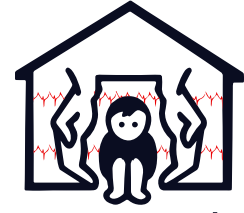


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Journal of Pediatric Emergency and Intensive Care Medicine



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# ÇOCUK ACİL ve YOĞUN BAKIM DERGİSİ

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# Nasogastric and Endotracheal Tubes as Risk Factors for Sinusitis in Critically Ill Children: A Retrospective Case-control Study

Kritik Hasta Çocuklarda Nazogastrik ve Endotrakeal Tüp Kullanımı ile Sinüzit Gelişimi Arasındaki İlişkinin İncelenmesi: Geriye Dönük Olgu-kontrol Çalışması

Özlem Sarıtaş Nakip<sup>1</sup>, Ekim Gümeler<sup>2</sup>, Selman Kesici<sup>1</sup>, Kıvanç Terzi<sup>1</sup>, Merve Erdem<sup>1</sup>, Benan Bayrakci<sup>1</sup>

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## Abstract

**Introduction:** Unknown fever in critically ill patients could be caused by occult sinusitis, which may also be related to healthcare interventions. The aim of this study was to uncover the correlation between a tube in the upper airways and children's susceptibility to sinusitis.

**Methods:** We retrieved data retrospectively and evaluated radiological images for the presence of nasogastric (NG) and endotracheal (ET) tubes, as well as any findings of sinusitis or nasopharyngeal (NF) secretions. We also recorded the intervals between the images.

**Results:** The study included 65 patients with a total of 162 images. The results showed a significant increase in the occurrence of sinusitis between the first (13/30, 43.3%) and second (20/30, 66.6%) images ( $p=0.039$ ). The cut-off time for the onset of sinusitis was found to be 2.5 days [area under the curve: 0.50, 95% confidence interval (CI): 0.355-0.646]. There was no significant difference in the occurrence of sinusitis or NF secretion formation between single or double tubes ( $p=0.389$ ). The presence of an NG or ET tube also did not show a significant relationship with sinusitis. However, the study found that NF secretions were present in 52% of images with an ET tube [ $p=0.004$ , odds ratio (OR): 6.21, 95% CI: 0.001-0.003] and 84% with an NG tube ( $p=0.003$ , OR: 6.9, 95% CI: 0.001-0.003).

**Conclusion:** The placement of NG and ET tubes, separately or combined, can raise the likelihood of sinusitis development in critically ill children due to reduced clearance of NF secretions.

**Keywords:** Sinusitis, nasogastric tube, endotracheal tube, critical care

## Öz

**Giriş:** Erişkinlerde iyi belirlenmiş bir risk faktörü olan okült sinüzit kritik çocuk hastalarda nedeni bilinmeyen ateşe neden olabilir ve sağlık bakımı ile ilişkili olabilir. Bu çalışmanın amacı çocuklarda nazogastrik ve endotrakeal tüp kullanımı ile sinüzite yatkınlık arasındaki ilişkiyi ortaya koymaktır.

**Yöntemler:** Verileri geriye dönük olarak elde ettik ve radyolojik görüntüleri nazogastrik (NG) ve endotrakeal (ET) tüplerin varlığının yanı sıra sinüzit veya nazofaringeal (NF) sekresyon belirtileri açısından değerlendirdik. Ayrıca görüntüler arasındaki aralıkları da kaydettik.

**Bulgular:** Toplam 162 görüntü ile 65 hasta çalışmaya dahil edildi. Sonuçlar, birinci (13/30, %43,3) ve ikinci (20/30, %66,6) görüntüler arasında sinüzit oluşumunda anlamlı bir artış olduğunu gösterdi ( $p=0,039$ ). Sinüzit başlangıcı için kritik süre 2,5 gün olarak belirlendi [eğri altında kalan alan: 0,50, %95 güven aralığı (GA): 0,355-0,646]. Tek ve çift tüp arasında sinüzit oluşumu ve NF sekresyonu açısından anlamlı fark yoktu ( $p=0,389$ ). NG veya ET tüpünün varlığı da sinüzit ile anlamlı bir ilişki göstermedi. Ancak ET tüplü görüntülerin %52'sinde [ $p=0,004$ , olasılık oranı (OO): 6,21, %95 GA: 0,001-0,003], NG tüplü görüntülerin ise %84'ünde ( $p=0,003$ , OO: 6,9, %95 GA: 0,001-0,003) NF sekresyonlarının olduğu belirlendi.

**Sonuç:** NG ve ET tüplerinin ayrı ayrı veya birlikte kullanımı, NF sekresyonların temizlenmesinin azalması nedeniyle kritik hasta çocuklarda sinüzit gelişme olasılığını artırabilir.

**Anahtar Kelimeler:** Sinüzit, nazogastrik tüp, endotrakeal tüp, yoğun bakım

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## Introduction

When treating critically ill pediatric patients, endotracheal (ET) and nasotracheal (NT) tubes are commonly used. The ET route is the preferred method of intubation for both adults and children. In contrast, nasotracheal intubation is less common, accounting for only 5.6% and 4% of advanced airway procedures in children and adults, respectively.<sup>1,2</sup> The use of ET and NT tubes has been identified as a significant risk factor for developing nosocomial sinusitis, which could lead to sepsis in critically ill adults.<sup>3,4</sup> Children may have a higher risk of developing sinusitis because of their smaller airways and anatomical differences compared with adults. This can be particularly concerning for pediatric intensive care unit (PICU) patients with intubation tubes.<sup>5</sup> According to research, proper aeration and clearance of mucosal secretions are crucial for preventing related sinusitis caused by NT. Typically, patients with an advanced airway receive their nutritional needs through nasogastric (NG) or orogastric tubes, but the link between these tubes and sinusitis in children is not well established.<sup>6,7</sup> This study investigated the potential development of sinusitis in PICU patients facilitated by NG or ET tubes.

## Materials and Methods

This research was conducted in the 16-bed PICU of Hacettepe University, a tertiary referral center in Turkey. The study included all patients (one month to 18 years old) who were referred to our PICU and underwent cranial radiological examination [computed tomography (CT) or magnetic resonance imaging (MRI)] from June 2011 to February 2018. Patients aged 4 months, those with primary immunodeficiency syndromes, recent chemotherapy for a neoplasm, fascial bone anomaly, known injury to facial bones or anterior cranial vault, and patients with only one image were excluded from the initial enrollment. In this study, patients with at least two cranial images were included and underwent radiological re-evaluations by a pediatric neuroradiologist. We recorded the presence of sinusitis, NG tube, ET tube, and secretions in the nasopharyngeal area and each study's timing and type of examination. The tube count of each test was also evaluated and categorized into "none," "one (NG or ET)," and two (NG+ET) tube groups. Ethical approval was obtained from the Ethical Committee of Hacettepe University Faculty of Medicine, and the study was performed according to the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

## Statistical Analysis

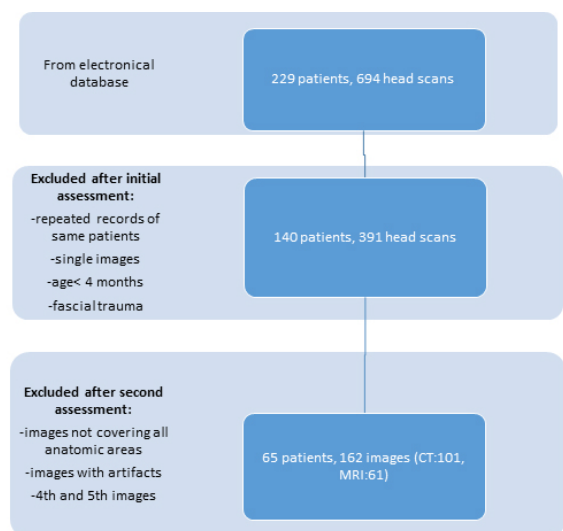
In this study, both normally and non-normally distributed variables were analyzed using SPSS v23.0. Mean and

standard deviations were used to represent normally distributed variables, whereas median and interquartile range were used for non-normally distributed variables. Categorical variables are presented as proportions and percentages. The Mann-Whitney U test was used to compare the median age of patients with and without sinusitis. In addition, the chi-square test was used to compare the ratios of sinusitis and the presence of NG tube alone, ET tube alone, and NG + ET. The McNemar test was used for the dependent variables. The time between two consequent examinations was considered to be between the NG tube duration and sinusitis occurrence. ROC curve analysis was performed to search for a cut-off time, and significant cut-off values were presented in terms of sensitivity, specificity, and positive and negative predictive values. A p-value of 0.05 was considered significant.

