:215-224.
13. Yazdani R, Esfahani EN, Kharazifard MJ. Relationship of oral health literacy with dental caries and oral health behavior of children and their parents. J Dent (Tehran). 2018; 15:275-282.
14. Shan Z, Liao C, Lu J, et al. Improvement of parents' oral health knowledge by a school-based oral health promotion for parents of preschool children: a prospective observational study. BMC Oral Health. 2023; 23:890.
15. Balasooriyan A, van der Veen MH, Bonifácio CC, et al. Understanding parental perspectives on young children's oral health (≤ 4 years) growing up in a disadvantaged neighborhood of Amsterdam, the Netherlands: an exploratory study. BMC Public Health. 2024; 24:627.
16. Mutluay AT, Mutluay M, Dulgergil T. The effectiveness of a caries preventive program in mothers and infants - An 18-month follow-up study. J Dent Sci. 2020; 15:536-541.
17. Mueller M, Schorle S, Vach K, Hartmann A, Zeeck A, Schlueter N. Relationship between dental experiences, oral hygiene education and self-reported oral hygiene behaviour. PLoS One. 2022; 17:e0264306.

18. Deinzer R, Shankar-Subramanian S, Ritsert A, et al. Good role models? Tooth brushing capabilities of parents: a video observation study. BMC Oral Health. 2021; 21:469.

19. Marshman Z, Ahern SM, McEachan RRC, Rogers HJ, Gray-Burrows KA, Day PF. Parents' experiences of toothbrushing with children: a qualitative study. JDR Clin Trans Res. 2016; 1:122-130.

20. Xu H, Ma X, Wang J, et al. Exploring the state and influential factors of dental caries in preschool children aged 3–6 years in Xingtai City. BMC Oral Health. 2024; 24:951.

21. American Academy of Pediatric Dentistry. Fluoride therapy. The reference manual of pediatric dentistry. Chicago, Ill.: American Academy of Pediatric Dentistry; 2024; 351-357.

22. European Academy of Paediatric Dentistry. Guidelines on the use of fluoride in children: an EAPD policy document. Eur Arch Paediatr Dent. 2019; 20:507-516.

23. Choi HS, Ahn HY. Effects of mothers involved in dental health program for their children. J Korean Acad Nurs. 2012; 42:1050-1061.

24. Das H, Janakiram C, Ramanarayanan V, et al. Effectiveness of an oral health curriculum in reducing dental caries increment and improving oral hygiene behaviour among schoolchildren of Ernakulam district in Kerala, India: study protocol for a cluster randomised trial. BMJ Open. 2023; 13:e069877.

J Pediatr Res 2025;12(1):14-21
DOI: 10.4274/jpr.galenos.2025.35545

Original Article

A Non-pharmacological Application to Reduce Neonatal Pain During Lumbar Puncture Procedure in Neonatal Intensive Care: Placing a Pillow on the Abdomen

Sema Tanrıverdi[1], Hümeyra Köse Yaman[2], Seniha Kahraman[1], Emine Kublay[1]

[1]Manisa Celal Bayar University Faculty of Medicine, Department of Neonatology, Manisa, Türkiye
[2]Manisa Celal Bayar University Faculty of Medicine, Department of Pediatrics, Manisa, Türkiye

ABSTRACT

Aim: Lumbar puncture is one of the most common painful procedures which newborn babies encounter during neonatal intensive care follow-up. It is important to control pain during this procedure. The aim of this study was to show the effects of using a pillow placed in the abdominal area as a non-pharmacological application in order to relieve neonatal pain during the lumbar puncture procedure.

Materials and Methods: Forty newborn babies who were monitored in the neonatal intensive care unit of our hospital and received an indication for lumbar puncture were included in this study. Babies who underwent lumbar puncture were randomly selected and divided into two groups. Lumbar puncture was performed on 20 babies in group 1 by placing a pillow which we had prepared in the abdominal area. In addition, lumbar puncture was performed on 20 babies in group 2 without placing a pillow in the abdominal area during lumbar puncture. The vital signs and the neonatal infants pain scale pain scores of the two groups were compared.

Results: Forty newborn babies were included in this study. Their average week of birth was 30.61±4.32 (24-38) weeks and their average birth weight was 1.531.25±951.34 (640-3.675) grams. Of the babies, 26 (65%) were male and 14 (35%) were female. When the pillow we prepared was placed on the abdominal area during lumbar puncture, the pain score was lower, although this difference was not significant.

Conclusion: Placing a pillow on the abdominal area during lumbar puncture, which is one of the painful procedures in neonatal intensive care, can be applied as a nonpharmacological method.

Keywords: Newborn, pain, lumbar puncture, pillow

Introduction

Newborn babies in neonatal intensive care units (NICUs) are exposed to repeated painful interventions. If appropriate approaches are not taken to alleviate pain in babies exposed to these interventions, permanent neurological and behavioral problems may occur in their later life. Not providing adequate pain control to those babies who are monitored for a long time in the NICU increases this risk. These negative consequences of pain may be caused by the undesirable effects of drugs such as analgesics and

Corresponding Author
Assoc. Prof. Sema Tanrıverdi, Manisa Celal Bayar University Faculty of Medicine, Department of Neonatology, Manisa, Türkiye
E-mail: sema.tanriverdi@cbu.edu.tr **ORCID:** orcid.org/0000-0002-5681-3647
Received: 02.10.2024 **Accepted:** 14.01.2025 **Epub:** 06.03.2025 **Publication Date:** 17.03.2025

Cite this article as: Tanrıverdi S, Köse Yaman H, Kahraman S, Kublay E. A Non-pharmacological application to reduce neonatal pain during lumbar puncture procedure in neonatal intensive care: Placing a pillow on the abdomen. J Pediatr Res. 2025;12(1):14-21

sedatives used for pharmacological intervention, as well as failures to prevent pain (1).

The main purposes of evaluating the pain response are; to detect the painful condition of the baby, to determine their pain levels and to reveal any needs for intervention. Thus, evaluating their pain responses aims to avoid inadequate or unnecessary treatment (2). There are more than forty methods for assessing pain responses in newborns. Of these, the neonatal infant pain scale (NIPS) is an assessment scale developed for newborns which behaviorally evaluates their responses to pain during invasive procedures (3).

Pain management is very important as it has been shown that pain in the newborn has permanent consequences. There are two types of treatment for pain: Pharmacological and non-pharmacological. However, the important thing is to reduce and eliminate painful stimuli as much as possible rather than treating them. Non-pharmacological methods, such as breastfeeding and breast milk, pacifiers, skin-to-skin contact, positioning the baby, touch, massage, and providing painless sensory stimulation with sound and smell can effectively reduce discomfort and pain in preterm and term babies (4). Positioning and keeping babies in a midline flexion posture during painful interventions may make it easier for them to calm down. Loosely swaddling the baby during interventions has been found to be effective on physiological and behavioral pain responses (5).

One of the most common painful procedures which newborn babies encounter during NICU follow-up is lumbar puncture. It is important to control pain during this procedure.

There are studies on the appropriate positioning of newborn babies to reduce pain during lumbar puncture (6); however, there is no study in the literature to date which investigates the effects on pain of placing a pillow on the abdominal region during lumbar puncture in newborn babies. In a study conducted in 2009 on the use of a pillow in the abdominal region during lumbar puncture in children with cancer aged 2-18, although not statistically significant, there was less pain and greater satisfaction in those children using a pillow (7).

Placing a pillow on the abdomen during a lumbar puncture provides lumbar flexion, allows the paravertebral muscles to relax, and improves the patient's position during the lumbar puncture, allowing them to maintain a proper position and relax. The aim of this study was to show the effects of applying a pillow to the abdominal area as a non-pharmacological application to relieve neonatal pain during a lumbar puncture procedure.

Materials and Methods

Forty newborn babies who were monitored in the NICU of our hospital and who received an indication for lumbar puncture were included in this study. This study was approved by the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval no.: 20.478.486/1400, date: 15/06/2022).

The inclusion criteria for this study were babies whose gestational week was over 28 weeks who required lumbar puncture (excluding those who had started antibiotics due to symptoms of sepsis or in cases of growth in blood culture or in cases where there was no response to antibiotic treatment) (8) were included in this study. Informed consent forms were obtained from those families who agreed to participate in this study.

Babies with congenital vertebral anomalies, major congenital anomalies, babies born asphyxiated or babies whose general condition was not suitable for lumbar puncture (babies with no signs of sepsis for whom antibiotic treatment was started after birth, babies with thrombocytopenia, babies with damaged skin integrity in the area to be punctured and babies with a meningomyelocele sac) were not included in this study.

The babies were randomized by a sealed envelope method and divided into two groups according to the method of lumbar puncture.

Lumbar puncture was performed on the babies in group 1 by placing a pillow which we had prepared in the abdominal area. Lumbar puncture was performed on the babies in group 2 without placing a pillow in the abdominal area during lumbar puncture. The pillows used were made separately for each baby by the same nurse, using bonnet material filled with cotton.

The bonnet and cotton used to prepare the pillow were disposable. Pillows were prepared in sizes appropriate for the baby's weight and abdominal circumference. The lumbar puncture procedure was performed in accordance with the rules of the aseptic technique (Figures 1, 2).

Each baby was monitored during lumbar puncture. Their heart rate, respiratory rate, perfusion index, and blood pressure were measured and recorded before (one minute before), during, and after (one minute after) the lumbar puncture. The NIPS pain scale was used by the same nurse before, during, and after the lumbar puncture (9). The NIPS pain score was calculated according to facial expression, crying, breathing pattern, arm movement, leg movement, and alertness. NIPS pain scores >3 indicate the presence of pain (Table I).

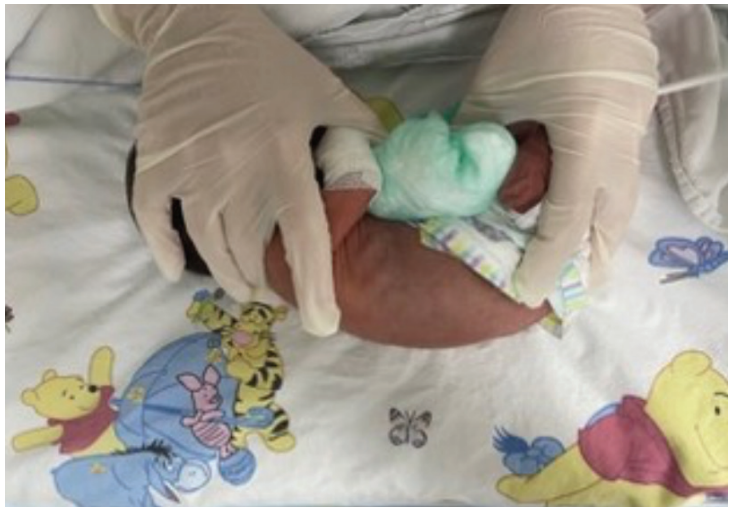


Figure 1. Lumbar puncture was performed on the babies by placing a pillow which we had prepared in the abdominal area. The pillows used were made separately for each baby by the same nurse, using bonnet material filled with cotton. The bonnet and cotton used to prepare the pillow were disposable. Pillows were prepared in sizes appropriate for the baby's weight and abdominal circumference

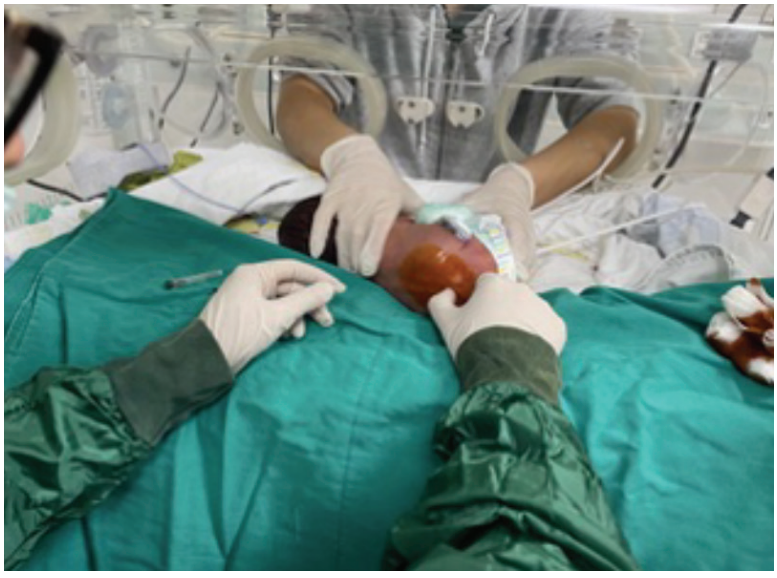


Figure 2. Lumbar puncture was performed on the babies by placing a pillow in the abdominal area. The lumbar puncture procedure was performed in accordance with the rules of the aseptic technique

Table I. NIPS

Parameters	**0 point**	**1 point**	**2 point**
Facial expression	Relaxed	Contracted	-
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than basal	-
Arms	Relaxed	Flexed/stretched	-
Legs	Relaxed	Flexed/stretched	-
Alertness	Sleeping/calm	Uncomfortable	-
>3 points: Pain			
NIPS: Neonatal infant pain scale			

The vital signs and pain scores of the two groups were compared.

Statistical Analysis

Statistical analysis was performed with SPSS 25. The Mann-Whitney U test was used to compare continuous variables, and the chi-square test was used to compare categorical variables. Statistical significance was determined as $p<0.05$.

Results

When the demographic characteristics of the babies included in this study were examined, their average gestational age was 30.61±4.32 (24-38) weeks, their average birth weight was 1.531.25±951.34 (640-3.675) grams, their average birth length was 39.50±7.72 (29.0-52.5) cm, and their average head circumference was 27.89±4.02 (23-36) cm. Of the babies, 26 (65%) were male and 14 (35%) were female.

The demographic and antenatal characteristics of group 1, in which a pillow was placed during lumbar puncture, and group 2, in which a pillow was not placed during lumbar puncture, are shown in Table II. There was no significant difference between the demographic and antenatal characteristics of the groups (Table II).

No significant difference was detected between respiratory support and nutrition during lumbar puncture of groups 1 and 2. The clinical features are shown in Table III.

In the comparison between groups 1 and 2, no significant difference was found in the vital signs (heart rate, respiratory rate, blood pressure) or NIPS pain scores before, during and after lumbar puncture; although no significance was detected, the heart rate, respiratory rate, blood pressure and NIPS pain scores of group 1 were lower than group 2 ($p>0.05$) (Table IV).

Table II. Comparison of demographic characteristics of patients in groups 1 and 2

	Group 1 (n=20)	**Group 2 (n=20)**	**p value**
Gestational age (weeks)	30.10±3.95 (25-36)	30.90±4.99 (24-38)	0.696
Birth weight (g)	1357.50±617.41 (680-2875)	1705.29±1209 (640-3975)	0.429
Birth length (cm)	39.40±6.43 (30-50)	39.61±9.36 (29.0-52.5)	0.955
Birth head circumference (cm)	27.65±3.19 (23-34)	28.16±4.97 (23-36)	0.789
Gender, n -Female -Male	 8 12	 6 14	0.639
Mode of birth, C/S, n	20	18	0.305
Apgar 1st	7 (6-9)	8 (6-10)	0.327
Apgar 5th	8 (8-10)	9 (8-10)	0.137
Maternal age	27.40±3.20 (19-44)	25.77±5.71 (23-32)	0.450
Number of maternal pregnancies, n	3 (1-5)	2 (1-4)	0.278
Number of maternal births, n	2 (0-3)	1 (0-3)	0.271

g: Gram, cm: Centimeter, C/S: Cesarean section

Table III. Comparison of clinical findings of patients in groups 1 and 2

	Group 1 (n=20)	**Group 2 (n=20)**	**p value**
The day the lumbar puncture was made	40.80±26.51 (6-67)	29.50±37.71 (5-119)	0.448
Sepsis, n -Clinic -Proven	 4 16	 10 10	0.307
Meningitis, n	0	0	1
Respiratory support when lumbar puncture is performed, n -Room air -Non-invasive ventilation -Intubate, mechanical ventilation	 10 8 2	 12 6 2	0.981

Table III. Continued			
	Group 1 (n=20)	**Group 2 (n=20)**	**p value**
Nutrition when lumbar puncture is performed, n -Total parenteral nutrion -Total parenteral nutrion+enteral -Enteral -Oral	 6 4 6 4	 4 8 6 2	 0.717
Hospital stay (day)	84.33±40.97 (18-141)	75.80±54.44 (14-162)	0.707
Mortality, n	0	2	0.330

Table IV. Babies in groups 1 and 2's comparison of vital signs and pain scores before, during and after LP			
Lumbar puncture before	**Group 1 (n=20)**	**Group 2 (n=20)**	**p value**
HR (min)	146.40±14.40 (121-172)	153±8.93 (142-168)	0.234
RR (min)	55.40±1.89 (52-58)	57.40±2.11 (56-62)	0.059
PI	0.91±0.30 (0.1-1.1)	0.69±0.25 (0.1-1)	0.095
SBP (mmHg)	68.77±6.97 (57-84)	75.11±12.74 8 (61-94)	0.209
DBP (mmHg)	41.33±9.88 (32-60)	47.44±11.69 (31-64)	0.249
MBP (mmHg)	52.00±7.64 (43-68)	57.88±9.84 (41-69)	0.176
NIPS pain score	0	0.30±0.94 (0-3)	0.331
Lumbar puncture during			
HR (min)	167.10±18.81 (143-212)	168.20±8.13 (156-178)	0.867
RR (min)	57.20±3.67 (52-64)	60.40±4.69 (54-68)	0.107
PI	0.83±0.36 (0.26-1.40)	0.67±0.35 (0.08-1.20)	0.320
SBP (mmHg)	74.87±12.36 (54-90)	85.00±17.00 (68-120)	0.195
DBP (mmHg)	49.25±16.48 (24-74)	49.50±10.70 (39-71)	0.972
MBP (mmHg)	56.62±9.70 (43-76)	64.12±16.50 (41-90)	0.287
NIPS pain score	1.90±1.44 (0-5)	2.40±1.34 (1-5)	0.435
Lumbar puncture after			
HR (min)	155.60±21.15 (108-181)	160.20±19.34 (117-184)	0.618
RR (min)	56.80±4.54 (52-68)	59.20±3.91 (54-66)	0.221
PI	0.97±0.41 (0.48-1.80)	0.66±0.22 (0.4-1)	0.054
SBP (mmHg)	77.11±10.81 (60-91)	77.88±7.57 (67-89)	0.862
DBP (mmHg)	46.11±5.84 (38-56)	47±5.72 (38-53)	0.749
MBP (mmHg)	55.11±4.67 (46-59)	58.22±8.01 (45-70)	0.329
NIPS pain score	1.10±1.28 (0-4)	1.30±0.94 (0-3)	0.697

LP: Lumbar puncture, HR: Heart rate, RR: Respiratory rate, PI: Perfusion index, SBP: Systolic blood, DBP: Diastolic blood pressure, MBP: Mean blood pressure, NIPS: Neonatal infant pain scale

Babies who have a pillow placed on their abdomen during a lumbar puncture tend to be more relaxed before, during, and after lumbar puncture.

Discussion

The purposes of evaluating pain response are; to detect painful conditions of the baby, to determine pain levels and to reveal any needs for intervention. Thus, the aim is to avoid inadequate or unnecessary treatment. Within the scope of the neonatal pain control program of the American Academy of Pediatrics and the Canadian Pediatric Association, both routinely and at regular intervals, it is recommended to evaluate both before and after painful interventions (2). More objective evaluation can be achieved

by using structured methods in the evaluation of pain in newborns. These structured methods are versatile, therefore, it is preferable to include several physiological, behavioral or other variables. Painful interventions cause physiological changes such as an increase in heart rate, blood pressure, respiratory rate and a decrease in oxygen saturation, changes in respiratory rhythm, and changes in skin color (3). Along with these changes, there are changes in crying, facial expressions (frowning, squinting, nasolabial wrinkles and opening of the mouth), hand and body movements, and muscle tone (10). Although the changes observed in preterm babies are parallel to those in term babies, they may be more subtle (11).

The "premature infant pain profile (PIPP)", the "crying, requires oxygen saturation, increased vital signs, expression, sleeplessness", the "NIPS", and the "neonatal pain agitation and sedation scale (N-PASS)'' are used in the evaluation of pain responses in newborns. There are many methods available, such as N-PASS and the "Neonatal Facing Coding System" (2).

NIPS, which was developed by Lawrence et al. (12) in 1993, is a method which is suitable and frequently used to evaluate procedural pain in premature and term babies.

One of the most common painful procedures which newborn babies encounter during their stay in the NICU is lumbar puncture. It is important to control pain during lumbar puncture.

Pain management is very important as it has been shown that pain in the newborn has permanent consequences. There are two types of treatment for pain: Pharmacological and non-pharmacological. However, the important thing is to reduce and eliminate painful stimuli as much as possible rather than treating them. Non-pharmacological methods, such as breastfeeding and breast milk, pacifiers, skin-to-skin contact, positioning the baby, touch, massage, and providing painless sensory stimulation with sound and smell, can effectively reduce discomfort and pain in preterm and term babies (4). Positioning and keeping babies in a midline flexion posture during painful interventions may make it easier for them to calm down. Loosely swaddling the baby during interventions has been found to be effective on physiological and behavioral pain responses (5).

It has been stated that changing their position provides significant comfort to newborns. Change of position is a practice which prevents the development of pain, reduces acute pain, increases blood circulation, and prevents muscle contraction and spasm (13). During painful procedures, keeping babies in a midline flexion posture and loose enough to allow them to put their hands to their mouths may make it easier for them to calm themselves (1). In the study by Çağlayan and Balcı (14) in which they evaluated pain scores during blood collection from the heel of 41 preterm newborns born under the 37th gestational week in both routine and fetal positions (facilitated tucking), those babies in the fetal position had lower pain scores. In the study conducted by Lopez et al. (15) with 42 preterm babies, the PIPP pain score was evaluated in order to determine the effectiveness of the fetal position on relieving pain during venous intervention, and the pain scores of the positioned group were found to be significantly lower than the control group.

Many studies have shown the benefits of non-pharmacological treatments, such as sucrose and kangaroo care, in reducing pain scores in newborns during mildly painful routine procedures (16). Skin-to-skin contact with the mother is an effective method of pain treatment during simple interventions (17). When glucose or sucrose is applied together with kangaroo care, it reduces neonatal pain related to minor procedures more than either of them alone (18). Other effective methods include vanilla scent and manual swaddling by the parent during interventions (19). It has been observed that sensory stimulation provided by massage, talking, eye contact, and/or perfume smell, when used together with glucose, provides more effective analgesia than using a pacifier with glucose (20). It was determined that using pacifiers, rocking and swaddling were the most effective methods in reducing pain (21). There are studies showing that visual stimulation consisting of touch, massage, talking, listening to music and in-utero sounds, and moving toys may have pain-reducing effects (22).

Before lumbar puncture procedure, non-drug pain control methods (such as sugary solutions, pacifiers, and breast milk) which are appropriate to the patient's clinic should be applied. If there is enough time, local anesthetic cream can be applied. There are also centers where subcutaneous lidocaine injection is performed (23). Before starting a painful procedure such as lumber puncture, the baby should be made to feel comfortable and safe, and disturbing sounds and lights should be avoided. In accordance with this, the baby can be fixed with a loose cover or by gently giving the baby's hand or foot a flexion posture (1).

The most common positions used to perform lumbar puncture are the lateral decubitus and sitting position. However, it is uncertain which position best improves patient outcomes. Most study participants were term

newborns (24). A study found that lumbar puncture performed in the prone position was safe, effective, and comfortable in premature and low birth weight infants (6). In a questionnaire study to evaluate the lumbar puncture procedure in neonates in Spanish hospitals examining the materials used and sedation-analgesia, the most commonly used measures were topical anesthetics (90.3%) and sucrose (82.2%). Other non-pharmacological interventions (aspiration, comfort measures, breastfeeding) were used at a rate of 7% (25).

In our study, it was thought that the baby would feel safer and more comfortable in the flexion position and with a pillow placed on the baby's abdomen before the lumbar puncture procedure. It was observed that the baby's vital signs, heart rate, respiratory rate, blood pressure and pain score, before, during and after lumbar puncture, were lower in the group in which the pillow was placed compared to the group in which the pillow was not placed, although not significantly. This practice has not been seen among the non-pharmacological methods used to reduce pain in neonatal lumbar puncture attempts in the literature. There is no study on this subject to date. There is sufficient evidence to support the use of non-pharmacological interventions, particularly breastfeeding, sweet-tasting solutions, and skin contact, as primary strategies for pain management during common needle puncture procedures. Music therapy, sensory saturation, rocking and holding, swaddling, appropriate positioning, pacifier retention, facilitated compression, and nonnutritive sucking are recommended for acute pain management in infants (5). Further research comparing individual non-pharmacological pain management interventions and their combined effects for commonly performed painful procedures in NICUs, such as lumbar puncture, is needed.

Conclusion

As a result of this study, placing a pillow on the baby's abdomen during lumbar puncture may be considered as a non-pharmacological intervention which can be used to alleviate the infant's pain response.

Ethics

Ethics Committee Approval: This study was approved by the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval no.: 20.478.486/1400, date: 15/06/2022).

Informed Consent: Informed consent forms were obtained from those families who agreed to participate in this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.T., H.K.Y., S.K., E.K., Concept: S.T., H.K.Y., S.K., E.K., Design: S.T., H.K.Y., S.K., E.K., Data Collection or Processing: S.T., H.K.Y., S.K., E.K., Analysis or Interpretation: S.T., Literature Search: S.T., H.K.Y., Writing: S.T., H.K.Y.

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

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

References

1. Yiğit Ş, Ecevit A, Köroğlu ÖA. Turkish Neonatal Society guideline on the neonatal pain and its management. Turk Pediatri Ars. 2018; 53:161-71.
2. American Academy of Pediatrics Committee on Fetus and Newborn, American Academy of Pediatrics Section on Surgery, Canadian Paediatric Society Fetus and Newborn Committee, et al. Prevention and management of pain in the neonate: an update. Pediatrics. 2006; 118:2231-41.
3. Maxwell LG, Malavolta CP, Fraga MV. Assessment of pain in the neonate. Clin Perinatol. 2013; 40:457-69.
4. Pillai Riddell RR, Bucsea O, Shiff I, et al. Non-pharmacological management of infant and young child procedural pain. Cochrane Database Syst Rev. 2023; 14:CD006275.
5. McNair C, Campbell-Yeo M, Johnston C, et al. Nonpharmacologic management of pain during common needle puncture procedures in infants: Current research evidence and practical considerations: An update. Clin Perinatol. 2019; 46:709-30.
6. Guo W, Ma D, Qian M, et al. Lumbar puncture in the prone position for low birth weight neonates. BMC Pediatr. 2022; 22:2.
7. Marec-Bérard P, Bissery A, Kebaïli K, et al. A positioning pillow to improve lumbar puncture success rate in paediatric haematology-oncology patients: A randomized controlled trial. BMC Cancer. 2009; 9:21.
8. Polin RA. Committee on fetus and newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012; 129:1006-15.
9. Yılmaz Bİ, Kanan N. Pain management in the newborn and the roles of nurses. Journal of General Health Sciences (JGEHES). 2021; 3:273-85.
10. Anand KJS, Eriksson M, Boyle EM, et al. Assessment of continuous pain in newborns admitted to NICUs in 18 European countries. Acta Paediatr. 2017; 106:1248-59.
11. Brummelte S, Grunau RE, Chau V, et al. Procedural pain and brain development in premature newborns. Ann Neurol. 2012; 71:385-96.
12. Lawrence J, Alcock D, McGrath P, et al. The development of a tool to assess neonatal pain. Neonatal Netw. 1993; 12:59-66.
13. Kılıç M, Öztunç G. Methods used in pain control and the role of the nurse. Fırat Sağlık Hizmetleri Dergisi. 2012; 7:35-51.

14. Çağlayan N, Balcı S. An effective model of reducing pain in preterm neonates: Facilitated tucking. F.N. Hem Derg. 2014; 22:63-8.

15. Lopez O, Subramanian P, Rahmat N, et al. The effect of facilitated tucking on procedural pain control among premature babies. J Clin Nurs. 2015; 24:183-91.

16. Stevens B, Yamada J, Ohlsson A, et al. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev. 2016; 16:CD001069.

17. Gray L, Watt L, Blass EM. Skin-to-skin contact is analgesic in healthy newborns. Pediatrics. 2000; 105:e14.

18. Chermont AG, Falcão LF, de Souza Silva EH, et al. Skin-to-skin contact and/or oral 25% dextrose for procedural pain relief for term newborn infants. Pediatrics. 2009; 124:1101-7.

19. Sizun J, Ansquer H, Browne J, et al. Developmental care decreases physiologic and behavioral pain expression in preterm neonates. J Pain. 2002; 3:446-50.

20. Bellieni CV, Bagnoli F, Perrone S, et al. Effect of multisensory stimulation on analgesia in term neonates: A randomized controlled trial. Pediatr Res. 2002; 51:460-3.

21. Riddell RRP, Racine NM, Gennis HG, et al. Non-pharmacological management of infant and young child procedural pain. The Cochrane Database Of Systematic Reviews, 2015; 2:CD006275.

22. Franck LS, Lawhon G. Environmental and behavioral strategies to prevent and manage neonatal pain. Semin Perinatol. 1998; 22:434-43.

23. Hall RW, Anand KJ. Pain management in newborns. Clin Perinatol. 2014; 41:895-924.

24. Pessano S, Bruschettini M, Prescott MG, et al. Positioning for lumbar puncture in newborn infants. Cochrane Database Syst Rev. 2023; 14:CD015592.

25. Jimeno Ruiz S, Riaza Gómez M, Cárdenas Rebollo JM, et al. Material and sedation-analgesia in the neonatal lumbar puncture procedure. An Pediatr (Engl Ed). 2021; 95:246-52.

J Pediatr Res 2025;12(1):22-6
DOI: 10.4274/jpr.galenos.2025.78614

Original Article

The Impact of the COVID-19 Pandemic on Invasive Group A *Streptococcal* Infections in Children

Nursel Atay Ünal[1], Meltem Polat[1], Nursel Kara Ulu[1], Elif Güdeloğlu[1], Elif Ayça Şahin[2], Tuğba Bedir Demirdağ[1], Hasan Tezer[1], Anıl Tapısız[1]

[1]Gazi University Faculty of Medicine, Department of Pediatric Infectious Diseases, Ankara, Türkiye
[2]Gazi University Faculty of Medicine, Department of Microbiology, Ankara, Türkiye

ABSTRACT

Aim: The aim of this study was to evaluate the impact of the coronavirus disease-2019 pandemic on the invasive group A *Streptococcus* (iGAS) infections in children. We also aimed to assess the demographic and clinical characteristics, and treatment outcomes of children with iGAS infections.

Materials and Methods: We conducted a retrospective analysis of the medical records for pediatric patients aged 1 month to 18 years who were diagnosed with iGAS infections and followed by a single pediatric infectious diseases department from January 2010 to December 2021. The study period was divided into two periods: the pre-pandemic period (January 2010-February 2020) and the pandemic period (March 2020-December 2021).

Results: A total of 40 patients (60% female) with a median age of 8 years (1-17 years) were included in this study. Among these, 20 had bacteremia, 13 patients had necrotizing soft tissue infection, 4 had pneumonia and empyema, 2 had septic arthritis, and 1 had acute bacterial meningitis. Two patients developed streptococcal toxic shock syndrome. In 6 patients, varicella infection, and in 4 patients, influenza infection preceded iGAS infection. The distribution of patients by year was as follows: 2 patients in 2010, 2011, and 2012; 3 in 2013; 0 in 2014; 4 in 2015; 6 in 2016 and 2017; 7 in 2018; and 8 in 2019, indicating a progressive increase in iGAS cases towards the last years of the pre-pandemic period. No cases were observed during the pandemic period. Three patients died.

Conclusion: Our study found that the number of iGAS cases progressively increased in the last years of the pre-pandemic period, while no cases were observed during the pandemic period. This may be attributed to a reduction in GAS transmission due to the preventive measures implemented during the pandemic, as well as a decrease in the incidence of infections such as influenza and varicella, which are significant risk factors for iGAS.

Keywords: Invasive group A *Streptococcal* infections, COVID-19 pandemic, children

Introduction

Invasive group A *Streptococcus* (iGAS) infections include bacteremia, pneumonia, osteomyelitis, septic arthritis, and any other infections in which GAS is isolated from a normally sterile body site. These infections also include necrotizing fasciitis (1). The clinical spectrum of iGAS disease in children differs from that in adults (2).

After the onset of the coronavirus disease-2019 (COVID-19) pandemic in March 2020, significant behavioral changes

Corresponding Author
Nursel Atay Ünal, MD, Gazi University Faculty of Medicine, Department of Pediatric Infectious Diseases, Ankara, Türkiye
E-mail: nur.sel@hotmail.com **ORCID:** orcid.org/0000-0002-0118-1961
Received: 05.11.2024 **Accepted:** 14.01.2025 **Epub:** 06.03.2025 **Publication Date:** 17.03.2025

Cite this article as: Atay Ünal N, Polat M, Kara Ulu N, et al. The impact of the COVID-19 pandemic on invasive group a *Streptococcal* infections in children. J Pediatr Res. 2025;12(1):22-6

occurred in society. Many countries adopted hygienic measures such as handwashing and widespread face masking, along with school closures and social distancing. These actions led to notable shifts in the epidemiology of viral and bacterial infections (3). iGAS infections have been associated with antecedent viral infections, such as varicella and influenza (1). Therefore, the number of new diagnoses for various infectious diseases was impacted by the pandemic. Our aim was to evaluate the impact of the COVID-19 pandemic on the number of iGAS infections in children. We also aimed to assess the demographic and clinical characteristics, and treatment outcomes of these children.

Materials and Methods

Pediatric patients aged 1 month to 18 years, admitted to Gazi University Hospital with iGAS infection between January 2010 and December 2021, were analyzed retrospectively. This study was approved by the Gazi University Clinical Research Ethics Committee Non-Interventional Research (decision no.: 226, dated: 20.03.2023). The study period was divided into two periods: the pre-pandemic period (January 2010-February 2020) and the pandemic period (March 2020-December 2021). We collected data from medical records, the infectious diseases consultation database, and the microbiology laboratory database regarding the patients' demographics (age, sex), admission dates, infection sites, risk factors, presenting symptoms, laboratory findings, culture results, antimicrobial treatments, the need for surgical drainage, complications [e.g., *Streptococcal* toxic shock syndrome (STSS)], and mortality. iGAS infections were defined as bacteremia, pneumonia, necrotizing soft tissue infection, or any other infection associated with the isolation of GAS from a normally sterile site (1).

Microbiological Methods

Tissue samples were inoculated onto blood and eosin-methylene blue agar. The aerob/anaerob blood culture bottles were incubated for 5 days in BacT/Alert System (Biomeriux, France). The growing microorganism was identified using matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (Biomeriux, France). Antibiotic susceptibility testing for the bacteria identified as GAS was performed using the Vitek 2 automated system (Biomeriux, France).

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences 21 (SPSS 21) (IBM SPSS Inc, Chicago, IL, USA). Data were analyzed by frequency and percentage (%) for qualitative variables, and median, minimum, and maximum values for quantitative variables. The Mann-Whitney U test was used to compare the median age values between the groups with and without bacteremia. Statistical significance was set at $p<0.05$.

Results

We identified 40 children (n=24; 60% female) with laboratory-confirmed iGAS infections during the study period. The median age was 8 years (range 1-17 years). The distribution of patients by year was as follows: 2 patients in 2010, 2011, and 2012; 3 in 2013; 0 in 2014; 4 in 2015; 6 in 2016 and 2017; 7 in 2018; and 8 in 2019, indicating a progressive increase in iGAS cases towards the last years of the pre-pandemic period (Figure 1). Of these patients, 20 (50%) patients had bacteremia, 13 (32.5%) had necrotizing soft tissue infection, 4 (10%) had pneumonia and empyema, 2 (5%) had septic arthritis, and 1 (2.5%) had acute bacterial meningitis (Figure 1).

Bacteremia was present in 20 (50%) of 40 patients; 12 (60%) patients with bacteremia had a source of skin and/or soft tissue infection, and 8 (40%) patients had bacteremia without a focus. The median age of those patients with bacteremia was 4 years (range: 1-8 years), which was significantly lower than that of those patients without bacteremia (median age 9 years, range: 3-17 years) ($p=0.02$).

In 6 (15%) patients, varicella infection, and in 4 (10%) patients, influenza infection preceded iGAS infection. Two (5%) patients met the criteria for STSS; one had pneumonia and empyema, while the other had a retropharyngeal abscess. Both patients presented to our hospital with septic shock and rapidly developed multiple organ failure, resulting in death within 24 hours. Both patients were previously healthy and had no underlying diseases.

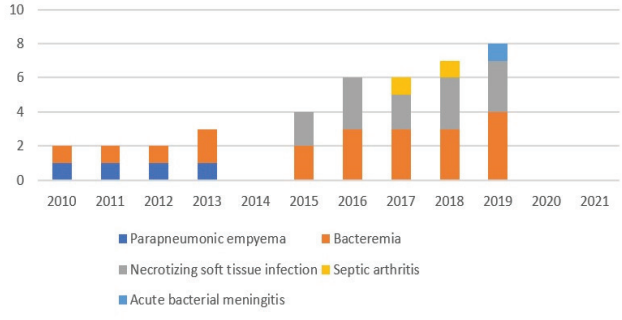


Figure 1. Annual numbers of children with invasive group A *Streptococcal* infections from 2010 to 2021

GAS meningitis was seen in a 7-year old boy who had a prior varicella infection and perforated otitis media. He presented with fever, headache, and signs of meningeal irritation. Cerebrospinal fluid (CSF) analysis revealed 1,250 cells/mm^3 with a glucose and protein concentrations of 20 and 232 mg/dL, respectively. Empiric treatment with intravenous (IV) ceftriaxone (100 mg/kg per day) and vancomycin (60 mg/kg per day) was initiated. A Gram stain of the CSF showed Gram-positive cocci, and CSF culture grew GAS (sensitive to penicillin). Blood and throat cultures remained negative. Vancomycin was discontinued, and since IV penicillin was not available at the hospital, the treatment was completed with ceftriaxone for 10 days. The patient was discharged in good condition on the 11th day of hospitalization.

The median white blood cell count was 15,670/mm^3 (790-42,000/mm^3) and C-reactive protein was 160 mg/L (40-240 mg/L). The median length of stay in hospital was 10 days (1-30 days). Four (10%) patients were admitted to the pediatric intensive care unit.

All patients were treated with antibiotic treatment: ampicillin-sulbactam+clindamycin (23 patients), ceftriaxone+clindamycin (10 patients), ceftriaxone+vancomycin (5 patients), and cefepime+teicoplanin (2 patients). Empiric treatment with cefepime+teicoplanin was initiated in 2 patients (1 patient with a retropharyngeal abscess and STSS, and another with necrotizing soft tissue infection with bacteremia) after a first dose of ampicillin- sulbactam+clindamycin, before the culture results were available. Both patients experienced rapid clinical deterioration, renal insufficiency, and eventual mortality.

All isolates were sensitive to penicillin. Clindamycin resistance was present in 7 (17.5%) patients, while erythromycin resistance was identified in 2 (5%) patients.

IV immunoglobulin was administered in 2 (5%) patients. Fifteen (37.5%) patients (13 with necrotizing soft tissue infection, 2 with septic arthritis) required a surgical procedure. Mortality was observed in 3 (7.5%) patients: 2 patients with STSS and 1 patient with a necrotizing soft tissue infection with bacteremia.