## Results

From 2011 to 2018, 3577 patients were monitored in the PICU. Of these patients, 229 had 694 head scans, either CT or MRI, for various reasons. Images of repeated scans of the same patients, single images, and scans of patients under 4 months of age or with facial trauma were excluded after the initial assessment. We conducted a second evaluation of the images and excluded those that did not cover all anatomical areas or had artifacts. We also removed the 4<sup>th</sup> and 5<sup>th</sup> images because of their small numbers. Our study included 65 patients and 162 images, of which 101 were CT and 61 were MRI (see Figure 1).

The median age of the patients was 6.4 years, ranging from 4 months to 17.4 years. Traumatic brain injury was the most common diagnosis (32.8%), followed by acute



**Figure 1.** Patient selection to the study  
MRI: Magnetic resonance imaging

neurological dysfunction (30.8%) due to various diseases such as hemorrhage, tumors, and meningitis. Approximately 15.2% of patients had a history of neoplasm, whereas others had respiratory diseases like pneumonia and acute respiratory distress syndrome, cardiovascular diseases like fatal arrhythmias and heart failure, shock, liver failure, and adrenal insufficiency.

No findings were suggestive of an invasive fungal infection. Of the first images taken, 46% (n=30) showed signs of sinusitis, regardless of whether the patient had an NG or ET tube (Table 1). Among the images where there was no sinusitis present in the first image (n=35), 12 (34.2%) of them had sinusitis in the second image, making the incidence of sinusitis 60% in the second image. Three patients who had sinusitis in the first image showed no signs in the second image. One patient had no NG tube in either image, another had both images taken on the same day, and the last one had an NG tube in both images taken 11 days apart. The median age of patients affected by sinusitis and those who were not were similar (p=0.445).

The median time between admission and the first images taken was 1 day (1-30 days). The time between the first and second images was a median of 2 (1-6) days, and the

time between the second and third images was 3.5 (1.5-8.5) days. There was no significant difference between single or double tube presence with sinusitis or NF secretion formation (p=0.389). Similarly, there was no significant relationship between the presence of an NG or ET tube. However, we found an NG tube in 84% of images with NF secretions and an ET tube in 52% (p=0.003 and p=0.004, respectively) (Table 2). Sinusitis was present in 17 (44.7%) of the images with at least one tube and 13 (48.1%) of the images without any tubing, with no significant difference between them (p=0.806). On the other hand, NF secretion was found in 17 of 38 images with at least one tube and in 2 of 27 images without a tube (p=0.001). Thirty patients had an NG tube in both the first and second images, and among these patients, there was a statistically significant increase in the incidence of sinusitis between the first (13/30, 43.3%) and second (20/30, 66.6%) images (p=0.039). ROC analysis showed that 2.5 days was the cut-off time for sinusitis, with an area under the curve of 0.50 and a 95% confidence interval (0.355-0.646). Thirteen (40.6%) of 32 patients with three sequential images had an NG tube during all three images, and there were no significant changes in the incidence of sinusitis and NF secretion over time (p=0.097 and p=0.264, respectively).

**Table 1. The proportions of the NG tube, ET tube, sinusitis, and NF secretion of the sequential images**

	First image (n=65)		Second image (n=65)		Third image (n=32)	
	+ n (%)	- n (%)	+ n (%)	- n (%)	+ n (%)	- n (%)
ET tube	17 (26)	48 (73)	14 (21)	51 (78)	9 (28)	23 (71)
NG tube	36 (55)	29 (44)	39 (60)	26 (40)	18 (56)	14 (43)
Sinusitis	30 (46)	35 (53)	39 (60)	26 (40)	17 (53)	15 (46)
NF secretion	19 (29)	46 (70)	25 (38)	40 (61)	10 (31)	22 (68)
Number of tubes						
None	27 (41)		25 (38)		12 (37)	
NG or ET tube	23 (35)		27 (41)		13 (40)	
NG plus ET tube	15 (23)		13 (20)		7 (21)	

ET: Endotracheal, NG: Nasogastric, NF: Nasopharyngeal

**Table 2. The proportions of the presence of NG tube, ET tube, sinusitis, and NF secretion in the first image**

	Sinusitis, n (%)*				NF secretion, n (%)*			
	Absent	Present	p	OR (95% CI)	Absent	Present	p	OR (95% CI)
ET tube								
Absent	27 (77)	21 (70)	0.514	1.62 (0.612-0.637)	39 (84)	9 (47)	0.004	6.21 (0.001-0.003)
Present	8 (22)	9 (30)			7 (15)	10 (52)		
NG tube								
Absent	15 (42)	14 (46)	0.758	1.16 (0.610-0.635)	26 (56)	3 (15)	0.003	6.9 (0.01-0.003)
Present	20 (57)	16 (53)			20 (43)	16 (84)		
Total	35	30			46	19		

\*: Percentages represent within columns, ET: Endotracheal, NG: Nasogastric, NF: Nasopharyngeal, CI: Confidence interval, OR: Odds ratio

## Discussion

In this retrospective study, we found that NG and ET tubes were significantly associated with increased nasopharyngeal secretions, which may increase the risk of sinusitis in critically ill children. The nasal cycle influences the mucosal lining over the nasal septum and nasal turbinates, which is responsible for alternating changes in turbinate sizes due to mucosal engorgement.<sup>8</sup> A foreign object such as NG, NT, or ET tubes may quickly interrupt this finely balanced mechanism. Although ET tubes do not seem to block any nasopharyngeal region, they are shown to be an independent risk factor for sinusitis in adults. A large adult study showed that compared with patients with only an NG tube, the risk for sinusitis was 41% greater in patients with an ET tube and 200% greater in patients with both tubes.<sup>9</sup> Another adult study reported sinusitis as a cause of fever of unknown origin (13.8%).<sup>10</sup> We hypothesized that lower age may be a risk factor for sinusitis because the pneumatization pattern is unique to each group of sinuses and the continuous change in the size and aeration of the sinus as a child grows. However, we did not find any significant relationship between age and the risk of sinusitis. This may be due to the small sample size.

The optimal imaging method for sinusitis is a topic of ongoing research and debate. Cranial CT scans are not typically recommended for routine diagnosis of sinusitis because they are not specific to the paranasal sinuses and may not provide the detailed imaging required for accurate assessment of sinus pathology. Paranasal sinus CT scans are specifically designed to visualize the paranasal sinuses. They have also been identified as the best imaging method for diagnosing sinusitis in children, emphasizing its importance in pediatric cases.<sup>11,12</sup> Furthermore, MRI provides excellent images for complex sinus disease, intracranial tumor extension, and aggressive fungal sinusitis without ionizing radiation, making it a valuable alternative to CT imaging.<sup>13</sup> Therefore, while cranial CT scans may provide some information about sinus pathology, they are not as specific or suitable as paranasal sinus CT scans for accurately diagnosing and evaluating sinusitis.<sup>12</sup> We used only cranial CT and/or MRI scans that were taken for other reasons, such as traumatic brain injury, seizures, and central nervous system infections. Thus, this may have caused misinterpretation of the imaging findings, leading to statistically insignificant results in this study.