Discussion

In our study, we found that the number of iGAS cases increased progressively during the pre-pandemic period, while no cases were observed during the pandemic. This situation may be attributed to a reduction in GAS transmission due to the preventive measures implemented during the pandemic, as well as a decline in the incidence of infections such as influenza and varicella, which are significant risk factors for iGAS.

Similarly, data from the centers for disease control and prevention indicate that the number of reported iGAS cases in the United States remained high between 2015 and 2019, with annual rates of 100 to 200 cases. In 2020, during the pandemic, only 74 cases were reported, a decrease that may also be linked to COVID-19 pandemic measures such as isolation and infection control (4). A study conducted in the Netherlands evaluated the pre-pandemic and post-pandemic periods, and found that, similar to our study, no cases of iGAS were reported during the pandemic in 2020. However, a significant increase in cases was observed during the post-pandemic period (5).

Clinicians in several European countries and the United States have reported an increase in cases of iGAS infections in children after overall low incidence rates during the years of the COVID-19 pandemic (6,7). This increase is thought to be associated with an increased circulation of respiratory viruses which predispose individuals to GAS infection following the relaxation of COVID-19 measures. This increase may also indicate that the incidence of iGAS infections has returned to levels which were observed in the pre-pandemic period (8).

Previous reports have identified the skin as a potential source for GAS bacteremia (9,10). In our findings, 60% of the patients with bacteremia had skin and/or soft tissue infections as a predisposing factor, which is consistent with previous studies. Additionally, it has been reported that varicella and influenza infections are among the main predisposing factors in children, and our study supports this conclusion (5,11).

GAS is highly susceptible to beta-lactam antibiotics. However, clinical failures can occur with penicillin treatment alone, particularly in patients with iGAS infections in which a larger number of bacteria may be present (12,13). Clindamycin may be a more effective agent for the treatment of iGAS infections than penicillin, as its efficacy is not impacted by inoculum size or the stage of growth (12-14). Additionally, clindamycin suppresses bacterial toxin production (14). However, clindamycin should not be used as a monotherapy, because it is not bactericidal, and GAS resistance to clindamycin is rising in certain geographic areas (1). Therefore, a combination of penicillin/beta-lactam antibiotics and clindamycin is recommended for the initial treatment of iGAS infections (15). In our study, 82.5% of the patients were treated with a combination of clindamycin and beta-lactam antibiotics.

According to our study findings, the overall mortality rate was 7.5% (3 out of 40 children). In various studies conducted in different countries, mortality rates have ranged from 2% to 8% (16,17).

Study Limitations

This study has several limitations. First, as a single-center study, the findings may not be generalizable to other regions or healthcare settings with different epidemiological patterns. Second, the relatively small sample size limits the statistical power and the ability to detect subtle trends in iGAS incidence. Additionally, the absence of cases during the pandemic period may be influenced by changes in healthcare-seeking behavior, diagnostic practices. Lastly, the study did not assess potential changes in circulating GAS strains or the impact of variations in antibiotic use, which could have influenced the observed trends. Future multicenter and prospective studies are needed to validate these findings and further explore the factors influencing iGAS epidemiology.

Conclusion

Our study revealed a progressive increase in iGAS cases during the pre-pandemic years, while no cases were observed during the pandemic period. This decrease may be attributed to a reduction in GAS transmission due to pandemic-related preventive measures, as well as a decline in the incidence of infections such as influenza and varicella, which are important risk factors for iGAS. Prospective surveillance studies are needed in order to better evaluate any changes in the epidemiology of iGAS infections.

Ethics

Ethics Committee Approval: This study was approved by the Gazi University Clinical Research Ethics Committee Non-Interventional Research (decision no.: 226, dated: 20.03.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.A.Ü., M.P., N.K.U., E.G., T.B.D., H.T., A.T., Concept: N.A.Ü., M.P., N.K.U., E.G., Design: M.P., Data Collection or Processing: N.A.Ü., M.P., E.A.Ş., Analysis or Interpretation: N.A.Ü., M.P., Literature Search: N.A.Ü., M.P., Writing: N.A.Ü., M.P.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this article.

Financial Disclosure: The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. American Academy of Pediatrics. Group A Streptococcal Infections. In: Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH, eds. Red book: 2024 Report of the Committee on Infectious Diseases. American Academy of Pediatrics; 2024, p. 785-98.
2. Stevens DL. invasive group a streptococcus infections. Clin Infect Dis. 1992; 14:2-11.
3. McBride JA, Eickhoff J, Wald ER. Impact of COVID-19 quarantine and school cancelation on other common infectious diseases. Pediatr Infect Dis J. 2020; 39:e449-e452.
4. Centers for disease control and prevention. Active bacterial core surveillance (ABCs). ABCs Report: group A Streptococcus, 2015-2020 https://www.cdc.gov/abcs/reports/index.html (accessed on March, 15, 2023).
5. van Kempen EB, Bruijning-Verhagen PCJ, Borensztajn D, et al. Increase in invasive group a streptococcal infections in children in the netherlands, a survey among 7 hospitals in 2022. Pediatr Infect Dis J. 2023; 42:e122-e4.
6. Massese M, La Sorda M, De Maio F, et al. Epidemiology of group a streptococcal infection: are we ready for a new scenario? Lancet Microbe. 2024; 5:620-1.
7. Polat M, Atay Ünal N, Kara Ulu N, et al. H. Streptococcal toxic shock syndrome following influenza a infection in two children. Pediatr Infect Dis J. 2023; 42:e182-e3.
8. Centers for Disease Control and Prevention. Increase in Invasive Group A Strep Infections, 2022–2023. Available at: https://www.cdc.gov/groupastrep/igas-infections-investigation.html (Accessed on December 08, 2024).
9. Cancellara AD, Melonari P, Firpo MV, et al. Multicenter study on invasive streptococcus pyogenes infections in children in Argentina. Arch Argent Pediatr. 2016; 114:199-208.
10. Sivagnanam S, Zhou F, Lee AS, O'Sullivan MV. Epidemiology of invasive group a streptococcus infections in Sydney, Australia. Pathology. 2015; 47:365-71.
11. Zachariadou L, Stathi A, Tassios PT, Pangalis A, Legakis NJ, Papaparaskevas J; Hellenic Strep-Euro Study Group. Differences in the epidemiology between paediatric and adult invasive streptococcus pyogenes infections. Epidemiol Infect. 2014; 142:512-9.
12. Stevens DL, Bryant AE, Yan S. Invasive group A streptococcal infection: New concepts in antibiotic treatment. Int J Antimicrob Agents. 1994; 4:297-301.
13. Stevens DL, Yan S, Bryant AE. Penicillin-binding protein expression at different growth stages determines penicillin efficacy in vitro and in vivo: an explanation for the inoculum effect. J Infect Dis. 1993; 167:1401-5.

14. Mascini EM, Jansze M, Schouls LM, Verhoef J, Van Dijk H. Penicillin and clindamycin differentially inhibit the production of pyrogenic exotoxins a and b by group a streptococci. Int J Antimicrob Agents. 2001; 18:395-8.

15. Babiker A, Li X, Lai YL, et al. Effectiveness of adjunctive clindamycin in β-lactam antibiotic-treated patients with invasive β-haemolytic streptococcal infections in US hospitals: a retrospective multicentre cohort study. Lancet Infect Dis. 2021; 21:697-710.

16. Tapiainen T, Launonen S, Renko M, et al. Invasive Group A Streptococcal Infections in Children: A Nationwide Survey in Finland. Pediatr Infect Dis J. 2016; 35:123-8.

17. O'Brien KL, Beall B, Barrett NL, et al. Epidemiology of invasive group a streptococcus disease in the United States, 1995-1999. Clin Infect Dis. 2002; 35:268-76.

J Pediatr Res 2025;12(1):27-30
DOI: 10.4274/jpr.galenos.2025.86300

Original Article

Overview of Microlithiasis in Infancy in Pediatric Urology

Hasan Turan[1], Özgür Özdemir Şimşek[2]

[1]İzmir Bakırçay University Faculty of Medicine, Department of Pediatric Urology, İzmir, Türkiye
[2]İzmir Bakırçay University Faculty of Medicine, Department of Pediatric Nephrology, İzmir, Türkiye

ABSTRACT

Aim: Infantile microlithiasis, defined as kidney stones smaller than 3 mm, is a multifactorial condition associated with genetic, environmental, and anatomical factors. Congenital anomalies of the kidney and urinary tract (CAKUT) are among the major structural anomalies linked to microlithiasis. This study investigated the prevalence of microlithiasis in infants with CAKUT and explored associated clinical and biochemical characteristics.

Materials and Methods: This retrospective study included 148 infants diagnosed with microlithiasis via ultrasonography at a single center in the prior 2 years. Demographic data, biochemical findings, and imaging results were analyzed. CAKUT anomalies, including ureteropelvic junction obstruction (UPJO) and vesicoureteral reflux (VUR), were documented. Follow-up data covering 12 months were reviewed in order to assess stone persistence and complications.

Results: Among the 148 infants, 56% were male. CAKUT anomalies were identified in 16 cases (10.8%), with UPJO being the most common (87.5%). Stones were detected incidentally in 82.4% of cases, while symptomatic presentations included urinary tract infections (9 cases) and hematuria (3 cases). Persistent stones were observed in 7.4% of patients during follow-up, primarily in those with structural anomalies. A family history of nephrolithiasis was reported in 72% of cases, and all patients received vitamin D supplementation.

Conclusion: Infants with microlithiasis demonstrate a notable association with CAKUT, particularly UPJO and VUR. Routine biochemical and imaging evaluations, coupled with long-term follow-up, are crucial for identifying at-risk patients and preventing complications. Multidisciplinary approaches are essential for optimizing outcomes in this population.

Keywords: CAKUT, infant, microlithiasis, pediatric, urinary anomalies

Introduction

Nephrolithiasis, a condition once considered rare in pediatric populations, has emerged as a significant clinical concern (1). Among its various forms, infantile microlithiasis, defined as kidney stones smaller than 3 mm, poses unique challenges for diagnosis and management. This condition is often asymptomatic but carries potential risks for recurrent urinary tract infections (UTIs), hematuria, and long-term renal dysfunction if left untreated (2,3).

Congenital anomalies of the kidney and urinary tract (CAKUT) are frequently implicated in the pathogenesis of microlithiasis. Structural abnormalities such as ureteropelvic junction obstruction (UPJO) and vesicoureteral reflux (VUR) create a conducive environment for stone formation due

Corresponding Author
Hasan Turan, MD., İzmir Bakırçay University Faculty of Medicine, Department of Pediatric Urology, İzmir, Türkiye
E-mail: hasanturan911@gmail.com **ORCID:** orcid.org/0000-0002-9853-9279
Received: 23.11.2024 **Accepted:** 09.01.2025 **Epub:** 18.02.2025 **Publication Date:** 17.03.2025

Cite this article as: Turan H, Özdemir Şimşek Ö. Overview of microlithiasis in infancy in pediatric urology. J Pediatr Res. 2025;12(1):27-30

to urinary stasis (4,5). Environmental factors, including vitamin D supplementation and inadequate hydration, further exacerbate this risk (6).

Understanding the epidemiology and clinical characteristics of microlithiasis in infants, particularly in the context of CAKUT, is crucial. This study aimed to provide insights into the prevalence of microlithiasis in infants with CAKUT and highlight associated clinical and biochemical profiles (7).

Materials and Methods

This retrospective study was conducted at a single tertiary pediatric care center. A total of 148 infants diagnosed with microlithiasis via ultrasonography were included. The study period spanned from January 2015 to December 2022. The inclusion criteria comprised infants with ultrasonographically confirmed microlithiasis (≤3 mm) and adequate clinical and biochemical data. The exclusion criteria included those patients with incomplete records or underlying systemic diseases unrelated to urinary anomalies.

Data Collection

Patient demographic details, including their age and gender, were recorded. Biochemical analysis included serum calcium, phosphate, parathyroid hormone, and the urine calcium/creatinine ratio. Imaging findings, including the presence of urinary anomalies, such as UPJO and VUR, were reviewed.

Follow-up

All patients were monitored for at least 12 months in order to assess stone persistence and complications such as UTIs or obstructive uropathy. Outcomes were categorized as stone resolution, persistence, or progression.

Statistical Analysis

The SPSS package program (IBM SPSS Statistics for Windows, version 25.0. Armonk, NY: IBMCorp, 2017) was used for statistical analysis. Variables with normal distributions are shown as mean values with standard deviation, variables with abnormal distribution are shown as median (range), and the rest are expressed as frequency. The chi-square test was used to compare categorical variables between groups. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of continuous variables between groups. All parameters were distributed abnormally, so they were evaluated by the Mann-Whitney U test. For this study, $p<0.05$ was considered statistically significant.

Ethics Statement

This study was conducted in compliance with the Declaration of Helsinki (2013 revision). Ethical approval was obtained from the İzmir Bakırçay University Non-Invasive Clinical Research Ethics Committee (approval no.: 1558, date: 17.04.2024). Informed consent was waived due to the retrospective nature of this study.

Results

Among the 148 infants included in this study, 56% were male. Their mean age at diagnosis was 10.2 months (range: 2-24 months). The majority of microlithiasis cases (82.4%) were detected incidentally during routine ultrasonography evaluations. Symptomatic presentations included UTIs in 9 patients and gross hematuria in 3 patients (5,7).

Associated Urinary Anomalies

Urinary tract anomalies were identified in 16 cases (10.8%). UPJO was the most common anomaly, accounting for 87.5% of these cases. VUR was observed in the remaining patients (7).

Biochemical Analysis

Patients were evaluated for the presence of hypercalciuria based on reference values determined by months in Turkish children (8). Biochemical evaluation revealed hypercalciuria in 32% of the patients. Elevated serum calcium and parathyroid hormone levels were observed in 14% and 10% of the cohort, respectively. Vitamin D supplementation was reported in all cases, with 18% receiving doses higher than recommended (6,9).

Laboratory analysis results of the patients are shown in Table I.

Follow-up Outcomes

After 12 months of follow-up, stone resolution was noted in 72% of the cases, while 7.4% exhibited persistent stones. Persistent stones were significantly associated with structural anomalies such as UPJO and VUR. Complications during follow-up included recurrent UTIs in 8 patients and worsening hydronephrosis in 2 patients (10).

Discussion

Although infantile microlithiasis is often asymptomatic, it presents significant challenges due to its association with long-term renal complications, especially when accompanied by CAKUT. The anatomical anomalies of CAKUT, such as UPJO and VUR, lead to urinary stasis, creating a favorable environment for stone formation (11,12).

Table I. Laboratory findings at the time of admission	
Laboratory findings	
Urea (mg/dL) median (Q1-Q3)	12.4 (6.1-35.4) mg/dL
Creatinine (mg/dL) median (Q1-Q3)	0.23 (0.17-0.31) mg/dL
Uric acid (mg/dL) median (Q1-Q3)	3.2 (1.4-4.6) mg/dL
Calcium (mg/dL) mean ± SD	10.5±0.4 mg/dL
Phosphorus (mg/dL) median (Q1-Q3)	5.7 (4.5-7.1) mg/dL
Parathormone (pg/mL) median (Q1-Q3)	27.1 (14.5-57.1) pg/mL
Vitamin D (ng/mL) median (Q1-Q3)	34.3 (9.3-69.2) ng/mL
Urine density median (Q1-Q3)	1006 (1000-1030)
Urine pH median (Q1-Q3)	6.5 (5-9)
Spot urine calcium/creatinine median (Q1-Q3)	0.34 (0.02-2.13)
SD: Standard deviation	

The high prevalence of UPJO observed in the studied cases supports previous research linking CAKUT to pediatric kidney stones (13,14).

The persistence of stones in cases with structural anomalies highlights the importance of timely and appropriate interventions. For instance, studies have shown that surgical correction of UPJO not only improves urinary flow, but also reduces the risk of stone formation (14). Moreover, advanced diagnostic techniques have facilitated the identification of such anomalies, enabling the development of tailored approaches which address individual patients' needs (4).

The biochemical abnormalities observed in this study further emphasize the multifactorial nature of microlithiasis. Hypercalciuria, observed in nearly one-third of our patients, is a well-known cause of stone formation. This finding aligns with studies emphasizing the synergistic role of metabolic factors and structural anomalies in pediatric stone disease (15). As this study was retrospective and evaluated from a pediatric urology perspective, only calcium and creatinine were measured in spot urine. One of the most important limitations of our study was that metabolic screening was not performed. Additionally, excessive vitamin D supplementation was noted in 18% of our cases, suggesting a potential contribution to hypercalciuria in susceptible infants, though this remains a topic for further investigation (16).

The resolution of stones in 67% of cases suggests that infantile microlithiasis can often be a transient condition. However, the persistence of stones in some patients underscores the importance of a patient-centered approach to follow-up and treatment. Proper hydration adjusted to body weight, low-oxalate diets, and periodic ultrasonographic follow-ups can lead to significant improvements in stone size and outcome (17,18).

These findings highlight the importance of routine screening for CAKUT in those infants diagnosed with microlithiasis. Advanced ultrasonography and voiding cystourethrography are valuable tools for the early detection of underlying anomalies (17). Early diagnosis is critical, as studies have demonstrated that timely identification and intervention can significantly slow the progression of nephrolithiasis and prevent associated complications. Structured follow-up and treatment protocols in infants with CAKUT have been shown to reduce recurrent stone formation and severe complications (11,12).

Injeyan et al. (18) reported that hydration plays a critical role in preventing stone formation, especially in those infants with CAKUT. They found that fluid intake increased in those infants with recurrent urinary stones. Their study emphasized that maintaining optimum urine output reduces the supersaturation of lithogenic substances such as calcium oxalate and uric acid (17). Adequate hydration has also been shown to prevent recurrent stones and alleviate urinary stasis in CAKUT patients. Regular fluid intake prevents crystal aggregation and dilutes solutes in urine, making it a cornerstone of pediatric nephrolithiasis management.

In addition to hydration, individualized management strategies, including dietary modifications and careful monitoring of vitamin D supplementation, are essential in reducing metabolic risks and preventing stone growth or even promoting spontaneous passage (15,16).

The strengths of this study lie in its use of robust imaging and biochemical analyses to elucidate the relationship between CAKUT and microlithiasis. High-resolution ultrasonography allowed for the precise identification of structural anomalies, while metabolic evaluations underscored the interplay between anatomical and biochemical factors. These approaches offer valuable insights into the multifactorial nature of stone formation in infants (11-16).

Study Limitations

However, the retrospective design and single-center setting of our study may limit its generalizability. Multicenter, prospective studies are needed in order to refine diagnostic, follow-up, and treatment protocols. CAKUT has been identified as the most significant factor in the development

of kidney stones in infants, with structural anomalies such as UPJO and VUR reported to account for 65% of cases. The presence of CAKUT was found to increase the likelihood of persistent stones by threefold compared to those infants without structural anomalies (19).

Similarly, CAKUT has been identified as the dominant risk factor in 60% of cases. The early diagnosis and management of CAKUT has been shown to significantly reduce complications such as recurrent infections and bilateral stones, underscoring the importance of screening for these anomalies in at-risk infants (11,13).

Conclusion

In infantile cases, the most critical factor is the presence of urological anomalies, which were evaluated in this study in line with the literature. In the absence of urological anomalies, we believe that routine follow-up is sufficient, and no additional interventions are required.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the İzmir Bakırçay University Non-Invasive Clinical Research Ethics Committee (approval no.: 1558, date: 17.04.2024).

Informed Consent: Informed consent was waived due to the retrospective nature of this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.T., Concept: H.T., Design: H.T., Data Collection or Processing: H.T., Ö.Ö.Ş., Analysis or Interpretation: H.T., Ö.Ö.Ş., Literature Search: H.T., Ö.Ö.Ş., Writing: H.T., Ö.Ö.Ş.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this article.