Among PICU patients undergoing cranial imaging for any reason, we observed a high incidence of sinusitis (46%) and a 30% increase over time. NG and ET tubes were associated with increased secretions and sinusitis. Although the AUC statistics showed weak strength and a lack of data regarding contributing factors such as preexisting adenoid vegetation and a history of allergic diseases, the threshold

time for developing sinusitis was 2.5 days. Nevertheless, having a facilitating factor for developing sinusitis and the need for a tube in the upper airways could accelerate the risk of sinusitis, and it could be faster than usual with a critical illness. Therefore, healthcare professionals should be aware of occult sinusitis as an etiology of fever, even in the short term. Healthcare-related infections, such as venous or urine catheter-related infections, have a crucial impact on morbidity and mortality. The burden of these infections is significant because of their preventable nature. Sinusitis is a common healthcare-related condition that frequently occurs in adult intensive care settings. It may be associated with fever of unknown origin and sepsis.<sup>3</sup>

Sinusitis is the most common (40.2%) predisposing factor in pediatric patients with orbital or preseptal cellulitis.<sup>14</sup> It can cause localized neurological diseases such as brain abscesses and subdural empyema, which could require intensive care treatments.<sup>15</sup> The incidental sinusitis rate in the PICU is approximately 50%.<sup>5</sup> We found that 46% of the 65 patients had sinusitis in their first cranial examination, which supports previous reports. Because PICU patients are often intubated and sedated or obtunded, sinusitis is often difficult to diagnose because there are no complaints of nasal congestion or drainage, facial pain, cough, or headache. Thus, radiological evaluation is the best screening tool for such patients.<sup>16</sup>

For intensive care patients, it is inevitable to have an artificial material for specific treatments, nutrition, and fluid balance monitoring (intravenous catheters, ET and NG tubes, urinary catheters, etc.). All these materials have their own risk of complications and increase the risk of nosocomial infections. It is wise to use them when necessary, and they should be removed as soon as possible to avoid the abovementioned risks. If they are needed longer, alternatives such as tracheostomy and gastrostomy should be considered and not delayed. In critically ill children with fever of unknown origin, occult sinusitis should not be missed, and empiric antibiotic treatment should be ordered accordingly. It has been reported that antibiotic-resistant Gram-positive bacteria, such as pneumococci, could be a source of septic shock in critical care settings.<sup>17,18</sup> Thus, local surveillance results should be considered when choosing antibiotics.

## Study Limitations

The current study's limitations were the retrospective nature, small sample size, precise duration between sequential images, and lack of data regarding fever, the need for change of antibiotic regimes, and inflammatory markers of the patients. The Lund-Mackay score for CT scans is an objective tool for adults; however, a validated scoring system in the pediatric population has yet to be widely used.<sup>19</sup> Although we did not use paranasal imaging and a well-defined scoring

system, a well-educated and experienced pediatric radiologist re-evaluated the images. We did not evaluate the CT and MRI images separately to avoid a significant decrease in size.

## Conclusion

The placement of NG and ET tubes, either alone or in combination, unequivocally leads to the accumulation of nasopharyngeal secretions, which significantly impairs clearance and predisposes critically ill children to sinusitis. This risk progressively increases over time and should be considered when managing critically ill children with these tubes.

## Ethics

**Ethics Committee Approval:** Ethical approval was obtained from the Ethical Committee of Hacettepe University Faculty of Medicine, and the study was performed according to the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

**Informed Consent:** Informed consent was obtained.

## Authorship Contributions

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

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# Perioperative Outcomes Following Surgery for Pediatric Brain Tumors: Assessment of Eight-year Single-center Short-term Results

## Pediyatrik Beyin Tümörlerinde Cerrahi Sonrası Perioperatif Sonuçlar: Sekiz Yıllık Kısa Vadeli Sonuçların Değerlendirilmesi

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### Abstract

**Introduction:** Various perioperative problems occur in patients operated on brain tumors. While many studies focused on the long-term effects of surgery, few focused on the perioperative period. The aim of this study to evaluate clinical and laboratory features and determining the factors which are effecting the outcome in operated patients for brain tumors our pediatric intensive care unit (PICU).

**Methods:** Patients who underwent intracranial tumor surgery in the PICU during the eight-year period were retrospectively screened.

**Results:** Seventy-four patients were included in the study, mean age was 60 (1.5-192) months, and supratentorial tumors were detected in 41 (55.4%) patients. The median length of stay (LOS) in PICU of the patients was 5 (1-150) days. When supratentorial tumor localization, ventriculoperitoneal shunt presence, central venous catheter related bloodstream infection, ventilator-associated pneumonia and other infections were evaluated, a statistically significant difference was found between the two groups when patients' LOS in the PICU is evaluated in 2 groups of more than 15 days (77%) and less than 15 days (23%). In the postoperative period, diabetes insipidus (DI) in 12 (16%), septicemia in 9 (12%), shunt infection in 8 (10%), hydrocephalus in 7 (9%), seizures in 5 (6%), cranial nerve palsy in 5 (6%) in patients.

**Conclusion:** Neurological sequelae increased with younger age and were more common in patients with infratentorial tumors. While a relationship was found between delta sodium and DI in the postoperative first 4 days, without relationship was found with neurological sequelae.

**Keywords:** Brain tumor, child, perioperative period problems, pediatric intensive care, delta sodium

### Öz

**Giriş:** Beyin tümörü nedeniyle ameliyat edilen hastalarda ameliyat sırasında çeşitli sorunlar ortaya çıkmaktadır. Pek çok çalışma ameliyatın uzun vadeli etkilerine odaklanırken, çok azı perioperatif döneme odaklandı. Bu çalışmanın amacı çocuk yoğun bakım ünitemizde (ÇYBÜ) beyin tümörü nedeniyle opere edilen hastaların klinik ve laboratuvar özelliklerinin değerlendirilmesi ve sonuca etki eden faktörlerin belirlenmesidir.

**Yöntemler:** Sekiz yıllık süreçte ÇYBÜ'de intrakraniyal tümör ameliyatı geçiren hastalar geriye dönük olarak tarandı.

**Bulgular:** Çalışmaya 74 hasta dahil edildi, ortalama yaş 60 (1,5-192) ay olup, 41 (%55,4) hastada supratentoryal tümör tespit edildi. Hastaların ÇYBÜ'de ortalama kalış süresi 5 (1-150) gündü. Supratentoryal tümör lokalizasyonu, ventrikülperitoneal şant varlığı, santral venöz kateter ilişkili kan dolaşımı enfeksiyonu, ventilatör ilişkili pnömoni ve diğer enfeksiyonlar değerlendirildiğinde, hastaların ÇYBÜ'de kalış süreleri 15 günden fazla (%77) ve 15 günden az (%23) olarak değerlendirildiğinde iki grup arasında istatistiksel olarak anlamlı fark bulundu. Ameliyat sonrası dönemde 12'sinde (%16) diyabet insipidus (Dİ), 9'unda (%12) septisemi, 8'inde (%10) şant enfeksiyonu, 7'sinde (%9) hidrosefali, 5'inde (%6) nöbet, hastaların 5'inde (%6) kraniyal sinir felci görüldü.

**Sonuç:** Nörolojik sekeller yaş ilerledikçe arttı ve infratentoryal tümörlü hastalarda daha sık görüldü. Ameliyat sonrası ilk 4 günde delta sodyum ile Dİ arasında ilişki bulunurken, nörolojik sekellerle ilişki saptanmadı.

**Anahtar Kelimeler:** Beyin tümörü, çocuk, perioperatif dönem sorunları, çocuk yoğun bakım, delta sodyum

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## Introduction

Central nervous system (CNS) tumors are the most common solid neoplasms in childhood.<sup>1</sup> One of four childhood cancers appear in CNS and CNS tumors account for the highest rate of death in children. Brain tumors are approximately 8-15% of pediatric cancers and third most common cancer type after leukemia (30%) and lymphoma (15%).<sup>2</sup> Although there are differences in tumor type and age at diagnosis, the 5-year survival rate of primary malignant and non-malignant brain tumors is 73%. Mass effect and treatment modalities (brain surgery procedure, radiotherapy, and chemotherapy) in the treatment of brain tumors create various difficulties for patients. Most of the first symptoms of CNS tumors are also seen in more common and less severe childhood diseases like gastroenteritis, migraine, and behavioral problems.<sup>3,4</sup>

Surgically removal of the tumor is the main treatment for brain tumors. Patients especially must be followed in pediatric intensive care unit (PICU) for managing surgical, neurological, infectious, and endocrinological problems and maintaining electrolytes in the postoperative period. Most of the studies focus on long-term outcomes of brain tumor patients but only a few study short-term outcomes. In our study, we evaluated demographic, clinical, and laboratory features of patients who operated on brain tumors and affecting factors of morbidity and mortality in our PICU.

## Materials and Methods

### Study Design and Study Population

In our study, there are 86 patients who followed up in PICU after intracranial tumor surgery between 2014-2022 in 8 years period. This retrospective was approved by the Local Ethics Committee of Ankara University Hospital (ethics committee number: İ11-696-22). Two of 86 patients were excluded due to lack of data while 10 of 86 patients were excluded due to length of stay (LOS) in PICU less than 24 hours. This study's main focus is on evaluating patients operated on brain tumor perioperative period.

### Data Collection

Patients' symptoms at admission, the time between diagnosis and symptoms, patients' pediatric risk of mortality (PRISM III) scores, pediatric logistic organ dysfunction (PELOD 2) scores, Glasgow Coma score (GCS), complete blood count, blood gas, biochemical indicators, radiological findings at admission, tumor localization, tumor origin, tumor grade, surgery technique, the existence of residue mass, postoperative imaging findings, tumor histology, existence of ventriculoperitoneal (VP) shunt and implantation time,

existence of external drainage and implantation time, complications after surgery were recorded. The patients were examined in terms of their characteristic features in subgroups with and without DI, with and without neurological sequelae.

### Definitions

Hyponatremia level was accepted as 135 mEq/L in the study. Patients' daily delta sodium values in the first 7 days were recorded. Delta sodium value is defined as the difference between the highest and lowest sodium values. In the study, delta sodium 5 is stated as the difference value between two measures is five and more as delta sodium 10 is stated as the difference value between the highest and lowest sodium measure is more than 10. DI was typically diagnosed with polyuria, polydipsia, high sodium level, and urine density below 1005. Whether tracheostomy is implemented, mechanical ventilation (MV) duration, usage of an inotrope, whether CRRT and PEX are done, and patients' outcomes were recorded. The reference range of different values is stated below.

Adrenocorticotrophic hormone (ACTH): 7.2-63.3 pf/mL, cortisol: 6.02-18.4 mcg/dL, thyroid-stimulating hormone (TSH): 0.38-5.33 microIU/mL.

### Statistical Analysis

The data were analyzed using the SPSS version 25.0 software (IBM Corp, Armonk, NY). Mean, standard deviation, median, frequency distribution, and percentage values were determined as descriptive statistics of the variables. Mean values were used in parametric tests and median values were used in non-parametric tests. Pearson's chi-square test and Fisher's Exact test were used to analyzing categorical variables. The data were tested for normal distribution using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). The independent samples t-test was used to analyze differences in normally distributed variables between two independent groups. The Mann-Whitney U test was used to analyze differences between the median values of non-normally distributed variables. P-values <0.05 were considered statistically significant.

## Results

### Patient Demographic Data

We enrolled 74 patients to this study and their mean age was 60 (1.5-192) months. 39% of the patients were male. There were 55.4% of the patients' tumor where in the supratentorial area (Figure 1). Patients' GCS, PRISM III scores, PELOD 2 scores median after surgery were 12.3 (3-15), 2.6 (0-8), 2.5 (0-40), respectively (Table 1).



### Postoperative Laboratory Data [Delta Sodium ( $\Delta$ Na)]

When patients are compared of having DI (16%) or not (84%), there was no statistical difference between 2 groups in age, hydrocephalus or convulsion existence, LOS in PICU, and hospital ( $p=0.21$ ,  $p=0.61$ ,  $p=0.59$ ,  $p=0.65$ ,  $p=0.53$ , respectively). Patients' delta sodium 5 ( $\Delta$ Na5 in Day 1,  $p=0.002$ ) and delta sodium 10 values ( $\Delta$ Na10 in Day 1,  $p=0.01$ ) on the first day are statistically significant between

the 2 groups. There was a statistical difference on the second day between delta sodium and delta sodium 5 values, while no difference between delta 10 sodium values ( $p<0.001$ ,  $p=0.001$ ,  $p=0.067$ ). There was a statistical difference on the third day between delta sodium and delta sodium 5 values, while no difference between delta 10 sodium values ( $p=0.002$ ,  $p=0.01$ ,  $p=0.79$ ). There were statistical differences in delta sodium values on the fourth and seventh days, while no difference in delta sodium 5 values ( $p=0.01$ ,  $p=0.32$ ,  $p=0.04$ ). Eleven patients (14.9%) in the DI patient group and 7 patients (9.5%) in other group had hypothalamic-pituitary-adrenal (HPA) axis defect ( $p<0.001$ ) (Table 2).

Table 1. Demographic characteristics of patients	
Parameters	Total patients
Age (months)	60 (1.5-192)
Age at being symptomatic (months)	59 (0.5-192)
Female, yes	35 (47.3%)
PRISM III score	2 (0-8)
PELOD 2 score	0 (0-40)
Hydrocephalus, n (%)	36 (59%)
Tumor location, supratentorial, n (%)	41 (55%)
High grade, n (%)	37 (50%)
Tumor resection, total, yes	46 (62.2%)
Time to diagnosis (months)	1 (0-74.5)
Number of symptoms	1 (1-4)
<b>Initial symptom</b>	
Headache	33 (44%)
Vomiting	28 (37%)
Cerebellar symptoms	19 (25%)
Nausea	17 (22%)
<b>Tumor location</b>	
Posterior fossa	29 (39%)
Midline	22 (29%)
Left hemisphere	12 (16%)
Right hemisphere	6 (8%)
Brainstem	4 (5%)
Bilateral hemispheres	1 (1%)
<b>Tumor histology</b>	
Astrocytoma, (%)	16 (21%)
Glioma, (%)	13 (17%)
Ependymoma, (%)	10 (13%)
Cranio-pharyngioma, (%)	9 (12%)
Medulloblastoma, (%)	6 (8%)
Germ, (%)	2 (2%)
Others, (%)	14 (18%)
MV usage, yes, (%)	25 (33.8%)
NIV usage, yes, (%)	4 (5.4%)
Inotrope usage, yes, (%)	6 (18%)
PICU length of stay (day)	5 (1-150)
Length of hospital stay (day)	21.5 (2-228)
28-day mortality rate, (%)	4%
Mortality, yes, (%)	11 (14%)

### Neurological Disabilities

When patients are analyzed into two groups; with neurological disabilities in 20 (27%) patients and without neurological disabilities in 54 (73%) patients. There was no statistical significance between the two groups in hydrocephalus existence, sodium value on the first day after surgery ( $p=0.54$ ,  $p=0.9$ , respectively). There was no statistical significance between the two groups in delta sodium levels for every days within the first 5 days ( $p=0.26$ ,  $p=0.57$ ,  $p=0.66$ ,  $p=0.66$ ,  $p=0.12$ , respectively). The mean age was  $50\pm 46$  months in the patient group with neurological disabilities whereas  $82\pm 54$  months in the patient group without having neurological disabilities ( $p=0.02$ ). Tumor localizations were the supratentorial area in 6 patients (30%) in the patients with neurological disabilities, and 35 patients (64%) in the patients without neurological disabilities ( $p=0.007$ ). According to the state of neurological disability, there was no statistical significance in terms of HPA axis defect and convulsion patients ( $p=0.06$ ,  $p=0.41$ ), respectively. When patients were compared with non-invasive ventilation (NIV) requirement, MV requirement, LOS in PICU and hospital, values were high in the patients with neurological disabilities and there was statistical significance between the two groups ( $p=0.01$ ,  $p<0.001$ ,  $p<0.001$ ,  $p<0.001$ ) (Table 3).