Financial Disclosure: The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. Penido MGMG, Alon US. Infantile urolithiasis. Pediatr Nephrol. 2021; 36:1037-40.
2. Çamlar SA, Soylu A, Kavukçu S. Characteristics of infant urolithiasis: A single center experience in western Turkey. J Pediatr Urol. 2020; 16:463.
3. Fallahzadeh MA, Hassanzadeh J, Fallahzadeh MH. What do we know about pediatric renal microlithiasis? J Renal Inj Prev. 2016; 6:70-5.
4. Marra G, Taroni F, Berrettini A, et al. Pediatric nephrolithiasis: a systematic approach from diagnosis to treatment. J Nephrol. 2019; 32:199-210.
5. Baştuğ F, Gündüz Z, Tülpar S, Poyrazoğlu H, Düşünsel R. Urolithiasis in infants: evaluation of risk factors. World J Urol. 2013; 31:1117-22.
6. Eskandarifar A, Roshani D, Tabarkhun A, Ataee E. Assessment of serum level of vitamin d in infants with nephrolithiasis. Iran J Kidney Dis. 2021; 1:116-20.
7. Güven AG, Koyun M, Baysal YE, et al. Urolithiasis in the first year of life. Pediatr Nephrol. 2010; 25:129-34.
8. Özdemir Şimşek Ö, Arslansoyu Çamlar S. Süt çocukluğu döneminde üriner sistem taş hastalığı. Türkmen MA, editör. Çocukluk Çağı Üriner Sistem Taş Hastalığı. 1. Baskı. Ankara: Türkiye Klinikleri; 2024. p. 51-5.
9. Copelovitch L. Urolithiasis in children: medical approach. Pediatr Clin North Am. 2012; 59:881-96.
10. Wani M, Mohamed AHA, Brown G, Sriprasad S, Madaan S. Challenges and options for management of stones in anomalous kidneys: a review of current literature. Ther Adv Urol. 2023; 15:17562872231217797.
11. Serdaroğlu E, Aydoğan M, Özdemir K, Bak M. Incidence and causes of urolithiasis in children between 0-2 years. Minerva Urol Nefrol. 2017; 69:181-8.
12. Baştuğ F, Ağbaş A, Tülpar S, et al. Comparison of infants and children with urolithiasis: a large case series. Urolithiasis. 2022; 50:411-21.
13. Andrioli V, Highmore K, Leonard MP, et al. Infant nephrolithiasis and nephrocalcinosis: natural history and predictors of surgical intervention. J Pediatr Urol. 2017; 13:355.e1-355.e6.
14. Skolarikos A, Dellis A, Knoll T. Ureteropelvic obstruction and renal stones: etiology and treatment. Urolithiasis. 2015; 43:5-12.
15. Yılmaz AÇ, Ünal N. Do dietary factors play a role in infantile urolithiasis? Pediatr Nephrol. 2022; 37:3157-63.
16. Yılmaz N, Yüksel S, Altıntaş F, Koçyiğit A. Nephrolithiasis during the first 6 months of life in exclusively breastfed infants. Pediatr Nephrol. 2021; 36:1227-31.
17. Bernardor J, Bidault V, Bacchetta J, Cabet S. Pediatric urolithiasis: what can pediatricians expect from radiologists? Pediatr Radiol. 2023; 53:695-705.
18. Injeyan M, Bidault V, Bacchetta J, Bertholet-Thomas A. Hydration and nephrolithiasis in pediatric populations: specificities and current recommendations. Nutrients. 2023; 15:728.
19. Çaltik Yilmaz A, Ünal N, Çelebi Tayfur A, Büyükkaragöz B. How important urolithiasis is under 2 years of age? Urolithiasis. 2022; 50:159-65.

J Pediatr Res 2025;12(1):31-37
DOI: 10.4274/jpr.galenos.2024.03342

Original Article

A Retrospective Evaluation of Pediatric Dental Emergencies: Distribution, Limitations, Treatment Approach, and Parental Satisfaction

Buse Nur Çınar, Dilşah Çoğulu

Ege University Faculty of Dentistry, Department of Pediatric Dentistry, İzmir, Türkiye

ABSTRACT

Aim: Pediatric dental emergencies involve sudden injuries and infections which can significantly impact a child's oral health and development, making immediate and specialized care essential in order to prevent lasting complications and ensure healthy, functional smiles. This study aimed to evaluate pediatric dental emergencies retrospectively, focusing on their distribution, limitations, the treatment modalities employed, and parental satisfaction with the care provided. This comprehensive assessment seeks to contribute to optimizing clinical practices in pediatric dentistry, ultimately enhancing patient outcomes and parental experiences.

Materials and Methods: This retrospective study reviewed 986 pediatric dental emergency cases involving patients aged 3-13 years who applied to the Department of Pediatric Dentistry at Ege University Faculty of Dentistry over six months. Data were systematically extracted from patient records, including demographic characteristics, the specific nature of the dental emergencies, the treatments administered, and the outcomes of subsequent follow-up visits. Parental satisfaction was assessed through a structured questionnaire, administered via telephone interviews. Statistical analyses were conducted by SPSS 25.0 (Chicago, Illinois, USA) using descriptive statistics and Pearson's chi-square test, with significance set at $p<0.05$.

Results: A total of 1,127 applications in 986 pediatric patients presenting with dental complaints were recorded at the emergency clinic. These patients accounted for 7.9% of a total of 12,500 patients who visited for dental diagnoses at the pediatric dentistry clinic. The male-to-female ratio was 1.68:1, indicating a significantly higher proportion of male patients (62.7%). The mean age of the patients was 8.12±2.37 years. The primary presenting complaints were pulpal inflammation (43%), dental trauma (39%), cases involving children with special needs (7%), and other issues (11%). Parental satisfaction was generally high, with 83% of parents reporting satisfaction with the promptness of care, 84% with the effectiveness of the treatment provided, and 82% with the communication and support offered by the dental staff.

Conclusion: These findings highlight a higher prevalence of pulpal inflammation and dental trauma among pediatric dental emergencies, underscoring the need for enhanced preventive measures and targeted patient education. The high levels of parental satisfaction reflect the critical importance of clinical efficacy and effective communication. This retrospective evaluation provides valuable insights into the distribution and management of pediatric dental emergencies. Future efforts are recommended in order to focus on implementing preventive strategies, refine treatment protocols, and maintain high standards of communication and support in order to further improve patient outcomes and parental satisfaction.

Keywords: Dental emergency, pain, pulpal inflammation, dental trauma, pediatric dentistry

Corresponding Author
Prof. Dr. Dilşah Çoğulu, Ege University Faculty of Dentistry, Department of Pediatric Dentistry, İzmir, Türkiye
E-mail: dilsah.cogulu@gmail.com **ORCID:** orcid.org/0000-0002-3156-9801
Received: 18.11.2024 **Accepted:** 30.12.2024 **Epub:** 18.02.2025 **Publication Date:** 17.03.2025

Cite this article as: Çınar BN, Çoğulu D. Retrospective evaluation of pediatric dental emergencies: Distribution, limitations, treatment approach, and parental satisfaction. J Pediatr Res. 2025;12(1):31-37

Introduction

Oral and dental health issues represent a substantial global health challenge, particularly among pediatric populations. Notably, for many individuals, the initial encounter with dental care occurs in response to an emergency situation rather than through preventive measures. This highlights the critical importance of establishing routine dental visits, particularly for children, in order to promote the early detection and management of oral health issues and to foster lifelong healthy dental practices (1-4). Despite the recognized importance of routine dental care, access to these services remains limited for many children. As a result, parents frequently seek dental care for their children only when severe problems arise, often leading to pain or discomfort (4). Research indicates that 28.5% of children attend their first dental visit in response to emergency situations. Pediatric dental emergencies are critical issues which require immediate and precise intervention to prevent long-term adverse outcomes (5).

A dental emergency refers to any acute oral health condition which demands immediate attention to relieve pain, stop bleeding, prevent infection, or preserve a tooth. These emergencies may be due to trauma, infections, or underlying dental conditions and can range from relatively minor issues, such as toothaches, to more severe conditions, such as abscesses or dental fractures. Prompt management is essential, as delays in treatment can result in complications such as systemic infections or tooth loss (6,7).

Dental emergencies are typically preceded by urgent conditions caused by infection, injury, accidents, disasters, or disease which require immediate medical intervention (8). The American Dental Association and the American Association of Oral and Maxillofacial Surgeons define dental emergencies as jaw and alveolar bone fractures, avulsed or displaced teeth, fractured teeth with pulp exposure, acute alveolar abscesses, airway obstruction, oral mucosal lacerations, acute dental pain and infection, and uncontrolled bleeding (9,10). The symptoms associated with these emergencies often create distress for both the patients and the dental professionals. As such, dentists must possess adequate knowledge and decision-making skills in order to quickly alleviate pain and discomfort, particularly when treating pediatric patients (6). Pediatric dental emergencies require prompt, specialized care which accounts for both the physical and emotional needs of the child. Early intervention and appropriate management are essential in order to prevent complications, preserve dental structures, and reduce the psychological impact of traumatic dental experiences (11). Expanding access to pediatric dental care and promoting preventative strategies are vital in reducing the incidence and severity of these emergencies. Understanding the etiology, treatment protocols, and potential outcomes of pediatric dental emergencies is critical for informing preventative care and enhancing acute treatment practices in dentistry (12). Timely intervention in pediatric dental emergencies is critical in order to prevent long-term complications. For example, delaying treatment of a fractured permanent tooth can result in pulp necrosis, potentially necessitating root canal therapy or extraction. Moreover, untreated dental infections in children can progress rapidly, leading to facial swelling, fever, and, in severe cases, systemic involvement requiring hospitalization (13). This retrospective study aimed to investigate the distribution of cases, limitations, treatment approaches, and parental satisfaction in pediatric patients who presented with dental emergencies at a university pediatric dentistry clinic.

Materials and Methods

This retrospective study analyzed 1,127 applications resulting from 986 pediatric dental emergency cases involving patients aged 3-13 years old who presented to the Department of Pediatric Dentistry at Ege University Faculty of Dentistry between September 2023 and February 2024. Ethical approval was obtained from the Ege University Faculty of Medicine Medical Research Ethics Committee (approval no.: 23-4T/54, date: 06.04.2023), and written informed consent was obtained from each parent. Informed consent was obtained via phone from the parents. Consent was documented through their response to a WhatsApp message stating, "I have read, understood, and approve". Data were systematically extracted from patient records, encompassing demographic variables, the specific nature of the dental emergencies encountered, the interventions administered, and the outcomes of follow-up evaluations.

Data collection followed a standardized protocol which included:

- Demographic information: Age, gender.
- Clinical presentation: Type of dental emergency, presenting symptoms, and duration since the onset of symptoms.
- Diagnostic procedures: Clinical examination findings and radiographic evaluations.
- Management: Immediate interventions, definitive treatments provided, and follow-up care.

- Outcomes: Assessment of pain relief, infection control, functional and aesthetic restoration, and parental satisfaction.

This study gathered detailed information regarding patient demographics, including age, gender, and the specific time, day, and month of the diagnosis. Diagnosis and treatment data, including the management provided by the on-duty dentist, and follow-up care, were collected from the electronic medical records by the clinic's dental emergency charting system. The analysis aimed to integrate clinical data with experiential insights in order to provide a comprehensive understanding of the effectiveness of emergency treatment strategies and the quality of patient and parental experiences. Dental emergency diagnoses were categorized into four main groups: dental trauma, pulp-related dental infections, special needs cases, and other conditions (eruption disorders, space maintainers, etc.). Additional data recorded included details of the affected teeth (primary vs. permanent), location (upper vs. lower jaw, anterior vs. posterior teeth), tooth number, type of dental trauma, and associated symptoms (e.g., swelling, abscess etc.).

The treatment approaches were classified into two broad groups: With treatment and without treatment (either because treatment was not indicated or was refused by the patient). The "with treatment" group was further subdivided into three categories: Dental treatment alone, medication alone, and a combination of dental treatment and medication. Dental treatments included restorative treatment, endodontic emergency procedures, repositioning and/or splints, and other multiple interventions. The need for a return visit was assessed by the responsible dentist, and the return visit rate was calculated based on whether patients adhered to the scheduled follow-up visits.

Parental satisfaction was evaluated through a structured questionnaire administered via telephone interviews. These interviews assessed multiple dimensions of the dental care experience, providing insight into overall parental satisfaction. The parental satisfaction survey, consisting of three questions (question 1: Satisfaction with the promptness of care, question 2: Satisfaction with the effectiveness of the treatment, question 3: Satisfaction with the communication and support offered by the dental staff), scored out of 5 (1-5 points, from "strongly disagree" to "strongly agree") according to Likert scaling, was carried out with the parents.

Statistical Analysis

Statistical analysis was conducted by SPSS 25.0 (Chicago, Illinois, USA) using descriptive statistics and Pearson's chi-square test, with a significance level of $p<0.05$.

Results

The present study was conducted retrospectively by analyzing Ege University Faculty of Dentistry, Department of Pediatric Dentistry records. A total of 1,127 applications were documented from 986 pediatric patients who presented with dental complaints to the emergency clinic, representing 7.9% of the 12,500 patients treated over a six-month period. The male-to-female ratio was 1.68:1, reflecting a significantly higher proportion of male patients (62.7%). The mean age of the patients was 8.12±2.37 years. Among the 986 patients, 270 (27%) were in their primary dentition, 410 (42%) were in their mixed dentition, and 306 (31%) were in their permanent dentition.

As shown in Figure 1, the primary reasons for emergency consultations included pulpal inflammation (43%), dental trauma (39%), cases involving children with special needs (7%), and other miscellaneous conditions (11%). Among the cases of pulpal inflammation, 53.7% involved primary teeth, while 46.3% affected permanent teeth, with the most commonly involved teeth being 85, 36, and 46, respectively.

In the cases of dental trauma, 38.4% involved primary teeth, and 61.6% involved permanent teeth, with teeth 11, 21, and 12 being the most frequently affected. Luxation was the most prevalent form of dental trauma in both primary and permanent dentitions. It was reported that among the patients admitted for dental trauma, 23% were involved in traffic accidents, 36% experienced falls at school, 21% sustained injuries from home accidents, and 20% were due to other causes. Furthermore, 12% of the patients had initially sought treatment at a medical emergency department before presenting at the emergency dental clinic. Additionally, 28% of the patients had previously

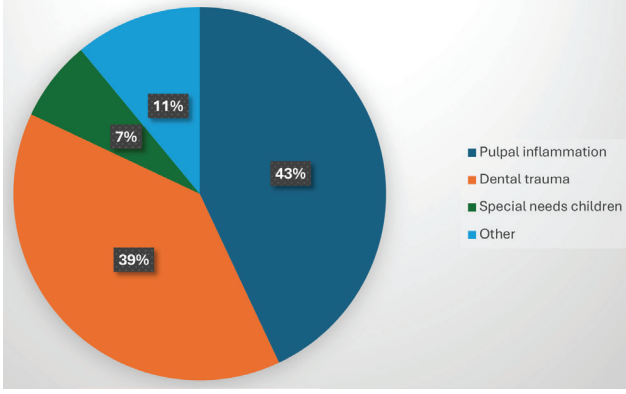


Figure 1. Primary reasons for dental emergency consultations

sought care at another dental clinic, with no treatment being administered to 81% of these cases.

Eruption related issues were predominantly observed in those children within the mixed dentition stage. A total of 27 patients (2.7%) presented to the emergency clinic with complaints associated with eruption related disturbances. Additionally, 13 patients (1.3%) sought emergency dental care due to complications related to space maintainers, such as broken wires, damaged appliances, or irritation.

The findings of the present study revealed that 905 patients (91.8%) received treatment during their emergency visits. Among these, 397 patients (43.9%) underwent dental treatment only, 52 patients (5.7%) received medication alone, and 456 patients (50.4%) received a combination of both dental treatment and medication. A total of 212 patients (23.4%) received restorative treatments, 423 patients (46.7%) underwent endodontic procedures, and 47 patients (5.2%) required extractions. Additionally, repositioning and splinting were performed on 158 (17.5%) patients due to trauma. Avulsion cases accounted for 43 patients, with replantation and splinting conducted in 32 of these instances. Emergency department dentists advised 928 patients (94.1%) to return for follow-up care; however, only 713 patients complied, resulting in a return rate of 72.3%.

The majority of pediatric patients were accompanied by their mothers (68.8%), while 20% were accompanied by their fathers, and 11.2% by other individuals. Additionally, a significant proportion of the children (57.6%) originated from distant districts, 22.1% resided in proximity to our clinic, and 20.3% traveled from other cities for emergency consultations.

Parental satisfaction levels were notably high, with 83% of respondents expressing satisfaction with the promptness of care, 84% reporting satisfaction with the effectiveness of the treatment provided, and 82% expressing contentment with the communication and support offered by the dental staff (Figure 2).

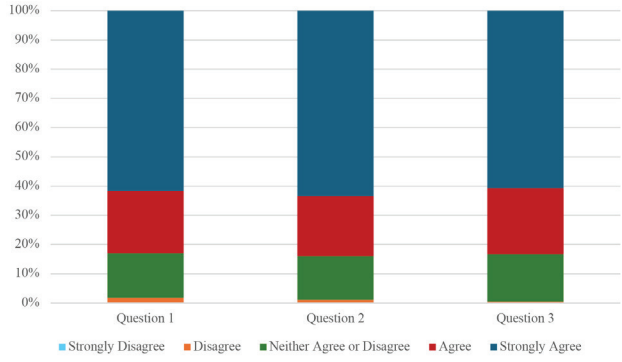


Figure 2. Responses for the parental satisfaction survey

Discussion

Emergency visits are one of the main reasons for parents to take their children to the dentist. Eliminating pain and avoiding emergency complications are an important part of the pediatric dental practice (6,7,14,15). This retrospective evaluation aimed to elucidate the patterns and management strategies associated with pediatric dental emergencies, while also capturing the perspectives and satisfaction levels of parents concerning the dental care their children received.

A total of 1,127 applications were documented from 986 pediatric patients who presented with dental complaints to the emergency clinic, representing 7.9% of the 12,500 patients treated at the Pediatric Dentistry Clinic overall. In the literature, no comprehensive studies have been conducted on the subject of emergency dental clinics. Despite the increasing demand for immediate dental care, there remains a significant gap in research which thoroughly examines the protocols, treatment outcomes, and patient experiences specific to this field. Most available studies tend to focus on general dental care or specific procedures rather than the unique challenges and needs of emergency dental settings (15-18). This highlights the necessity for further in-depth investigations to improve care standards and optimize treatment strategies in emergency dental practice.

The male-to-female ratio was 1.68:1, reflecting a substantially higher representation of male patients, who accounted for 62.7% of the total. These results were found to be consistent with the literature (17-20). It has been particularly reported that the majority of pediatric patients presenting to emergency dental clinics due to trauma are boys (18). This trend aligns with existing studies, which often attribute the higher incidence of dental trauma in boys to factors such as increased participation in physical activities and higher levels of risk-taking behaviors. These findings underscore the importance of targeted prevention strategies and tailored treatment approaches in managing dental trauma among boys in emergency settings. The results of our study were found to be consistent with the existing literature.

In the present study, the primary reasons for presentation included pulpal inflammation (43%), dental trauma (39%), cases involving children with special needs (7%), and various other concerns (11%). In a similar study in the literature, the majority of emergency dentistry cases were reported to involve dental trauma (21).

Additionally, a significant portion of patients presented with pulpal infections, highlighting the importance of these conditions in emergency dental care (22). The distribution

of cases in this study was found to be consistent with the literature, confirming the prominence of both dental trauma and pulpal infections as common reasons for emergency dental visits. These findings emphasize the need for effective management protocols to address the diverse range of conditions seen in emergency dental settings.