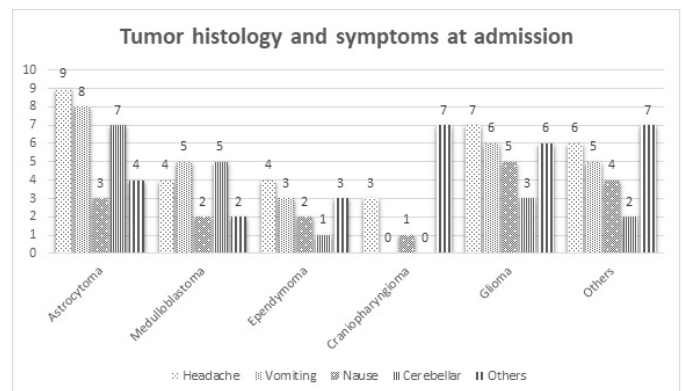


Figure 1. Tumor histology and symptoms at admission

PRISM III: Pediatric Risk of Mortality III, PELOD2: Pediatric Logistic Organ Dysfunction 2, NIV: Non-invasive ventilation, MV: Mechanical ventilation, PICU: Pediatric intensive care unit

### Patient Characteristics, Preoperative and Postoperative Endocrine Laboratory Data

Hormonal studies were performed on 15 patients before surgery and 19 patients after surgery. Patients' preoperative ACTH median value was 11.8 (1.1-38), cortisol median value was 6.7 (0.5-22), TSH median value was 1.2 (0.1-4.4). Patients' postoperative ACTH median value was 4.8 (1-38),

cortisol median value was 15.3 (0.5-45.3), TSH median value was 0.4 (0-11.5). In the preoperative period, ACTH was low in 5 patients (33%), TSH was low in 3 patients (20%), and cortisol was low in 8 patients (53%). In the postoperative period, ACTH was low in 11 patients, TSH was low in 8 patients (42%), cortisol was low in 8 patients, and high in 8 patients.

**Table 2. Comparison of the characteristics of patients with and without diabetes insipidus**

Parameters	Total (n=74)	DI, no (n= 62)	DI, yes (n=12)	p-value
Age (months)	60 (1.5-192)	60 (1.5-192)	79 (13-170)	0.21*
Supratentorial, n (%)	41 (54%)	30 (40.5%)	11 (14.9%)	<b>0.006***</b>
Hydrocephalus, yes	36 (59%)	32 (52.5%)	4 (6.6%)	0.61***
Na value, first day	138 (124-166)	137 (122-148)	138 (129-148)	0.06*
ΔNa, first day (n=69)	2 (0-28)	2 (0-18)	8.5 (0-14)	<b>0.01*</b>
ΔNa 5, first day	23 (33.3%)	14 (20.3%)	9 (13%)	<b>0.002***</b>
ΔNa 10, first day	10 (14.5%)	5 (7.2%)	5 (7.2%)	<b>0.01***</b>
ΔNa, second day (n=54)	3.5±4.8	2.26±2.7	8±7.6	<b>&lt;0.001**</b>
ΔNa 5, second day	14 (25.9%)	6 (11.1%)	8 (14.8%)	<b>0.001***</b>
ΔNa 10, second day	5 (9.3%)	2 (3.7%)	3 (5.6%)	0.067***
ΔNa, third day (n=53)	2 (0-11)	1 (0-11)	3 (1-8)	<b>0.002*</b>
ΔNa 5, third day	9 (17%)	4 (7.5%)	5 (9.4%)	<b>0.01***</b>
ΔNa 10, third day	1 (1.9%)	1 (1.9%)	0	0.79***
ΔNa, fourth day (n=50)	2±2.7	1.54±1.6	3.9±4.6	<b>0.01**</b>
ΔNa, fifth day (n=51)	2.6±4.4	1±3	3±7.4	0.32*
ΔNa, seventh day	3.2±5.3	1±5.3	3±5	<b>0.04*</b>
HPA axis damage, yes	18 (24.3%)	7 (9.5%)	11 (14.9%)	<b>&lt;0.001***</b>
Seizure, yes	5 (6.8%)	4 (5.4%)	1 (1.4%)	0.59***
PICU length of stay	5 (1-150)	4.5 (1-150)	6.5 (1-30)	0.65*
Length of hospital stay	21.5 (2-228)	21 (2-238)	24.5 (8-46)	0.53*

ΔNa: Delta sodium, ΔNa 5: Delta sodium 5, ΔNa 10: Delta sodium 10, HPA: Hypothalamic-pituitary-adrenal, PICU: Pediatric intensive care unit, \*: Independent samples t-test, \*\*: Mann-Whitney U test, \*\*\* Fischer's Exact test

**Table 3. Comparison of patient characteristics according to neurological sequelae**

Parameters	Total (n=74)	NS, no. (n=54)	NS, yes (n=20)	p-value
Age (months)	73.7±53.8	82±54	50±46	<b>0.02*</b>
Supratentorial, n (%)	41 (54%)	35 (47%)	6 (8.1%)	<b>0.007***</b>
Hydrocephalus, yes	36 (59%)	27 (44%)	9 (14%)	0.54***
Na value, first day	138 (124-166)	137 (128-148)	137 (122-148)	0.9**
ΔNa first day (n=69)	2 (0-18)	2 (0-17)	3 (0-18)	0.26**
ΔNa second day (n=54)	2 (0-28)	1 (0-28)	2 (0-13)	0.57**
ΔNa fifth day (n=51)	1 (0-25)	1 (0-25)	1 (0-17)	0.12**
HPA axis damage, yes	18 (24.3%)	16 (21.6%)	2 (2.7%)	0.06***
Seizure, yes	5 (6.8%)	3 (4.1%)	2 (2.7%)	0.41***
NIV usage, yes	0.3±1.7	0.04±0.2	1.1±3.2	<b>0.01*</b>
MV usage, yes	5.4±17.7	0.7±2	18.3±30	<b>&lt;0.001*</b>
PICU length of stay	14.3±27.4	6.9±7.7	34±46	<b>&lt;0.001*</b>
Length of hospital stay	32±38	20±16	62±16	<b>&lt;0.001*</b>

NS: Neurological sequelae, ΔNa: Delta sodium, ΔNa 5: Delta sodium 5, ΔNa 10: Delta sodium 10, HPA: Hypothalamic-pituitary-adrenal, NIV: Non-invasive ventilation MV: Mechanical ventilation, PICU: Pediatric intensive care unit, \*: Independent samples t-test, \*\*Mann-Whitney U test, \*\*\* Fischer's Exact test

## The Patient Characteristics According to the Median LOS in PICU

When the patients were divided into 2 as less than 15 days (77%) and over (23%) according to the number of intensive care hospitalization days, respectively; patients with hydrocephalus on admission imaging were 26 (42.6%) and 10 (16.4%) ( $p=0.48$ ). The tumor was located supratentorially in 36 (48.6%) patients in the group hospitalized for less than 15 days and in 5 (6.8%) patients in the group hospitalized for 15 days or more ( $p=0.01$ ). The frequency of VP shunt, central venous catheter (CVC) associated, VAP, and accompanying infections was higher in the group with intensive care hospitalization for 15 days or more ( $p<0.001$ ,  $p=0.009$ ,  $p=0.009$ ,  $p<0.0001$ , respectively). The characteristics of the patients according to the number of intensive care hospitalization days are given in the supplemental file.

## Patients' Outcome and Mortality

Patients' median LOS in PICU was 5 (1-150) days, whereas the mean LOS in hospital was 21.5 (2-228) days. The median day of MV requirement was 0 days (0-132), whereas the mean day of NIV requirement was 0 days (0-12). One (1%) patient needed CRRT. Patients' mortality rate was 4% on the 28<sup>th</sup> day and 14% at discharge ( $n=11$ ).

## Discussion

There could be delays and difficulties in the diagnosis process since brain tumors are childhood's third most common tumor and having non-specific symptoms. Target treatments like genetic defining and immunotherapy will increase survival on this type of tumor in the future. Patients must be evaluated with multidisciplinary approach and patients' clinics, vitals and laboratory values must be carefully monitored to decrease morbidity and mortality. In the perioperative period, problems like convulsion, cranial nerve paralysis, muscle strength loss, cerebellar syndrome, central salt loss, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), DI, CNS infection, shunt infection, HPA axis damage, endocrine disorders, and biochemical imbalances can be seen according to tumor's type, localization, surgery technique, the trend of patients' endocrinal and biochemical values.

Ten percent of children with CNS tumor has convulsions. The timing of convulsions divides into two groups early period inside the first week and the late period. Uncontrolled convulsions have bad effects on neurological outcome. A study made in adults suggests that using antiepileptics decreases convulsions in adults although no such benefit couldn't be shown in child patients. A study of Saadeh et al.<sup>5</sup> researched risk factors of convulsions after supratentorial tumor resection and relations between convulsions, age, tumor localization, extent of resection, pathology, occurrence

of hydrocephalus and sodium levels, found factors that were evaluated with multiple variant regression, which are temporal lobe localization, age less than 2 years, the existence of hydrocephalus before surgery, convulsions before surgery and parietal lobe localization statistically significant. Three of our patients had convulsion as presenting symptom and 5 of our patients had convulsions after surgery. Three of 5 patients had convulsions after surgery was less than 2 years and 3 patients' tumors were localized in supratentorial area. All of three patients' had convulsions as presenting symptoms, delta sodium levels were high, and developed DI. Hydrocephalus and sodium levels were found related whereas no relations were found between DI occurrence and neurological disability.

A study by Houdemont et al.<sup>6</sup> that researched postoperative neurological complications and outcomes with 117 pediatric patients who were operated on brain tumors, found a relation between LOS in PICU and severity of neurological complications ( $p=0.006$ ). In a study of Houdemont et al.<sup>6</sup> researched short-term complications in the postoperative period with 117 children in 2011, complications caused by tumor localization were cranial nerve paralysis (60 patients, 51.7%), motor deficit (21 patients, 18.1%), cerebellar syndrome (40 patients, 34.5%), convulsion (7 patients, 6%) and endocrine disorder (14 patients, 12.1%) they found statistically significant. In the postoperative period, postoperative hydrocephalus in 3 patients (2.6%), cerebrospinal fluid leak in 8 patients (6%), meningitis in 10 patients (8%), ventriculitis in 1 patient (1%) and brain abscess in 1 patient (1%) detected. Twenty-seven patients (23%) had a better neurological state, while 9 patients (7.6%) had a worse neurological state.<sup>6</sup> In our study DI in 12 patients (16%), sepsis in 9 patients (12%), hydrocephalus in 7 patients (9%), convulsion in 5 patients (6%), cranial nerve paralysis in 5 patients (6%), shunt infection in 4 patients (5%), intracranial hemorrhage in 4 patients (5%) and central salt loss in 3 patients (4%), were seen in the postoperative period. In the postoperative period, 39% of the complications were seen in the first 2 days, 31% between 3 and 7 days, and 29% of them were seen in 8 days or more. Accompanying infections in 21 patients (28%), shunt infection in 8 patients (10%), CVC infection in 5 patients (6%), ventilator-associated pneumonia in 5 (6%) patients, and sepsis in 4 patients (5%) were seen during patients' PICU follow-up.<sup>6</sup> Neurological disabilities were seen more in younger age and patients with infratentorial tumors. No relation was found between neurological disability and first-day delta sodium level and delta sodium. Fluctuations in sodium levels could cause temporary mental status change and convulsions unless intervened but change in sodium levels were not related to neurological disabilities in our center particularly.

Hypothalamo-hypophyseal hormone deficiencies are seen in 40-87% of children with craniopharyngioma and 73%

of adults. GH, FSH/LH, ACTH, TSH, and ADH values can be deficient at diagnosis and a spectrum from one hormone deficiency to panhypopituitarism can be seen.<sup>7</sup> Hypophyseal tumors could cause many hormones and water metabolism deficiencies other than mass effects to critical areas. Brain surgeons are trying to protect and restore pituitary functions while they resect tumors and remove the mass effect on critical areas. Checking hypophyseal hormones before surgery is important for understanding deficiency situations and excluding possible hormone-secreting tumors. In hypophyseal TSH, LH, FSH, IGF1, prolactin, morning ACTH and cortisol values must be looked at before surgery. A prospective study by Chen et al.<sup>8</sup> with 385 patients found hypothyroidism of 36%, hypogonadism of 41%, hypoprolactinemia of 18%, and GH deficiency of 61%. One of three hypothyroidism patients has also hypocortisolism.<sup>9</sup> In our study 5 patients' ACTH levels, 3 patients' TSH levels, and 8 patients' cortisol levels were low in the preoperative period.

A study by Sorba et al.<sup>10</sup> which evaluated the postoperative period of 174 hypophyseal surgery patients, defined 13 (7.5%) DI and 11 (6.3%) SIADH patients. Patients who developed DI has more LOS in the hospital than SIADH patients. Four patients were discharged with persistent DI and 2 patients were discharged with SIADH.<sup>10</sup> Kruis et al.'s<sup>11</sup> retrospective study with 120 child patients who was performed surgery on their sellar and suprasellar areas, found a relation between high plasma sodium levels, sodium level fluctuation during the day, and postoperative neurological status. Thus the importance of monitorization of patients' sodium level with sellar lesions was emphasized. DI was detected in 67% of patients. The difference between the highest and lowest sodium values in the first 10 days of DI patients was  $\geq 10$  mmol/L/24 hours in 75.3% of the patients. Mental status changes were more detected in DI patients than in non-DI patients and related to low sodium levels. At the end of the study, it was suggested that patients with sellar and suprasellar lesions must be monitored and followed up in experienced medical centers since mental status changes related to sodium level fluctuations in the first 10 days.<sup>11</sup> In our study, DI-developed patients' mean age was found more than DI undeveloped patients, and the development of DI was not found to affect PICU and hospital LOS. Patients' delta sodium level differences who had convulsions were  $\geq 10$  mmol/L/24 hours. A relation was detected between DI and the first 5 days' delta sodium levels but no relation was detected between DI and convulsion. A relation was found between DI, tumor localization, and HPA axis defect.

Infectious, endocrinological, and surgical complications and shunt infections can be seen in short and long-term periods of patients who were operated on brain tumors.

One of the most important ones is hyponatremia seen after supratentorial tumor surgery. A hyponatremia level of 130 mEq/L and below was related to 21% of patients with convulsions and 41% of patients with mental status changes. A hyponatremia level of 130 mEq/L and below was also found related to poor neurological outcomes.<sup>12</sup> Schipman et al.'s<sup>13</sup> study which researched complications in the first 30 days with 2511 adult patients, showed nosocomial infections in 305 patients (12.1%), cerebrospinal fluid (CSF) leak in 156 patients (6.2%), surgical site infections in 104 patients (4.1%), surgical site bleeding in the postoperative period in 95 patients (3.8%), hydrocephalus in 30 patients (1.2%). Our study found no relation between hyponatremia, supratentorial localization, and neurological disabilities. Hyponatremia and hydrocephalus at admission were found related while PICU LOS was not found related. Obstructive hydrocephalus and young age were found related to hyponatremia in our study.