In the present study, luxation injuries appeared more frequently in both primary and permanent dentition. According to the literature, luxation injuries were the most frequently occurring type other than avulsion in both primary and permanent dentition (23). In contrast, a study assessing the dental injury types in a university-based pediatric dentistry postgraduate outpatient clinic reported that luxation injuries were seen more often in primary dentition, whereas tooth fractures were more common than luxation in permanent dentition (24). Primary incisors tended to be luxated more than permanent teeth (25). Some authors have attributed this difference to the spongy nature of the supporting structures surrounding primary dentition in young children and to the lower root/crown ratio compared to permanent teeth, thereby favoring luxation injuries over fractures (26).

Eruption related problems commonly occur in children with mixed dentition. A total of 27 children (7.4%) visited the emergency clinic due to eruption related problems. A review of the literature reveals a consistent finding regarding the prevalence of patients presenting to emergency dental clinics due to complications associated with dental eruption (27). Numerous studies indicate that issues such as delayed eruption, impaction, and malocclusion are significant contributors to the need for urgent dental care (28). Specifically, patients experiencing these eruption related problems often seek emergency treatment due to associated pain, infection or functional impairment. This trend underscores the importance of early detection and management of eruption anomalies in order to minimize the incidence of emergency visits and enhance overall oral health outcomes.

In the present study, 1.3% of the patients applied to the emergency clinic due to complications related to space maintainers, such as broken wires, damaged appliances, or irritation. The incidence of patient referrals to emergency dental clinics due to complications associated with space maintainers is consistent with the findings documented in the existing literature (29). Research indicates that issues such as dislodgment, failure to adequately maintain arch space, and resultant discomfort are prevalent among pediatric patients utilizing these appliances. Studies consistently demonstrate that complications related to space maintainers not only contribute to patient morbidity, but also necessitate urgent dental intervention to prevent further orthodontic complications. This correlation underscores the critical need for vigilant monitoring and effective management of space maintainers throughout orthodontic treatment. Furthermore, the alignment of these findings with the literature highlights the imperative for enhanced patient education regarding the appropriate use, maintenance, and potential complications of space maintainers. Such educational initiatives may play a pivotal role in reducing the frequency of emergency visits attributable to space maintainer-related issues, thereby improving overall treatment outcomes in pediatric orthodontics (29,30).

In the present study, the majority of children (78.8%) were accompanied by their mothers, while 10% were accompanied by their fathers and 11.2% by other individuals. This finding underscores the predominant role of mothers in managing pediatric dental emergencies, reflecting their primary caregiving responsibilities in many family structures. This trend may be influenced by several factors, including the mothers' closer involvement in their children's daily routines and health needs, as well as their heightened awareness of symptoms indicating pain or discomfort. Furthermore, mothers are typically more likely to recognize the significance of early dental intervention, driven by a strong commitment to their child's immediate well-being and long-term health. This maternal role in emergency dental care underscores the importance of educating primary caregivers, particularly mothers, on recognizing and promptly addressing dental emergencies, which can significantly improve treatment outcomes and mitigate potential complications (31).

In the present study, the majority of children (57.6%) resided in distant suburban areas, while 22.1% lived in close proximity to the clinic, and 20.3% came from other cities. The university hospital where this study was conducted serves as a major referral center, receiving a high volume of patients from diverse locations. The large number of patients presenting to the emergency dental clinic from distant areas and neighboring provinces reflects the hospital's reputation and central role in providing specialized care. This influx of patients from various regions highlights both the accessibility and the demand for the high-quality emergency dental services which our institution uniquely offers, underscoring the necessity for streamlined and efficient management protocols to address the needs of a broad patient demographic.

Patient satisfaction has emerged as a key goal for healthcare services (32). In the present study, parental satisfaction levels were notably high, with 83% expressing satisfaction with the promptness of care, 84% with the quality and effectiveness of treatment, and 82% with the communication and support provided by the dental team. High patient satisfaction is essential for pediatric patients with pain, as it promotes adherence to follow-up care and builds trust between the families and the healthcare providers, supporting long-term dental health.

Study Limitations

This study identifies pulpal infections and traumatic injuries as the most common pediatric dental emergencies, emphasizing the importance of timely treatment, follow-up care, and preventive measures such as oral hygiene education and protective gear during sports. While the single-center design limits generalizability, further multicenter studies and research on long-term outcomes and socio-economic factors could inform equitable and effective dental care strategies.

Conclusion

This retrospective study provides key insights into the prevalence, management, and outcomes of pediatric dental emergencies. It emphasizes the importance of timely intervention to minimize complications and accelerate recovery. These findings highlight the need for standardized protocols and advocate for public health initiatives focusing on prevention and oral health education in order to reduce emergencies and promote long-term oral health in children.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ege University Faculty of Medicine Medical Research Ethics Committee (approval no.: 23-4T/54, date: 06.04.2023).

Informed Consent: Informed consent was obtained via phone from the parents. Consent was documented through their response to a WhatsApp message stating, "I have read, understood, and approve".

Acknowledgments

The authors would like to express their sincere gratitude to all the pediatric patients who contributed to the data for this study, to their families for their cooperation, to the colleagues in the emergency dental clinic for their invaluable support, and to Assoc. Prof. Dr. Timur Köse for his assistance with the statistical analysis.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.N.Ç., D.Ç., Concept: B.N.Ç., D.Ç., Design: B.N.Ç., D.Ç., Data Collection or Processing: B.N.Ç., D.Ç., Analysis or Interpretation: B.N.Ç., D.Ç., Literature Search: B.N.Ç., D.Ç., Writing: B.N.Ç., D.Ç.

Conflict of Interest: One author of this article, Dilşah Çoğulu, is a member of the Editorial Board of The Journal of Pediatric Research. However, she did not involved in any stage of the editorial decision of the manuscript. The other author declared no conflict of interest.

Financial Disclosure: The author(s) received no financial support for this research, authorship, and/or the publication of this article.

References

1. Daou MH, Eden E, Osta NE. Age and reasons of the first dental visit of children in Lebanon. J Med Liban. 2016; 64:18-22.
2. Cunha RF, Pugliesi DM, de Mello Vieira AE. Oral trauma in Brazilian patients aged 0-3 years. Dent Traumatol. 2001; 17:210-12.
3. Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century – the approach of the WHO Global Oral Health Programme. Community Dent Oral Epidemiol. 2003; 31:3-23.
4. Peres MA, Macpherson LMD, Weyant RJ, et al. Oral diseases: a global public health challenge. Lancet. 2019; 394:249-60.
5. Agostini FG, Flaitz CM, Hicks MJ. Dental emergencies in a university-based pediatric dentistry postgraduate outpatient clinic: a retrospective study. ASDC J Dent Child. 2001; 68:316-21.
6. Lygidakis NA, Marinou D, Katsaris N. Analysis of dental emergencies presenting to a community paediatric dentistry centre. Int J Paediatr Dent. 1998; 8:181-90.
7. Quinonez C, Gibson D, Jokovic A, Locker D. Emergency department visits for dental care of nontraumatic origin. Community Dent Oral Epidemiol. 2009; 37:366-71.
8. Wong NH, Tran C, Pukallus M, Holcombe T, Seow WK. A three-year retrospective study of emergency visits at an oral health clinic in south-east Queensland. Aust Dent J. 2012; 57:132-7.
9. American Dental Association Council on Dental Practice; American Dental Association Council on Government Affairs. The U.S. approach to dental emergency preparedness and disaster response. JADA. 2009; 140:546-7.
10. Troulis MJ, Ward BB, Zuniga JA. Emerging technologies: findings of the 2005 AAOMS Research Summit. J Oral Maxillofac Surg. 2005; 63:1436-42.
11. Martens LC, Rajasekharan S, Jacquet W, et al. Paediatric dental emergencies: a retrospective study and a proposal for definition and guidelines including pain management. Eur Arch Paediatr Dent. 2018; 19:245-53.
12. Ramos-Gomez FJ, Crystal YO, Ng MW, Crall JJ, Featherstone JD. Pediatric dental care: prevention and management protocols based on caries risk assessment. J Calif Dent Assoc. 2010; 38:746-61.

13. Lee SM, Yu YH, Karabucak B. Endodontic treatments on permanent teeth in pediatric patients aged 6-12 years old. J Dent Sci. 2023; 18:1109-15.

14. Graham DB, Webb MD, Seale NS. Pediatric emergency room visits for nontraumatic dental disease. Pediatr Dent. 2000; 22:134-40.

15. Sakai VT, Magalhaes AC, Pessan JP, Silva SM, Machado MA. Urgency treatment profile of 0 to 15 year-old children assisted at urgency dental service from Bauru Dental School, University of Sao Paulo. J Appl Oral Sci. 2005; 13:340-4.

16. Brecher EA, Keels MA, Best AM, Quiñonez RB, Roberts MW. Management of after-hours pediatric dental emergencies among pediatric and general dentists. Pediatr Dent. 2018; 40:352-8.

17. Okunseri C. Limiting dental benefits may lead to hospital emergency department visits for nontraumatic dental conditions. J Evid Based Dent Pract. 2018; 18:185-6.

18. Meisha DE, Al-Khotani A, Alhurishi SA, et al. Pattern of pediatric emergency dental care during COVID-19 pandemic in Saudi Arabia. Saudi Dent J. 2024; 36:1350-6.

19. Jung CP, Tsai AI, Chen CM. A 2-year retrospective study of pediatric dental emergency visits at a hospital emergency center in Taiwan. Biomed J. 2016; 39:207-13.

20. Kurt A, Guduk OF, Erbek SM, Baygin O, Tuzuner T. Retrospective evaluation of patients admitted to Karadeniz Technical University Pediatric Dentistry clinic due to trauma. Eur Oral Res. 2019; 53:74-9.

21. Nourwali IM, Maddhar AK, Alsaati BH, et al. Emergency management of dental trauma: a survey of public knowledge, awareness, and attitudes in Al-Madinah Al-Munawwarah. Clin Cosmet Investig Dent. 2019; 11:279-84.

22. Franciscatto GJ, Brennan DS, Gomes MS, Rossi-Fedele G. Association between pulp and periapical conditions and dental emergency visits involving pain relief: epidemiological profile and risk indicators in private practice in Australia. Int Endod J. 2020; 53:887-94.

23. Lauridsen E, Hermann NV, Gerds TA, Kreiborg S, Andreasen JO. Pattern of traumatic dental injuries in the permanent dentition among children, adolescents, and adults. Dent Traumatol. 2012; 28:358-63.

24. Ng L, Malandris M, Cheung W, Rossi-Fedele G. Traumatic dental injuries presenting to a paediatric emergency department in a tertiary children's hospital, Adelaide, Australia. Dent Traumatol. 2020; 36:360-70.

25. de Paula Barros JN, de Araújo TAA, Soares TRC, et al. Profiles of Trauma in Primary and Permanent Teeth of Children and Adolescents. J Clin Pediatr Dent. 2019;43:5-10.

26. Andreasen JO, Andreasen FM, Andersson L. Textbook and color atlas of traumatic injuries to the teeth. 4th ed. Blackwell Munksgaard; Oxford, 2007.27.

27. Wilson S, Smith GA, Preisch J, Casamassimo PS. Nontraumatic dental emergencies in a pediatric emergency department. Clin Pediatr (Phila). 1997; 36:333-7.

28. Aldowsari M, Alsaif FS, Alhussain MS, et al. Prevalence of delayed eruption of permanent upper central incisors at a tertiary hospital in Riyadh, Saudi Arabia. Children (Basel). 2022; 9:1781.

29. Caprioglio A, Pizzetti GB, Zecca PA, et al. Management of orthodontic emergencies during 2019-NCOV. Prog Orthod. 2020; 21:10.

30. Popat H, Thomas K, Farnell DJ. Management of orthodontic emergencies in primary care-self-reported confidence of general dental practitioners. Br Dent J. 2016; 221:21-4.

31. Divaris K, Lee JY, Baker AD, et al. Influence of caregivers and children's entry into the dental care system. Pediatrics. 2014; 133:e1268-76.

32. Goswami M, Talwar S, Goswami M, Goswami MM. Evaluation of the satisfaction level of patients visiting dental emergency services. J Family Med Prim Care. 2022; 11:3830-3.

J Pediatr Res 2025;12(1):38-44
DOI: 10.4274/jpr.galenos.2024.34467

Case Report

What is the Optimal Treatment for this Rare Entity: A Pediatric Case with the Hyalinizing Clear Cell Carcinoma of the Nasopharynx

Eda Ataseven[1], Şebnem Önen Göktepe[2], Göksel Turhal[3], Derya Demir[4], Serra Kamer[5], Mehmet Kantar[1]

[1]Ege University Faculty of Medicine, Department of Pediatric Hematology and Oncology, İzmir, Türkiye
[2]University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, Clinic of Pediatric Hematology and Oncology, İzmir, Türkiye
[3]Ege University Faculty of Medicine, Department of Ear Nose Throat, İzmir, Türkiye
[4]Ege University Faculty of Medicine, Department of Pathology, İzmir, Türkiye
[5]Ege University Faculty of Medicine, Department of Radiation Oncology, İzmir, Türkiye

ABSTRACT

Hyalinizing clear cell carcinoma (HCCC) is a rare low-grade malignant tumor of the minor salivary glands of the head and neck. It can also arise in the nasopharynx in rare cases. Only a few cases of nasopharyngeal HCCC (NHCCC) have been reported in the literature, and most patients are in their sixth decade of life. Due to this disease's rarity, there is no consensus on its optimal treatment. Surgical excision is the mainstay of treatment. However, the role of postoperative radiotherapy is unknown. Herein, we report on a case of NHCCC in a 14-year-old female, treated successfully with sur-gical resection and adjuvant radiotherapy. This patient is the youngest case of NHCCC reported in the literature.

Keywords: Hyalinizing clear cell carcinoma, nasopharynx, childhood, treatment, surgery

Introduction

Hyalinizing clear cell carcinoma (HCCC) is a rare low-grade malignant tumor of the head and neck salivary glands which was first described in detail by Milchgrub et al. (1) in 1994. HCCC represents 1% of all salivary gland tumors (1,2). They arise mainly from the palate, base of the tongue, and floor of the mouth and also in the nasopharynx, maxilla, oral mucosa, or nasal cavity in rare cases (1-4).

HCCCs are low-grade malignant tumors, and they have an indolent course. Most patients are in their sixth decade of life and have a female predominance (3). They usually present with painless mass and manifest site-specific symptoms such as epistaxis, tinnitus, or nasal obstruction due to the local mass effect (2,3).

Its definitive diagnosis is based on histological examination. HCCC has a broad differential diagnosis which

Corresponding Author
Assoc. Prof. Eda Ataseven, Ege University Faculty of Medicine, Department of Pediatric Hematology and Oncology, İzmir, Türkiye
E-mail: edataseven@yahoo.com **ORCID:** orcid.org/0000-0003-3419-5814
Received: 17.09.2024 **Accepted:** 02.12.2024 **Epub:** 18.02.2025 **Publication Date:** 17.03.2025

Cite this article as: Ataseven E, Önen Göktepe Ş, Turhal G, Demir D, Kamer S, Kantar M. What is the optimal treatment for this rare entity: a pediatric case with the hyalinizing clear cell carcinoma of the nasopharynx. J Pediatr Res. 2025;12(1):38-44

includes other clear cell-containing head and neck tumors (3). Hence, it is sometimes challenging to distinguish HCCC from the other salivary gland tumors with clear cell variants based on a small biopsy sample. Antonescu et al. (5) identified a consistent Ewing sarcoma breakpoint region 1 (EWSR1) - *activating transcription factor-1 fusion* gene in HCCC, and this molecular signature is not present in the other clear cell tumors. Shah et al. (6) recently found that *EWSR1* rearrangements were not a feature in the other salivary gland tumors, suggesting that this EWSR1 rearrangement is specific to HCCC and so it can be used to distinguish this lesion from other salivary gland neoplasms.

There have been only a few cases of nasopharyngeal HCCC (NHCCC) reported in the literature. Due to this disease's rarity, there is no consensus on its optimal treatment. Surgical excision is the mainstay of treatment. However, the role of adjuvant radiotherapy remains unknown. Although there is no standardized treatment regimen, positive surgical margins and particularly aggressive tumors are frequently treated with radiotherapy in order to decrease the risk of recurrence (4).

Case Report

A fourteen-year-old female patient presented with nasal congestion and epistaxis for three months. On her physical examination, a large polypoid mass obliterated the left nasal cavity. Her head and neck examination showed no other lesions or lymphadenopathy. Magnetic resonance imaging showed a protruding nasopharyngeal mass measuring 3x2.5x2 cm in diameter, arising from the left lateral and posterior wall, obstructing the entire nasopharynx, and extending to the Rosenmüller fossa and torus tubarius (Figure 1). A homogeneous contrast enhancement was apparent. There were also bilateral retropharyngeal and cervical lymph nodes of less than 1 cm.

A biopsy was performed, and it showed submucosal diffuse infiltration by neoplastic epithelial cells with clear cytoplasm, round-oval nuclei, and inconspicuous nucleoli. Tumor cells were positive for periodic acid schiff with diastase soluble in histochemistry. Immunohistochemistry revealed that the neoplastic cells were positive for epithelial membrane antigen (EMA), cytokeratin (AE1/AE3), but no expression of DOG1, SOX-10, or p63. This was compatible with clear cell carcinoma. To rule out metastasis from the kidney, a positron emission tomography (PET) scan and abdominal ultrasonography (USG) were performed. The PET scan revealed an abnormal accumulation of fluorodeoxyglucose (SUV_{max}: 2.5) in the nasopharyngeal mass without any tumors in other sites of the body. Abdominal USG was normal. Tumor markers, such as alpha-fetoprotein, human chorionic gonadotropin and neuron specific enolase were within normal limits. The tumor stage was pT2N0M0. Following this, the patient underwent complete tumor resection.

The tumor originated from the left Rosenmüller fossa, and the boundaries of the resection were the base of the sphenoid sinus superiorly, the lateral nasopharyngeal wall laterally, and the midline posterior nasopharyngeal wall medially. The Torus tubarius and cartilaginous Eustachian tubes were included in the resection. The deep surgical

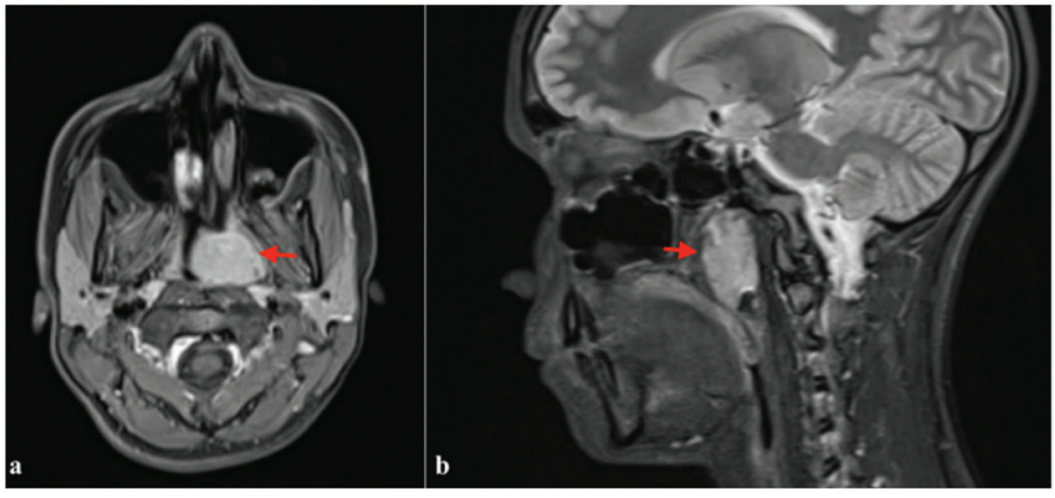


Figure 1. Corrected MRI scan reveals a 3×2.5×2 cm lobulated, expansile, nasopharyngeal mass which obliterates the nasopharynx and extends into the left Rosenmüller fossa

MRI: Magnetic resonance imaging

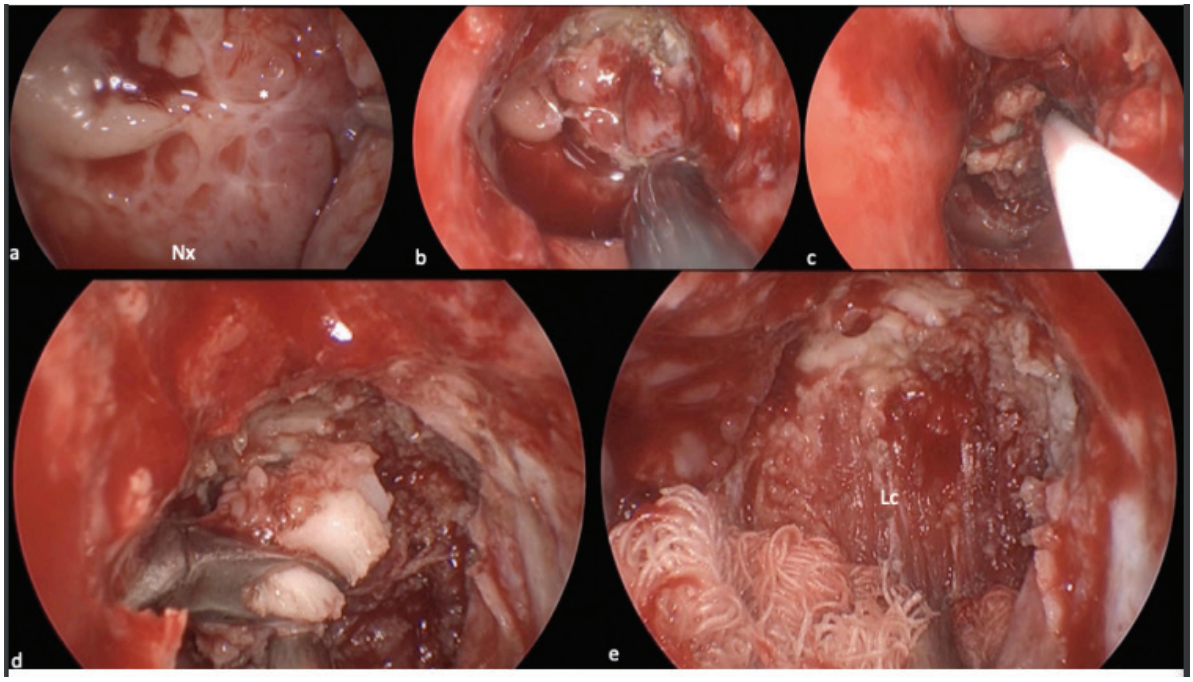


Figure 2. (a-c) Endoscopic views of the nasopharynx from the left nasal cavity (Nx: nasopharynx, *: tumor) **d)** En-bloc removal of the tumor **e)** View of the nasopharynx following resection

Lc: Longus capitis muscle

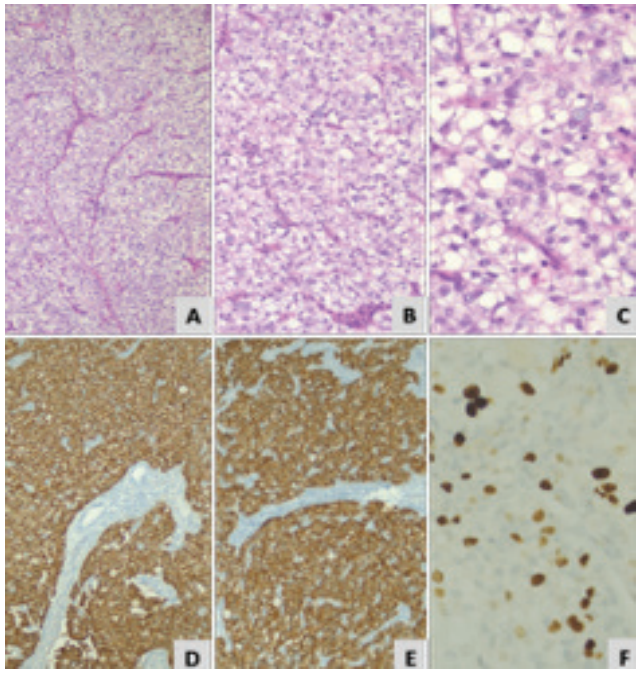


Figure 3. Biopsy shows submucosal infiltration by neoplastic epithelial cells with clear cytoplasm (HE, x100) **(A)**, the nuclei of neoplastic cells round-oval nuclei, inconspicuous nucleoli, and some pleomorphism (HE, x200; x400) **(B, C)**, immunohistochemically, epithelial cells express cytokeratin (AE1/AE3) (IHC, x100) **(D)**, EMA (IHC, x100) **(E)**, Ki-67 (IHC, x400) **(F)**

IHC: Immunohistochemistry, EMA: Epithelial membrane antigen

margin was clear along longus capitis and longus colli muscles. An endoscopic partial nasopharyngectomy was performed using the transnasal route (Figure 2).

The resection of the tumor demonstrated the same histological features as the biopsy. Immunohistochemistry showed that neoplastic cells with clear cytoplasm expression of cytokeratin (AE1/AE3) and EMA, but no expression of p63, alpha-smooth muscle actin, S100, PAX8, TFE-3, DOG1, or SOX-10. The Ki-67 proliferation index was approximately 15% in the neoplastic epithelial cells. Chromogenic in situ hybridization (CISH) for Epstein-Barr virus-encoded small RNA was negative. Fluorescence in situ hybridization (FISH) revealed *EWSR-1* gene rearrangement in the neoplastic cells. Given the morphology, immunophenotype, CISH, and FISH, the exact diagnosis was clear cell carcinoma (Figure 3). Since the patient had no evidence for the involvement of the renal tissue, besides immunohistochemically, and with TFE-3 being negative in the tumor, renal cell carcinoma was excluded.

After discussing adjuvant treatment at the tumor board, the patient underwent an intensity-modulated radiation therapy of 66 Gy targeting the nasopharynx. There was no recurrent or residual disease after 4 years of follow-up.

Table I. Cases of nasopharyngeal HCCC reported in the literature

Study	Age/sex	Primary tumor	Metastasis	Surgery	Radiotherapy/ dosage	Outcome
Cheng et al. (11) 2008	63/F	Right side of the nasopharynx with extension to the left choana	No	Endoscopic resection of the nasopharyngeal tumor	Performed/dosing unspecified	12 months tumor free
Dosemane et al. (12) 2015	22/F	Arising from the roof of the nasopharynx	No	Endoscopic wide excision	Performed/60 Gy	3 years tumor free
Goyal and Tanveer (13) 2009	20/M	Arising from the nasopharynx and extending into the left nasal cavity and orbit	No	Subtotal maxillectomy with left orbital exenteration and neck dissection	Performed/60 Gy	6 months tumor free
Nakashima et al. (14) 2015	27/F	Right side of the nasopharynx obstructing the eustachian tube	No	Wide resection, with 1 cm margin	No	2 years tumor free
Nakano et al. (15) 2014	27/F	Nasopharynx	No	Surgical resection	No	18 months tumor free
Fukuda et al. (16) 2015	63/F	Roof of the nasopharynx	No	Surgical excision	No	1 year tumor free
Shah et al. (6) 2013	Unspecified	Nasopharynx	Unspecified	Unspecified	Unspecified	Unspecified
Tang et al. (9) 1995	51/F	Nasopharynx	Unspecified	Transpalatal excision	Performed after second recurrence, 60 Gy	Multiple recurrences over 11 year period
Ceballos Sáenz et al. (8) 2014	38/M	Mass obliterating the lumen of the nasopharynx and extending into the left nasal cavity.	Local lymph node metastasis, no distant metastasis	Surgical excision, with residual disease	Radiotherapy and chemotherapy performed, unspecified	Not known
Malfitano et al. (4) 2019	48/M	Right side of the nasopharynx	No	Endoscopic resection of the mass and right-sided neck dissection	Performed/66 Gy	9 weeks tumor free
Wang and Fu (10) 2010	57/M	Left side of nasopharynx	No	Biopsy	Neoadjuvant chemotherapy and radiotherapy/dose unspecified	2 months tumor free
Chapman et al. (17) 2018	62/M	Nasopharynx	No	Excisional biopsy	Unspecified	5 months tumor free
Antonescu et al. (5) 2011	77/F	Nasopharynx	No	Unspecified	Performed/dosing unspecified	Unspecified
Bilodeau et al. (18) 2013 reported 3 cases	Unspecified	Nasopharynx	Unspecified	Unspecified	Unspecified	Unspecified
Hara et al. (19) 2018	18/F	Nasopharynx	No	En bloc surgical resection	No	12 months tumor free

Table I. Cases of nasopharyngeal HCCC reported in the literature

Study	Age/sex	Primary tumor	Metastasis	Surgery	Radiotherapy/ dosage	Outcome
Albergotti et al. (2) 2016 reported 2 cases	Unspecified	Nasopharynx	Unspecified	Unspecified	Unspecified	Unspecified
Zhao et al. (20) 2018	62/M	Nasopharynx	No	Unspecified	Unspecified	8 months tumor free
Arifi et al. (21) 2022	63/M	Nasopharynx	No	Biopsy	Chemotherapy and radiotherapy/70 Gy	12 months tumor free
Chang and Wu (22) 2024	44/M	Nasopharynx	No	Endoscopic wide excision	Chemotherapy and radiotherapy/70 Gy	12 months tumor free
Sun et al. (23) 2024 reported 2 cases	61/F 72/F	Nasopharynx	1) Local LN 2) No	Surgical excision	Chemotherapy and radiotherapy	1) 2.5 years 2) 8 months tumor free
Zhai et al. (24) 2023 reported 26 cases	30-82 years old F/M: 16/10	Nasopharynx	5 patient lymph node metastasis	Surgery: 20 patients	only RT (3 pt) S+RT (5 pt) S+ Chemo (1 pt)	5 patients died of disease
Our patient	14/F	Nasopharynx	No	Partial nasopharyngectomy	RT, 66 Gy	48 months tumor free

HCCC: Hyalinizing clear cell carcinoma, F: Female, M: Male, RT: Radiotherapy, LN: Lymph node, Gy: Gray

Discussion

HCCCs are rare low-grade malignant tumors, and they have an indolent course. To date, 50 cases of NHCCC have been reported in the literature (Table I) (4-24). Due to the rarity of this tumor, most of these reports are clinical case reports. As of 2023, only 21 cases had been reported in the literature. However, in October 2023, Zhai et al. (24) published the largest case series to date, reporting on 26 cases from a single institution. Of these 50 cases, only 43 had detailed information on clinical presentation, treatment, and follow-up. The mean age of the reported 43 patients was 52 years (18-82 years), and twenty-six (60%) were female. To our knowledge, our patient is the youngest patient reported in the literature to date.

Most of the time, HCCCs have an excellent prognosis (4). Local or distant metastases at presentation are uncommon in HCCC. Solar et al. (7) reviewed 52 cases of HCCC independent from localization, reported local lymph node metastasis at 23%, and recommended careful evaluation of the neck and the removal of regional lymphatics. There were no cases of NHCCC presenting with distant metastases in the literature - only seven patients from 43 cases (16%) presented with local cervical lymph node involvement (8,23,24).

There is currently no consensus on the standard treatment. The recommended treatment for HCCC is a wide surgical resection, followed by partial or modified neck dissection in the presence of cervical lymph node metastases (4,8). The effects of chemotherapy and irradiation after surgery are controversial because of the rarity of HCCC.

In the 17 single case reports, four patients were treated with complete surgical excision, and six were treated with surgery and postoperative adjuvant radiotherapy. Of these six patients, five had an excellent prognosis with no evidence of mortality. Only Tang et al. (9) reported a patient who experienced multiple recurrences; However, this case had an incomplete initial surgical excision. Of the 17 reported cases, six presented with extensive disease, and two had local lymph node metastasis (8,10,21-23). These six cases were treated with chemotherapy, surgery, and radiotherapy.

We evaluated the study by Zhai et al. (24) separately from the others because it is the largest case series in the literature, consisting of 26 cases reported retrospectively from a single center. Of the 26 patients included in their

study, the treatment details of 23 patients were available. Of these 23 patients, 14 had surgery alone, 5 had combined surgery and radiotherapy, 3 had only radiotherapy, and one was treated with chemotherapy and surgery due to advanced disease. In this cohort, tumor recurrence and death occurred in 2 of the 14 patients who underwent surgery alone. Tumor recurrence was detected in 3 of the 5 patients treated with surgery and radiotherapy, but all survived. Three patients who received only radiotherapy died due to progressive disease.

According to these results, complete surgical resection is the mainstay of treatment, and the role of radiotherapy remains uncertain. Case reports both with and without adjuvant radiotherapy are limited. The average follow-up for the single case reports was one year (9 weeks-3 years), excluding one case reported by Tang et al. (9) (with multiple recurrences over 11 years). These follow-up times are too short to assess the role of radiotherapy.

When compared with the literature, Zhai et al. (24) reported a high recurrence rate (23%) (6/26 patients). However, their study has longer follow-up periods (6-192 months) compared to the other single-case reports.

In the present case, we employed endoscopic partial nasopharyngectomy and adjuvant radiotherapy. An adequate safety margin could not be obtained due to the anatomical complexity of the nasopharynx, and the long-term risk of recurrence remains unknown. Albergotti et al. (2) reviewed patients with head and neck clear cell carcinomas treated by surgical resection without documented positive margins or evidence of metastasis at resection, reporting a 20.4% risk of recurrence. There was one case of recurrent NHCCC among the 17 single case reports in the literature, and no patients died from disease progression. However, as mentioned earlier, there are limited cases of NHCCC, and the follow-up periods in these reports are too short. When reviewing the study by Zhai et al. (24) it is evident that the risk of seeing relapse and/or mortality becomes higher with longer-term follow-ups. As a result, long-term follow-ups of these patients are necessary.

The case presented here highlights the importance of a detailed evaluation for a definitive diagnosis. In the treatment of NHCCC, wide local excision is recommended. Despite ongoing controversy regarding the role of radiation in its treatment, adjuvant radiotherapy should be recommended when total surgical removal of the primary tumor is not achieved or for clinically aggressive tumors. Since the reported cases of NHCCC are rare, more cases are needed in order to discuss the role of postoperative radiotherapy, and long-term follow-ups of these patients are essential.

Ethics

Informed Consent: The written informed consent form was taken from the patient and family to publish the case.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.A., Ş.Ö.G., G.T., D.D., S.K., M.K., Concept: E.A., Ş.Ö.G., Design: E.A., Data Collection or Processing: E.A., Ş.Ö.G., Analysis or Interpretation: E.A., Literature Search: E.A., Ş.Ö.G., S.K., M.K., Writing: E.A., Ş.Ö.G., G.T., D.D., S.K., M.K.

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

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

References

1. Milchgrub S, Gnepp DR, Vuitch F, Delgado R, Albores-Saavedra J. Hyalinizing clear cell carcinoma of salivary gland. Am J Surg Pathol. 1994; 18:74-82.
2. Albergotti WG, Bilodeau EA, Byrd JK, et al. Hyalinizing clear cell carcinoma of the head and neck: case series and update. Head Neck. 2016; 38:426-33.
3. Weinreb I. Hyalinizing clear cell carcinoma of salivary gland: a review and update. Head Neck Pathol. 2013; 7(Suppl 1):20-9.
4. Malfitano MJ, Norris MN, Stepp WH, et al. Nasopharyngeal hyalinizing clear cell carcinoma: a case report and review of the literature. Allergy Rhinol (Providence). 2019; 10:1-7
5. Antonescu CR, Katabi N, Zhang L, et al. EWSR1-ATF1 fusion is a novel and consistent finding in hyalinizing clear-cell carcinoma of salivary gland. Genes Chromosomes Cancer. 2011; 50:559-70.
6. Shah AA, LeGallo RD, van Zante A, et al. EWSR1 genetic rearrangements in salivary gland tumors: a specific and very common feature of hyalinizing clear cell carcinoma. Am J Surg Pathol. 2013; 37:571-8.
7. Solar AA, Schmidt BL, Jordan RC. Hyalinizing clear cell carcinoma: case series and comprehensive review of the literature. Cancer. 2009; 115:75-83.
8. Ceballos Sáenz C, Argyris PP, Manivel JC, Urias Barreras CM, Koutlas IG. Nasopharyngeal hyalinizing clear cell carcinoma: report of the histopathlogic features of a case showing EWSR1 rearrangements by FISH and literature review. Int J Surg Pathol. 2014; 22:667-72.
9. Tang SK, Wan SK, Chan JK. Hyalinizing clear cell carcinoma of salivary gland: report of a case with multiple recurrences over 12 years. Am J Surg Pathol. 1995; 19:240-1.
10. Wang F, Fu Z. Primary clear cell carcinoma of the nasopharynx: a case report. Chin Ger J Clin Oncol. 2010; 9:493-94.

11. Cheng LH, Lin YS, Lee JC. Primary clear cell carcinoma of the nasopharynx. Otolaryngol Head Neck Surg. 2008; 139:592-93.

12. Dosemane D, Lobo FD, Sreedharan SS. Primary clear cell carcinoma of the nasopharynx. J Cancer Res Ther. 2015; 11:928-30.

13. Goyal R, Tanveer N. Primary clear cell carcinoma of nasopharynx-a rare entity. Indian J Sure Oncol. 2020; 11:134-37.

14. Nakashima T, Yasumatsu R, Yamauchi M, et al. Hyalinizing clear cell carcinoma of the nasopharynx oper- ated by trans-oral and trans-palatal approach. J Laryngol Otol. 2015; 129 Suppl 2:95-7.15.

15. Nakano T, Yamamoto H, Nishijima T, et al. Hyalinizing clear cell carcinoma with EWSR1-ATF1 fusion gene: report of three cases with molecular analyses. Virchows Arch. 2015; 466:37-43.

16. Fukuda A, Tagami Y, Takasawa A, et al. Nasopharyngeal hyalinizing clear cell carcinoma with EWSR1 rearrange- ments diagnosed by fluorescence in situ hybridization. Auris Nasus Larynx. 2015; 42:412-15.

17. Chapman E, Skalova A, Ptakova N, et al. Molecular profiling of hyalinizing clear cell carci-nomas revealed a subset of tumors harboring a novel EWSR1-CREM fusion. Am J Surg Pathol. 2018; 42:1182-89.18.

18. Bilodeau EA, Weinreb I, Antonescu CR, et al. Clear cell odontogenic carcinomas show EWSR1 rearrangements: a novel finding and a biological link to salivary clear cell carcinomas. Am J Surg Pathol. 2013; 37:1001-5.

19. Hara M, Otsuki N, Yanagisawa S, et al. A case of nasopharyngeal clear cell carcinoma diagnosed by molecular analysis. Acta Oto-Laryngologica Case Reports. 2018; 3:34-8

20. Zhao YN, Wang X, Liang FH, et al. Hyalinizing clear cell carcinoma of salivary glands: A retrospective study focused on uncommon morphology, immunohistochemistry, and detection of gene fusion using fluorescence in situ hybridization. Pathol Res Pract. 2018; 214:380-84.

21. Arifi S, Hammas N, Ait Erraisse M. Clear cell carcinoma of minor salivary glands: the nasopharynx, an uncommon site of origin. Cureus. 2022; 14:e25033.

22. Chang YW, Wu HM. Hyalinizing clear cell carcinoma in the nasopharynx: a case report and literature review. Medicine (Baltimore). 2024; 103:e39163.

23. Sun H, Yuan J, Cheng Q, et al. Case report: Successful management of primary hyalinizing clear cell carcinoma in nasopharynx: a report of 2 cases and system analysis. Front Oncol. 2024; 14:1384913.

24. Zhai C, Yuan C, Sun J, et al. Clinical and histopathologic analyses of nasopharyngeal hyalinizing clear cell carcinoma: a series of 26 cases with molecular confirmation. Am J Surg Pathol. 2023; 47:1168-75.