The purpose of Helmbold et al.'s<sup>14</sup> study with 70 pediatric patients was to assess settled risk factors and to define factors related to new inflammations and postoperative VP shunt implantation. Postoperative shunt implantation was done in patients who had surgery before age of 3, external ventricular drainage (EVD) implantation before surgery, hydrocephalus signs after postoperative imaging, FOHR index more than 0.46 in the postoperative period, intraventricular hemorrhage, CRP levels more than 40 in the first 48 hours after surgery, CSF leak. Datas in hand suggest that reducing intraventricular hemorrhage could decrease the frequency of shunt implantation but aseptic inflammation pathways behind shunt need and CRP levels increase must be researched more.<sup>14</sup> Four (72%) patients were implanted shunt before or after surgery in our study. 58.1% of patient's tumor resected who didn't have shunts while 12% of patient's tumor resected who had shunts. It was statistically significant between those two groups. No relation was found between CRP, intraventricular hemorrhage, and VP shunt. In our study, 31 patients were put external drainage 8 of them before surgery and 23 of them during surgery.

MV was applied to 25 (33%) of the patients in our study. The median of MV administration was 7 (0.5-130) days. In the follow-up of 4 patients who were intubated, NIV was needed. In the follow-up, tracheostomy was performed on 5 patients. Inotrope was started in 6 patients who were followed up for sepsis. The 28<sup>th</sup>-day mortality of the patients was 4% (3 patients). Two of the 3 patients who died were clinically and radiologically diagnosed with brain death. One patient died due to sepsis. Fifteen (75%) of the patients with neurological sequelae needed MV. We think that our results are good considering the disease severity of the patient population we follow.

## Study Limitations

The limitation of the study is that it is a single center and retrospective study.

## Conclusion

In our study, neurological sequels were related to NIV need MV to need, longer PICU, and hospital LOS. Neurological disabilities were seen more in younger age and patients with infratentorial tumors. No relation was found between neurological disability and first-day delta sodium level and fifth-day delta sodium. Fluctuations in sodium levels could cause temporary mental status change and convulsions unless intervened but change in sodium levels were not related to neurological disabilities in our center particularly. Hyponatremia and hydrocephalus at admission were found related with neurological sequelae while PICU LOS was not found related. Obstructive hydrocephalus and young age were found related to hyponatremia in our study. Patients' delta sodium level differences who had convulsions were  $\geq 10$  mmol/L/24 hours. A relation was detected between DI and the first 5 days' delta sodium levels but no relation was detected between DI and convulsion. A relation was found between hydrocephalus and sodium levels whereas no relation was found between hydrocephalus, DI development, and neurological disabilities. Patients operated of intracranial surgery must be evaluated with a multidisciplinary approach and for reducing morbidity, complications, and mortality during perioperative period patients must be followed up in experienced medical centers.

## Ethics

**Ethics Committee Approval:** This work has not been published or is being considered for publication elsewhere. Written permission was obtained from the Local Ethics Committee of Ankara University Faculty of Medicine (ethics committee number: İ11-696-22).

**Informed Consent:** Written informed consent was obtained from all patients' relatives or legal authorities when necessary. Our study was conducted in accordance with the ethical principles of the World Medical Association Declaration of Helsinki.

## Authorship Contributions

Concept: F.K., M.A.Ü., E.Ü., T.K., Design: F.K., A.G., H.U., İ.D., G.K., H.U.D., E.Ü., T.K., Data Collection or Processing: F.K., A.D.A., M.Z., M.H., Analysis or Interpretation: M.Z., M.H., İ.D., G.K., H.U.D., M.A.Ü., Literature Search: F.K., M.H., Writing: F.K., E.Ü.

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# Determining the Difficulties of Parents with Children in Home Care Who Were Discharged from Intensive Care

## Çocuğu Yoğun Bakımdan Taburcu Edilen Ebeveynlerin Evde Bakımda Yaşadıkları Güçlüklerin Belirlenmesi

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### Abstract

**Introduction:** This study was performed to determine the difficulties experienced by parents with children in home care who were discharged from intensive care.

**Methods:** A phenomenological qualitative method was used to determine the difficulties experienced by the parents. The sample of the study consisted of parents (n=22) whose children met the inclusion criteria and needed home care. The data were analyzed in the MAXQDA qualitative data analysis program in accordance with Colaizzi's seven-stage method.

**Results:** The average age of the children in the study group was 85.63±58.40 months. 56.7% of them were male. 40% of the children were followed up with a diagnosis of neurological disease. All children discharged from the intensive care unit had tracheostomy. 95.4% of them used home-type mechanical ventilators, and 95.3% were fed enterally. In line with the data obtained from the interviews of the parents, it was determined that there were difficulties in terms of feelings about discharge, physical conditions for home care, family relationship, social relationship, difficulty in physical care, inadequacy in support systems and financial status.

**Conclusion:** The home care of children, who are dependent on medical technology and discharged from intensive care, is mostly performed by their families. Children dependent on medical technology should be supported by home care personnel to avoid potential risks.

**Keywords:** Home care, child, intensive care

### Öz

**Giriş:** Bu çalışma, çocuğu yoğun bakımdan taburcu edilen ebeveynlerin evde bakımda yaşadıkları güçlükleri belirlemek amacıyla yapılmıştır.

**Yöntemler:** Ebeveynlerin yaşadığı güçlüklerin belirlenmesinde fenomenolojik kalitatif yöntem kullanılmıştır. Çalışmanın örneklemini dahil edilme ölçütlerine uyan, çocuğu evde bakım gereksinimi olan ebeveynler (n=22) oluşturmuştur. Veriler, Colaizzi'nin yedi aşamalı yöntemi doğrultusunda MAXQDA nitel veri analiz programında analiz edilmiştir.

**Bulgular:** Çalışma grubundaki çocukların; ortalama yaşının 85,63±58,40 ay olduğu, %56,7'sinin erkek ve %40'ının nörolojik hastalık tanısı ile takip edildiği saptanmıştır. Yoğun bakımdan taburcu edilen çocukların tamamının trakeostomisi olduğu, %95,4'ünün ev tipi mekanik ventilatör kullandığı ve %95,3'ünün enteral yolla beslendiği belirlenmiştir. Ebeveynlerin görüşmelerinden elde edilen veriler doğrultusunda; taburculuğa ilişkin duygular, fiziki koşullar, aile ilişkisi, sosyal ilişki, fiziksel bakımda zorluk, destek sistemlerinde yetersizlik ve ekonomik güçlük olmak üzere yedi tema elde edilmiştir.

**Sonuç:** Yoğun bakımdan taburcu edilen tıbbi teknolojiye bağımlı çocuklar evde bakım hizmetleri ekiplerinden yeterince destek almamaktadır. Bu hastaların evde bakımları ailelere tarafından yapılmaktadır.

**Anahtar Kelimeler:** Evde bakım, çocuk, yoğun bakım

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## Introduction

Owing to the development of intensive care technologies, the number of patients who are taken care of at home (connected to a home mechanical ventilator) is increasing.<sup>1</sup> It has been determined that 6.6 out of every 100,000 people in Europe<sup>2</sup> 9.9 in Australia, and 12 in New Zealand<sup>3</sup> survive using a mechanical ventilator at home. The number of children in Turkey who are taken care of at home using a ventilator remained unknown.<sup>4</sup>

Patients who need intensive care survive more in parallel with technological developments. Some health problems of the intensive care patients, who are treated and followed up during the critical period, may become chronic in the future. Long-term stay of chronic intensive care patients in the intensive care leads to bed occupation, an increase in the cost, mortality, morbidity and workload. In order to use the limited number of intensive care beds more efficiently, to reduce the complications of staying in the intensive care unit, to provide moral support and to improve the quality of life, it is recommended that the stable intensive care patient whose emergency condition improves, should be taken care of at home.<sup>1,5-8</sup>

The length of hospital stay of patients is prolonged due to insufficient discharge planning and home care services. The home care team should coordinate the health care of children who are dependent on complex medical technology and need home care. In recent years, the number of children who are dependent on complex medical technology and followed up at home was reported to increase significantly.<sup>9</sup> It was emphasized that taking care of patients at home instead of the hospital has been cost-effective to if those patients needed long-term care. In the USA, the cost of daily care of intensive care patients connected to mechanical ventilators was reported to be between 600-1500 dollars,<sup>10,11</sup> whereas the monthly health care costs were 21,570 dollars in the intensive care and 7.050 dollars in home care and therefore the home care should be promoted.<sup>12</sup> It has been demonstrated that with the development of home care services, discharging children became easier and hospitalization reduced, in addition to many other advantages including social factors and low cost.<sup>13</sup> The needs of technology-dependent children and families should be clarified.<sup>9</sup> Determining the difficulties experienced in home care of children discharged from intensive care will provide more insight in terms of the management of home care services. This study was carried out to determine the difficulties experienced by parents with children in home care who were discharged from the intensive care unit.