J Pediatr Res 2025;12(1):45-47
DOI: 10.4274/jpr.galenos.2024.20270

Case Report

Pharmacological Treatment Leading to Complete Resolution in Kasabach-Merritt Phenomenon-Case Report

Jenith Vijayalakshmi, Manas Ranjan Behera, Nirmal Mohakud, Swarnalata Das, Bharati Agarwal, Palash Das

Kalinga Institute of Medical Sciences KIIT Deemed to be University, Department of Pediatrics, Bhubaneshwar, India

ABSTRACT

Kasabach-Merritt syndrome is a rare vascular tumor usually seen in infancy. It is locally aggressive and infiltrates the skin, subcutaneous tissue, and muscles. It is characterized by coagulopathy with thrombocytopenia, microangiopathic hemolytic anemia, and raised d-dimer levels. In small infants, this can cause life-threatening bleeding and can be fatal. We report on a two-month-old female child who presented to us with a rapidly enlarging purplish swelling on the right arm. It was also associated with petechial spots all over the body. A clinical diagnosis of hemangioma with Kasabach-Merritt phenomenon was made and was further confirmed by hematological investigations which showed anemia, and thrombocytopenia with hypofibrinogenemia. Imaging of the limb confirmed the diagnosis. After taking parental consent, the baby was started on injections of vincristine weekly with oral prednisolone. There was a significant reduction in the tumor's size and improved blood parameters. After 6 weeks of steroid therapy, the medication was tapered and the child was changed to single agent sirolimus with monitoring of serum levels. There was a remarkable response to sirolimus with complete resolution of the tumour and Kasabach-Merritt phenomenon. Kasabach-Merritt syndrome can be a life-threatening complication in infants. Appropriate pharmacological therapy with stringent monitoring can bring complete resolution.

Keywords: Kasabach-Merritt phenomenon (KMP), kaposiform hemangioendothelioma (KHE), thrombocytopenia, coagulopathy, sirolimus

Introduction

Kasabach-Merritt phenomenon (KMP) is a life-threatening event with the triad of anemia, thrombocytopenia and, coagulopathy in association with vascular tumors (1). Most cases present in infancy and the mortality rate varies from 10-37% in various studies (2). They usually present with a rapidly enlarging firm solitary purpuric, a soft to a firm cutaneous lesion, anemia, thrombocytopenia, and varying degrees of coagulopathy. Complete surgical resection offers the best form of cure; however, in many cases due to extensivity and coagulopathy, surgery is not possible. In such a circumstance, pharmacological therapy is the best option.

Case Report

We report on a 2-month-old female infant who presented with a history of erythematous lesion over the right arm from day 10 of life. It started gradually, initially

Corresponding Author
Assoc. Prof. Palash Das, Kalinga Institute of Medical Sciences KIIT Deemed to be University, Department of Pediatrics, Bhubaneshwar, India
E-mail: palash.das@kims.ac.in **ORCID:** orcid.org/0000-0002-4205-1194
Received: 29.05.2024 **Accepted:** 19.11.2024 **Epub:** 18.02.2025 **Publication Date:** 17.03.2025

Cite this article as: Vijayalakshmi J, Behera RB, Mohakud N, Das S, Agarwal B, Das P. Pharmacological treatment leading to complete resolution in Kasabach-Merritt phenomenon-case report. J Pediatr Res. 2025;12(1):45-47

small in size near the posteromedial aspect of the right arm, and progressed rapidly to reach the present size. It was associated with an edematous change of the right upper limb. She was a first-order child with a birth weight of 3 kilogram (kg) and had an uneventful perinatal period.

At admission, the child was conscious, alert, and playful with a weight of 4.6 kg and had stable vitals, with a normal general and systemic examination. Local examination of the right arm showed a tumor of size 8.5 centimeter (cm)×14 cm, warm, non-tender, firm in consistency, associated with edema of the right upper limb with distal pulses clearly palpable. The skin above the lesion was reddish-violaceous with small petechiae without signs of compromise in the blood supply (Figure 1).

Initial investigations including a complete blood count (CBC) revealed a total leukocyte count of 6,700 cells/cu.mm, hemoglobin (Hb) of 6.9 g/dL, total platelet count (TPC) of 4.000/cu.mm (thrombocytopenia) with peripheral smear showing microcytic hypochromic anemia with thrombocytopenia, with prothrombin time: 11.6 seconds (sec), activated partial thromboplastin time: 25.8 secs, internationalized normal ratio: 1.05 (normal), D-dimer: 13.23 ug/mL (high), and serum fibrinogen: <40 mg/dL. (low). Liver and renal functions were normal. Ultrasound examination of the abdomen and pelvis was normal and there was no evidence of hemangiomas elsewhere.

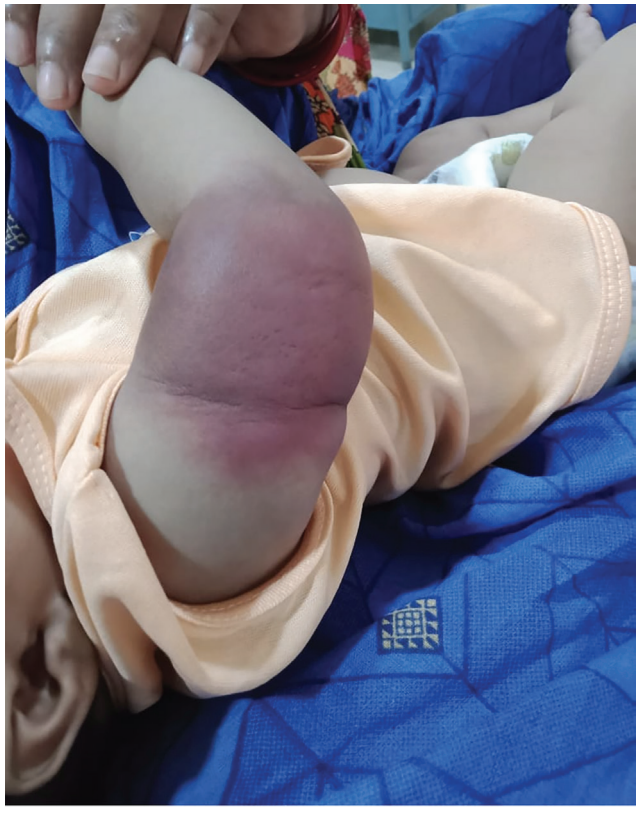


Figure 1. Vascular purplish tumour on right arm at presentation

A Doppler study of the right upper limb showed thickened heterogenous soft tissue over the right arm, and proximal forearm with prominent vessels showing arterial and venous flow with dilated vessels in the subcutaneous plane and intramuscular plane with features suggestive of hemangioma/hemangioendothelioma.

Magnetic resonance imaging of the affected limb revealed ill-defined T2 weighted short tau inversion recovery hyperintense soft tissue thickening involving subdermal fat planes in the arm and forearm.

Computed tomography angiogram of the right upper limb showed ill-defined to dense soft tissue thickening, mild homogenous enhancement of skin and subcutaneous plane of the right arm and forearm region on a post-contrast study and retention of contrast in delayed phases with likely hemangioma.

The baby had worsening anemia and received a packed red blood cell transfusion at 10 mL/kg owing to the anemia and thrombocytopenia with hypofibrinogenemia in the presence of a rapidly increasing vascular tumor, the child was diagnosed as a case of KMP. After parental counseling, the child was started on a standard regimen of oral prednisolone at 2 mg/kg/day and IV vincristine 0.05 mg/kg weekly.

After the second dose of vincristine, her CBC parameters improved (Hb: 8.7 gr/dL and TPC: 16,000/cu.mm). No platelet transfusion was given as platelet transfusions have been associated with tumoral bleeding.

On serial monitoring, the edema and the lesion gradually decreased in size, and at the time of discharge after 2 weeks of therapy, the size had reduced to 7 cm×13 cm. The parents were advised to follow up at our outpatient department regularly and were given vincristine and steroids for 4 weeks.

One month after follow-up, because of the persistent considerable size of the tumor, the child was started on sirolimus at 0.8 mg/m^2/dose twice daily along with a tapering dose of the steroids.

The steroids were stopped after 6 weeks and the child continued with sirolimus with regular CBC monitoring. Continuing with sirolimus, the size of the tumor was further reduced and there was no recurrence of thrombocytopenia or anemia. After 4 weeks of continuous sirolimus therapy, it was discontinued and the tumor had completely resolved by then. On follow-up, three months post-stoppage of the

therapy, there was no increase in the size of the tumor or any recurrence of KMP (Figure 2).

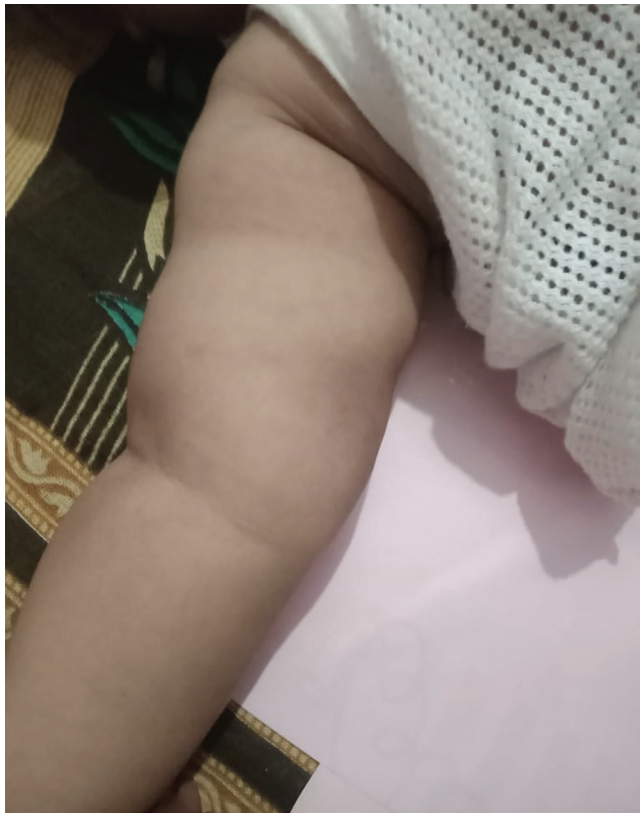


Figure 2. Complete resolution after sirolimus based therapy

Discussion

KMP is a potentially life-threatening disorder and pharmacologic treatment is now considered the first line of management (3). While the North American group recommends daily steroids plus weekly vincristine, European centers recommend a combination of steroids with ticlopidine and sirolimus. The duration of treatment is not well defined with most of the groups recommending vincristine and steroids until clinical response occurs, with sirolimus being recommended for at least 1 year. However, as seen in our case, remission was induced with a much shorter duration of treatment and this needs to be explored further. Sirolimus as a stand-alone treatment can also bring remission and is relatively safe, although serum drug levels have to be measured routinely. However, recent trials have suggested Sirolimus along with steroids to be the best first-line treatment (4).

KMP is a sign of an aggressive vascular tumor and has the propensity to cause severe bleeding which might be life-threatening. While steroids have been considered the first line of therapy, they carry a risk of infections, growth stunting, and developmental delay. Sirolimus is an inhibitor of mammalian target for rapamycin (5). Various study groups have shown sirolimus to be effective even in cases where high-dose corticosteroids have failed to get a response. Sirolimus has been shown to have a pooled odds ratio of 0.91 and minimal side effects (6). We conclude that sirolimus as a stand-alone treatment or with vincristine or steroids is a promising therapy and should be explored more in KMP.

Ethics

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.R.B., N.K.M., S.D., P.D., Concept: J.T., B.A., P.D., Design: M.R.B., N.K.M., S.D., B.A., P.D., Data Collection or Processing: J.T., B.A., Analysis or Interpretation: M.R.B., N.K.M., S.D., P.D., Literature Search: M.R.B., P.D., Writing: J.T., M.R.B., B.A., P.D.

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

Financial Disclosure: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

References

1. Mahajan P, Margolin J, Iacobas I. Kasabach-Merritt phenomenon: Classic presentation and management options. Clin Med Insights Blood Disord. 2017; 16:10:1179545X17699849.
2. Radović SV, Kolinović M, Ljubić D. Propranolol in the preoperative treatment of Kasabach-Merritt syndrome: A case report. J Med Case Rep. 2017; 27:308.
3. Ji Y, Chen S, Zhou J, et al. Sirolimus plus prednisolone vs sirolimus monotherapy for kaposiform hemangioendothelioma: A randomized clinical trial. Blood. 2022; 17:1619-30.
4. Harbers VEM, van der Salm N, Pegge SAH, et al. Effective low-dose sirolimus regimen for kaposiform haemangioendothelioma with Kasabach-Merritt phenomenon in young infants. Br J Clin Pharmacol. 2022; 88:2769-81.
5. O'Rafferty C, O'Regan GM, Irvine AD, et al. Recent advances in the pathobiology and management of Kasabach-Merritt phenomenon. Br J Haematol. 2015; 17:38-51.
6. Kai L, Wang Z, Yao W, et al. Sirolimus, a promising treatment for refractory Kaposiform hemangioendothelioma. J Cancer Res Clin Oncol. 2014; 140:471-6.

J Pediatr Res 2025;12(1):48-51
DOI: 10.4274/jpr.galenos.2025.90836

Case Report

Chest Wall Mass in a Healthy Infant: Considering Self-Limiting Sternal Tumors of Childhood (SELSTOC)

Francisco José Sanz-Santaeufemia[1], Berta Gato Moro[1], Isabel Rozas Gómez[2], María Esther García Talavera[3], María Lourdes Calleja Gero[1], Azucena Retuerta Oliva[1]

[1]Niño Jesús University Children's Hospital, Clinic of Pediatrics, Madrid, Spain
[2]Niño Jesús University Children's Hospital, Clinic of Radiology, Madrid, Spain
[3]Health Center Los Castillos, Primary Health Care, Alcorcon, Spain

ABSTRACT

Chest wall tumors, especially those with rapid growth are one of the main reasons for consultation due to their risk of developing into a threatening situation. Differential diagnosis must be made regarding osteoarticular infections, inflammatory or connective tissue diseases and bone, vascular or muscle neoplasm in this region. Self-limiting sternal tumors affect children below two years of age, having a benign origin, typical ultrasound image and complete clinical recovery with conservative management within 1-3 months. We present a new case with this condition and make a brief review of recent publications in the literature.

Keywords: Tumor, sternal, children

Introduction

Sternal masses are not frequent in children and include a variety of benign bone cyst, fibrous dysplasia, osteoblastoma, osteochondroma, and venolymphatic malformations among others, or malign (Ewing's sarcoma, Langerhans histiocytosis, chondrosarcoma or soft tissues sarcomas) tumors as well infectious or inflammatory diseases such as arthritis, recurrent chronic multifocal osteomyelitis or anatomical variants of the ribcage. We present a case in a toddler aged 8 months with a non-painful, palpable and inflamed sternal lesion who was finally diagnosed with self-limiting sternal tumors of childhood (SELSTOC) after repeated ultrasound studies and progressive involution of the mass after careful and patient follow-up.

Case Report

An 8.5-month-old girl who came to the emergency room showed a 2.5x2.5 cm supraxiphoid mass of solid consistency along with mild skin erythema around it (Figure 1). She had no fever and her parents explained that the erythema had grown quickly over the previous 5 days. A blood test was ordered and no alterations in hemogram, but elevated pro-inflammatory biomarkers were observed; the erythrocyte sedimentation rate was 56 mm/h and C

Corresponding Author
Asst. Prof. Francisco José Sanz-Santaeufemia, Niño Jesús University Children's Hospital, Clinic of Pediatrics, Madrid, Spain
E-mail: sanzsantaeufemiafj@gmail.com **ORCID:** orcid.org/0000-0002-1592-3575
Received: 16.10.2024 **Accepted:** 23.01.2025 **Epub:** 25.02.2025 **Publication Date:** 17.03.2025

Cite this article as: Sanz-Santaeufemia FJ, Gato Moro B, Rozas Gómez I, García Talavera ME, Calleja Gero ML, Retuerta Oliva A. Chest wall mass in a healthy infant: Considering self-limiting sternal tumors of childhood (SELSTOC). J Pediatr Res. 2025;12(1):48-51

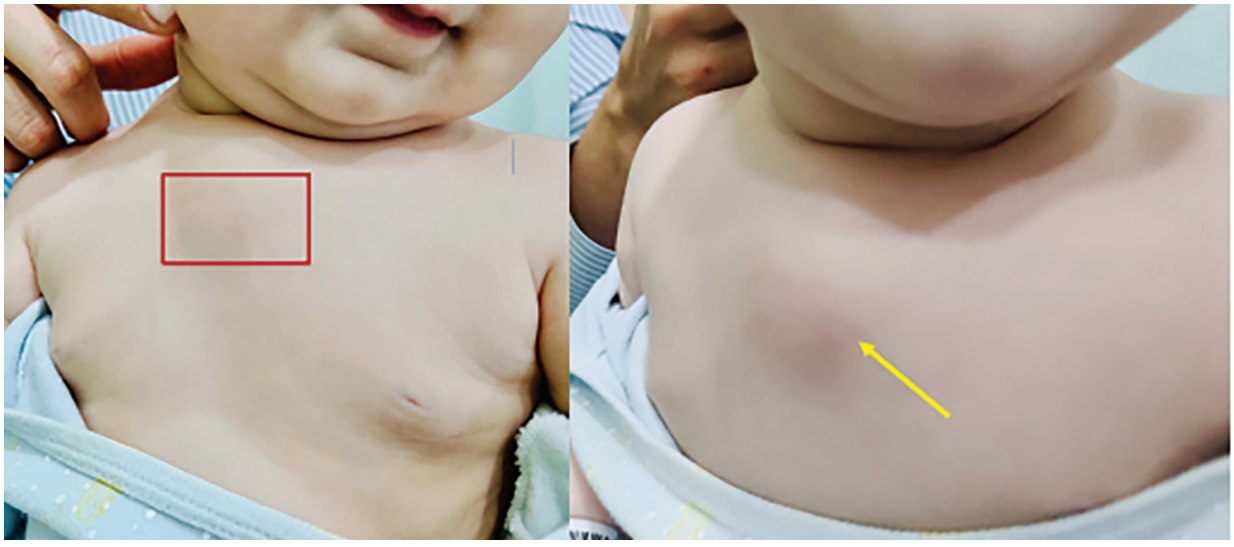


Figure 1. Sternal mass over 2.5 cm of diameter (square) with mild erythema around it (arrow)

Reactive protein was 3 mg/dL. In a chest X-ray, no unusual findings were seen.

The thoracic ultrasonography showed a dumbbell-shaped hypoechoic non-vascularized image with the following measurements: 10x4 mm on the left side and 8x4 mm on the right (Figure 2), which had no connection to the skin and did not affect the underlying bone and muscle. Despite being apyretic, the infant received endovenous cefotaxime as the initial therapy for osteoarticular sternal infection.

The radiologist warned that the image was highly suggestive of SELSTOC, recommending a new ultrasound study after a further 48 hours. In this second study, a slight decrease in the size of the lesion (8x3.3 mm and 7x3 mm for left and right sides respectively) was seen, and so the antibiotic therapy was removed given the low likelihood of osteomyelitis and a new appointment in 3 weeks at the outpatient level was proposed in order to conduct another ultrasonography. At this follow-up ultrasonography, the practical disappearance of the tumor previously seen in ecography was observed (Figure 3) and the chest wall tumor was mildly palpable and nearly unappreciable, confirming the suspected diagnosis from one month earlier.

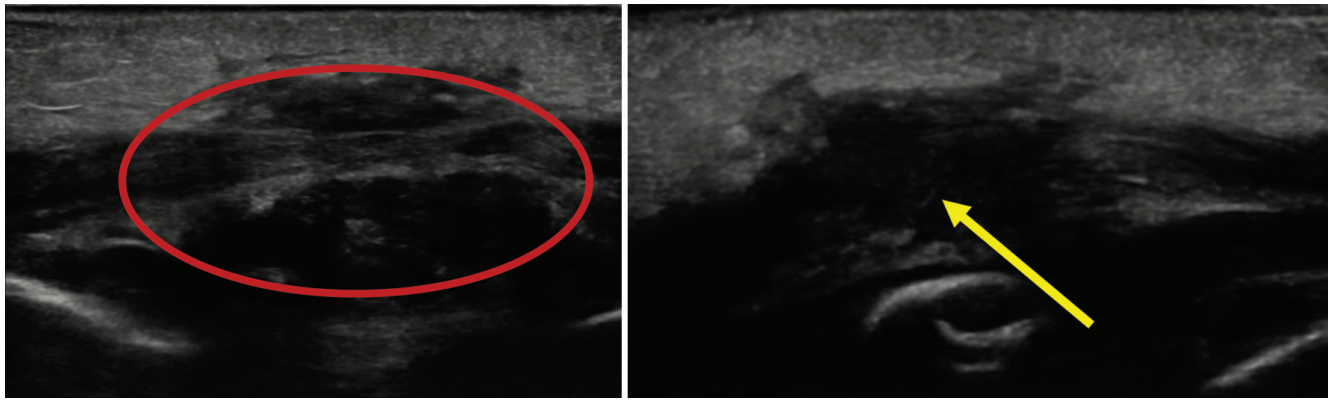


Figure 2. Dumbbell-shaped hypo-echoic and avascular lesion (arrow) with integrity of bone and muscle structures (circle)

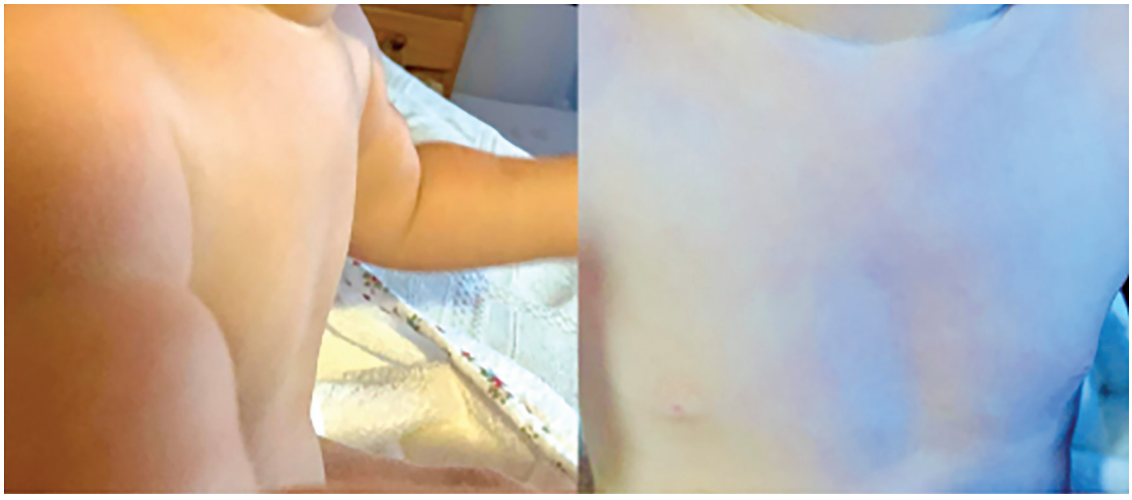


Figure 3. Picture taken 1 month later, showing complete clinical recovery (arrow)

Discussion

SELSTOC is a strange condition characterized by aseptic inflammation behaving as a cold abscess whose clinical symptoms are: Rapid growth, age below two years, no other clinical signs, unremarkable past history, typical sternal ultrasound (double lobed image dumbbell-shaped, hypoechoic and poorly vascularized) as well as complete clinical resolution within 1-3 months. First described by te Winkel et al. (1) in 2010 who collected 14 cases, where 6 of them required biopsy, and pathological studies showing unspecific inflammation despite being treated with antibiotics. Echography was carried out in 13 cases and a computed tomography (CT) was performed on 4 patients.

In recent years, there have been many reports on this issue (see Table I). For instance, Alonso Sánchez et al. (2) published 5 cases in 2020 with their classical characteristics being either clinical or radiological, with 3 children receiving antibiotics and one of them demonstrating 1 *Staphylococcal* infection after incision and drainage of the lesion, although the more likely reason could be an incidental situation on primary SELSTOC on the basis of typical ultrasound.

Table I. Patient characteristics diagnostic and therapeutic information

References	No. cases	Definition	Age median (range)	Biopsy/Joint puncture	Radiology data	Antibiotics (No.)	Resolution Median (range)
te Winkel et al. (1)	14	SELSTOC	16 mo (7-50)	5 Bi/6 incision	13 US. 4 CT	6/14	6 mo (1-6)
Alonso Sánchez et al. (2)	5	SELSTOC	9 mo (3-18)	1 Bi/1 incision	5 US. 1 MRI	3/5	6 mo (1-12)
Nikolarakou et al (3)	3	Chondroesternal arthritis	8 mo (8-12)	0 Bi/2 incision	3 US. 1 CT	3/3	2 mo (2-2)
Ilivitzki et al. (4)	3	Sternal pseudotumor	7 mo (7-16)	1 Bi/1 incision	3 US. 1 MRI	3/3	6 mo (4-18)
Adri and Kreindel (5)	2	SELSTOC	17 mo (12-22)	0/0	2 US	0	1 mo (1-1)
Fuente-Lucas et al. (6)	1	SELSTOC	7 mo	1/1	US. MRI	0	3 mo
Moreira and Marchiori (7)	1	SELSTOC	9 mo	0	US. MRI	0	2 wk
Arnés Parra et al. (8)	1	SELSTOC	9 mo	0	US. MRI	0	3 mo
Sanz-Santaeufemia (present case)	1	SELSTOC	8 mo	0	US	0	3 wk

No.: Number, mo: Months, wk: Weeks, Bi: Biopsy, US: Ultrasonography, CT: Computed tomography, MRI: Magnetic resonance image, SELSTOC: Self-limiting sternal tumors of childhood

Other papers found in the literature over the previous ten years include Nikolarakou et al. (3) in 2014 who described 3 affected children treated with antibiotics with 2 cases undergoing drainage and a CT for one patient due to multiple doubts about the nature of the mass; finally diagnosing this illness as chondrosternal arthritis but recognizing the great similarity with SELSTOC. Ilivitzki et al. (4) treated 3 patients with antibiotics, performing magnetic resonance image (MRI) and needle aspiration in one of them. They named this condition sternal pseudotumour. Adri and Kreindel (5) in 2018 presented 2 cases with the same definition, radiological studies and therapy as ours. Likewise, isolated cases with similar symptoms and evolution have been reported over this decade, such as Fuente-Lucas et al. (6) in 2021 reporting on the involvement of costochondral cartilages requiring biopsy and MRI to rule out malignancy. Moreira and Marchiori (7) in 2020 wrote a case report very similar to Fuente-Lucas et al. (6), except that pathological studies were not performed and Arnés Parra et al. (8) in 2022 published one case with age, clinical symptoms and conservative therapy nearly identical to our case, only differentiated by MRI which was performed in order to confirm the diagnosis. In all publications, the clinical data, ultrasound appearance along with the spontaneous regression during their clinical course are extremely similar. In general, it is not mandatory to conduct invasive tests such as biopsy or special radiologic studies such as MRI or CT, although they occasionally help in differential diagnosis (9). The complete resolution of the tumor within 1 to 3 months is the usual evolution, without the need for pharmacological or surgical therapies. Treatment can be based on careful observation with or without anti-inflammatory drugs, repeated ultrasound studies and a patient attitude while avoiding absolutely unjustified diagnostic procedures or therapeutic decisions (7), so demonstrating an application of quaternary prevention.

Conclusion

Sternal tumors in infants below 2 years of age, even in toddlers younger than 12 months, with no alarm signs or fever are highly suggestive of SELSTOC. Once this possibility is established, there is no need to carry out ionizing radiological examinations or invasive procedures in order to confirm or discard the clinical suspicion as the tumor is self-involuting and it originates from an exacerbated immune response to an aseptic inflammatory process. Despite swelling or local signs consistent with infection, a "do not touch" approach must be taken and a "wait-and-see" follow-up will prove it was the correct option.

Ethics

Informed Consent: There are parental permissions for the use of images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.J.S., B.G.M., A.R.O., Concept: F.J.S., A.R.O., Design: F.J.S., A.R.O., Data Collection or Processing: F.J.S., B.G.M., M.E.G.T., A.R.O., Analysis or Interpretation: F.J.S., I.R.G., M.L.C.G., Literature Search: F.J.S., I.R.G., A.R.O., Writing: F.J.S., M.E.G.T., A.R.O.

Conflict of Interest: The authors declare that they have no conflict of interest in this paper as well.

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

References

1. te Winkel ML, Lequin MH, de Bruyn JR, et al. Self-limiting sternal tumors of childhood (SELSTOC). Pediatr Blood Cancer. 2010; 15:81-4.
2. Alonso Sánchez J, Gallego Herrero C, García Prieto J, et al. Self-limiting sternal tumors of childhood (SELSTOC): A diagnostic challenge. Radiologia (Engl Ed). 2021; 63:400-5.
3. Nikolarakou A, Dumitriu D, Docquier PL. Chondrosternal arthritis in infant: an unusual entity. Case Rep Orthop. 2014; 652539.
4. Ilivitzki A, Sweed Y, Beck N, et al. Sternal pseudotumor of childhood: don't touch the lesion. J Ultrasound Med. 2013; 32:2199-203.
5. Adri D, Kreindel T. Self limiting sternal tumors of childhood: Two case reports. Radiologia (Engl Ed). 2019; 61:167-70.
6. Fuente-Lucas G, Planells-Alduvin MC, Tallón-Guerola P, et al. Tumor esternal autolimitado en una lactante de 7 meses. An Pediatr (Barc) 2021; 95:57-9
7. Moreira BL, Marchiori E. Self-limiting sternal tumor of childhood: A "do not touch" lesion. J Pediatr. 2020; 221:260-61.
8. Arnés Parra ML, Vereas Martínez A, Merino Bonilla JA, et al. Tumor esternal autolimitado de la infancia (SELSTOC) con hallazgos atípicos en ecografía y manejo conservador. Rev Pediatr Aten Primaria. 2022; 24:391-5.
9. Yamane A, Yasui D, Ichikawa T. A case of self-limiting sternal tumor of childhood. Radiol Case Rep. 2020; 16:602-3

J Pediatr Res 2025;12(1):52-54
DOI: 10.4274/jpr.galenos.2025.48265

Letter to the Editor

An Alternative Option for Catheterization at End-stage Central Venous Access in Children with Intestinal Failure

Betül Aksoy[1], Maşallah Baran[2], Onur Işık[3], Yeliz Çağan Appak[2], Muhammet Akyüz[3], Sinem Kahveci[1], Selen Güler[1], Şenay Onbaşı Karabağ[1], İlker Mercan[3], Cem Tuğmen[4]

[1]University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Clinic of Pediatric Gastroenterology, Hepatology and Nutrition, İzmir, Türkiye
[2]İzmir Kâtip Çelebi University, İzmir Tepecik Education and Research Hospital, Clinic of Pediatric Gastroenterology, Hepatology and Nutrition, İzmir, Türkiye
[3]University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Clinic of Pediatric Cardiovascular Surgery, İzmir, Türkiye
[4]University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Clinic of Organ Transplantation and General Surgery, İzmir, Türkiye

Keywords: Intestinal failure, central venous catheter, end-stage central venous access, direct intra-atrial catheter

Introduction

Intestinal failure (IF) has been defined as "the reduction of functional gut mass below the minimal amount necessary for digestion and absorption adequate to satisfy the nutrient and fluid requirements for growth in children" (1). Children with IF are dependent on intravenous fluids and parenteral nutrition (2,3). A functional central venous catheter (CVC) is essential for their survival until intestinal adaptation occurs. End-stage central venous access is defined as a critical restriction in the patency of the superior vena cava (SVC) or the major vessels draining into it, with or without inferior vena cava (IVC) occlusion (2). It has been reported that direct intra-atrial catheters may be used in children with end-stage central venous access (2).

In this case report, we present two patients who were candidates for ITx with end-stage central venous access where direct intra-atrial catheter was inserted.

Case 1

A 9-month-old girl who was diagnosed with microvillus inclusion disease was referred to our centre for ITx. Thrombosis of the left and right subclavian veins, internal jugular veins, and femoral veins were observed via radiological imagings. A direct intra-atrial 5-French (Fr) implantable port catheter was inserted (Figure 1a). Heparin was administered via a line lock to 1/1000 with taurolidine to prevent catheter-related bloodstream infections (CRBSI). A cadaveric ITx was performed when the patient was 14 months old. A catheter infection related to Candida

Corresponding Author
Betül Aksoy, University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Clinic of Pediatric Gastroenterology, Hepatology and Nutrition, İzmir, Türkiye
E-mail: drbetulaksoy@gmail.com **ORCID:** orcid.org/0000-0002-7657-8007
Received: 19.01.2025 **Accepted:** 27.02.2025 **Epub:** 06.03.2025 **Publication Date:** 17.03.2025

Cite this article as: Aksoy B, Baran M, Işık O et al. An alternative option for catheterization at end-stage central venous access in children with intestinal failure. J Pediatr Res. J Pediatr Res. 2025;12(1):52-54

parapsilosis (C. parapsilosis) was observed during the fifth month in a direct intra-atrial catheter. Only the port catheter chamber was changed for revision purposes. The direct intra-atrial catheter was used for 11 months with only one CRBSI without the need for replacement until the patient died due to sepsis at 21 months of age.

Case 2

A 9-month-old boy with short bowel syndrome was referred to our centre. He had end-stage central venous access. A direct intra-atrial 4-Fr implantable port catheter was inserted. The distal tip of the catheter was observed as being outside of the atrium with inspiration due to the short line of the catheter on the ninth day (Figure 1b). The catheter was removed and a direct intra atrial 5-Fr implantable port catheter was inserted again (Figure 1c). The port of the catheter was changed because of recurrent catheter infections related to Staphylococcus spp. in the fifth month of the direct intra-atrial catheter. CRBSI with C. parapsilosis was observed. This direct intra-atrial catheter was replaced with a new one at the seventh month. The patient was monitored with an intra-atrial catheter for nine months until the time of writing.

Discussion

Technique, mechanical complications, the risk of thrombotic and infective complications, the duration of the anticipated central venous access and the physician's experience affect the choice of vein for CVC placement. Femoral insertion is associated with higher risks of catheter colonization and thrombotic complications (4). Therefore, a femoral CVC is not recommended, especially in children who are candidates for ITx. An alternative but more invasive access for CVC placement in children with IF who have end-stage central venous access is a direct right atrial insertion through a sternotomy. We preferred venous access which was either transhepatic or direct intra-atrial in our patients who had end-stage central venous access, and we opted for direct intra-atrial catheters. A direct intra-atrial implantable port catheter was inserted via midline sternotomy in our patients. The surgical procedure was the same in both patients: the thorax was entered through the fourth intercostal space with a right anterolateral mini-thoracotomy. The pericardium was incised from the anterior of the phrenic nerve. A bladder-mouth suture was placed in the right atrial appendix, and the catheter was inserted into the IVC through the incision made in this area. The catheter was thrust from the thorax to the subcutaneous tissues through the third intercostal space. The port chamber was inserted in the pocket which was opened at the level of the second intercostal space on the right side. Rodrigues et al. (2) reported four children who had a double-lumen CVC which went directly to the right atrium through a sternotomy before ITx. They also reported complications from a serous pleural effusion requiring drainage which developed within 24 hours in one patient. This line was inadvertently dislodged on the third day and at 15 months in two patients after receiving direct intra-atrial catheters via midline sternotomy (2). We observed that the distal tip of the catheter not in the atrium due to the short line of the catheter on the ninth day after insertion in our Case 2 patient.

Rodrigues et al. (2) reported that in one patient, a direct intra-atrial tunnelled CVC was removed and replaced by a subcutaneous port at 12 months; unfortunately, the patient died of bacterial endocarditis 6.5 years after transplantation. The other three transplant recipients who had a direct intra-atrial catheter all had their CVCs removed within three months of the transplant operation (2). They found that these catheters were adequate for the perioperative management of an uncomplicated transplantation (2). In one of our patients, a direct intra-atrial implantable port catheter was used in the perioperative and postoperative periods of ITx.

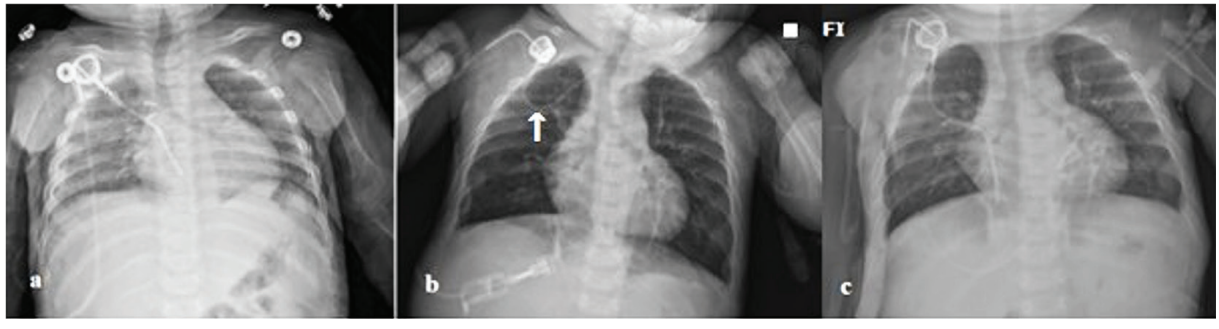


Figure 1. a) A direct intra-atrial catheter in Case 1. b) The distal tip of the catheter was not in the atrium in Case 2. c) The direct intra-atrial catheter was reinserted in Case 2

Taurolidine is effective in preventing CVC–related sepsis and should be used during long-term catheter use in children with IF (5). We used taurolidine with heparin as a line lock in order to prevent thrombosis and CRBSI in patients with direct intra-atrial implantable port catheters. CRBSIs were observed at 11 and 9 months in Cases 1 and 2, respectively. Changing the port of the catheter alone with a minimally invasive technique was effective for the treatment of CRBSI in our patients.

In conclusion, a direct intra-atrial implantable port catheter can be used for prolonged periods in children with IF who have end-stage central venous access. It is adequate for the management of the perioperative and postoperative periods of ITx. Changing the port of the catheter can be an efficient method for the treatment of CRBSI.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.I., M.A., İ.M., C.T., Concept: B.A., M.B., Design: B.A., M.B., Y.Ç.A., Data Collection or Processing: S.K., Analysis or Interpretation: Ş.O.K., Literature Search: S.G., Writing: B.A., M.B.

Conflict of Interest: One author of this article, Yeliz Çağan Appak, is a member of the Editorial Board of The Journal of Pediatric Research. However, she did not involved in any stage of the editorial decision of the manuscript. The other authors declared no conflict of interest.

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

References

1. Duggan CP, Jaksic T. Pediatric intestinal failure. N Engl J Med. 2017; 377:666-675.
2. Rodrigues AF, van Mourik ID, Sharif K, et al. Management of end-stage central venous access in children referred for possible small bowel transplantation. J Pediatr Gastroenterol Nutr. 2006; 42:427-433.
3. Van Ommen CH, Tabbers MM. Catheter-related thrombosis in children with intestinal failure and long-term parenteral nutrition: how to treat and to prevent? Thromb Res. 2010; 126:465-470.
4. Kolaček S, Puntis JWL, Hojsak I; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Venous access. Clin Nutr. 2018; 37:2379-2391.
5. Chu HP, Brind J, Tomar R, Hill S. Significant reduction in central venous catheter-related bloodstream infections in children on HPN after starting treatment with taurolidine line lock. J Pediatr Gastroenterol Nutr. 2012; 55:403e7.