## Study Question

What are the difficulties experienced by parents with children in home care who were discharged from the intensive care?

## Materials and Methods

### Type of Research

The research was carried out using the phenomenological research method from qualitative research. The data were obtained between January and June 2018 by using quantitative and qualitative methods. Qualitative research method was used to determine the difficulties experienced by parents in home care.<sup>14</sup> The obtained data were evaluated using Colaizzi's seven-stage data analysis method.<sup>15</sup>

### Study Population and Sample

The population of this study consisted of 42 children who were cared for at home after being discharged from the pediatric intensive care unit of a university hospital. In qualitative research, sample size varied according to sample diversity and data saturation.<sup>16</sup> Data saturation was achieved when no new information emerged in the interviews.<sup>17</sup> Therefore, the sample of the study consisted of 22 parents who agreed to participate in the study. Inclusion criteria for the study were: (1) The parent had a child who needed home care after intensive care, (2) the child was under 18 years old, (3) the parent had no communication problems (sight, hearing, mental), (4) the parent could speak Turkish.

### Data Collection Tools

"Descriptive information form" was used to describe the socio-demographic characteristics of the parents and the "Semi-structured interview form" was used to determine the difficulties experienced.

**Descriptive information form:** It was obtained by the "data collection form" prepared by the researchers in accordance with the current literature.<sup>1,2,18</sup> The data collection form consisted of 28 questions and two sections.

**Semi-structured interview form:** For the purpose determined in the research, the semi-structured interview form was prepared by the researchers in accordance with the literature in order to examine the feelings and difficulties of the parents in depth and to guide the interview.<sup>19-21</sup> There were 13 questions in the semi-structured interview form. Opinions of seven experts were taken for the content validity of the semi-structured interview form.

**Voice recorder:** Kingboss HS-27 voice recorder was used to record the interviews. The voice recorder had a capacity of 8 GB and can record for 24 hours.

### Data Collection

A pilot study was carried out with the data collection tools, which were finalized with expert suggestions. In the pilot

study, three parents were interviewed and these parents were not included in the sample.

The parents were informed about the purpose of the study by considering voluntariness in study participation, and their written and verbal consents were obtained.

In-depth interviews were conducted at home in accordance with the scheduled appointment. These interviews were performed by a researcher. During the interviews, audio recordings were made with the permission of the parents. After the data collection process was completed, the audio recordings were converted into written texts by the researchers.

### Statistical Analysis

Descriptive data were analyzed using number, percentage and mean statistical tests in the Statistical Package for Social Sciences (SPSS) 21.0 package program.

Colaizzi's seven-stage method was used for the analysis of qualitative data. At first, the voice conversations were recorded. Then, the interviews were deciphered using MAXQDA program. Each written transcript has been read multiple times by all authors. Secondly, important statements about the difficulties experienced by the parents were determined from the transcripts. Next, the important statements that emerged were formulated. At the fourth step, the formulated meanings reflecting the difficulties experienced by the parents were grouped into clusters of seven themes. In the fifth step, the basic structure of the difficulties experienced by the parents were defined. At the last stage, the findings were confirmed by contacting the parents again (Colaizzi, 1978). The relationship of codes with subcodes was analyzed with MAXQDA in coding and creating themes.

For the internal validity of the study, a semi-structured interview form was created in line with the literature. As a result of the content analysis, integrity was ensured by checking the hierarchical relationship between themes, codes and subcodes. In addition, an expert opinion was consulted at this stage. The texts belonging to two parents were randomly selected from the interview data and given to an expert in this field and expert confirmation was provided to ensure that the data collected during the interview reflected the real situation. At the same time, all of the findings obtained from the parents were given directly without comment.

For the external validity of the study, the researcher submitted all data collection tools, raw data, coding made during the analysis phase, and the perceptions, notes, writings and inferences that form the basis of the report to the expert review and confirmation review was carried out. In addition, the findings were verified by contacting the parents again.

## Results

The average age of the children enrolled in the study was  $85.63 \pm 58.40$  (min-max: 15-216) months. 54.5% (n=12) of them were boys and 45.5% (n=10) of them were girls. The mean ages of the mothers and fathers were  $35.13 \pm 6.48$  (min-max: 28-53) and  $39.23 \pm 6.38$  (min-max: 28-53) years respectively.

When the diagnoses of the children in the study group were examined, it was detected that 36.3% (n=8) of them were discharged with a neurological disease. The rest of the children were discharged with a metabolic disease (31.8%, n=7), drowning (13.6%, n=3) and post-op non-extubating and an infectious disease (9%, n=2). It was determined that the children who were taken care of at home after the intensive care unit spent an average of  $64.43 \pm 42.45$  (min-max: 15-180) days in the intensive care unit, and  $27.40 \pm 21.16$  (min-max: 4-94) months at home (Table 1).

The findings revealed that all of the children were discharged with tracheostomy. 95.4% of them used home-type mechanical ventilators, and 95.3% of them were fed with enteral nutritional support systems (gastrostomy, nasogastric or orogastric tube) (Table 2).

**Table 1. Characteristics of children and families (n=22)**

Characteristics	Min-max	Mean $\pm$ SD
<b>Length of stay in intensive care (days)</b>	15-180 days	64.43 $\pm$ 42.45
<b>Length of stay in the service (days)</b>	7-210 days	46.78 $\pm$ 58.78
<b>Home care period (months)</b>	4-94 months	27.40 $\pm$ 21.16
	<b>n</b>	<b>%</b>
<b>Mother's education</b>		
Primary school	12	54.5
Middle school	6	27.3
Higher education	4	18.2
<b>Father's education</b>		
Primary school	7	31.8
Middle school	10	45.4
Higher education	5	22.8
<b>Occupation status of parents</b>		
Mother not working	20	90.9
Father not working	2	0.9
<b>Family type</b>		
Nuclear family	19	86.3
Extended family	3	13.7
<b>Family income</b>		
Income less than expenses	11	50
Income equal to expenses	10	45.4
Income more than expenses	1	4.6
SD: Standard deviation		



When the trainings given while preparing for discharge were examined, it was observed that all families were informed about care practices (mouth, eye, general body care, etc.), tools used, what to do in an emergency, aspiration and nutrition. 90.9% (n=20) of the families were informed about treatment practices and tracheostomy care. Similarly, 90.9% (n=20) of them were trained for wound care and infection prevention, and 63.6% (n=14) of them were informed about basic life support training. It was detected that 90.9% (n=20) of the mothers and 9.1% (n=2) of the others took care of the child after discharge.

86.7% of the families applied to the home health services center, but only 36.7% of them benefited from these services. When the services provided by the home health services center were investigated, it was determined that 60% of the families did not receive any service, 23.3% of them received medical treatment/follow-up, 6.7% of them had physiotherapy, 6.7% of them had care and finally one person received an ambulance service.

When the services provided by the home care teams were examined, it was detected that the blood was withdrawn from six patients for the laboratory, wound care was provided to two patients and psychological support was provided to one patient. Tracheostomy replacement, tracheostomy care, aspiration, nasogastric/orogastric tube and urinary catheter

insertion, body care etc. were not performed by home care teams.

### Content Analysis of Qualitative Findings

In accordance with the data obtained from the interviews of the parents within the scope of the study, seven themes were obtained including feelings about discharge, physical conditions for home care, family relationship, social relationship, difficulty in physical care, inadequacy in support systems and financial difficulties.

#### Theme 1. Feelings About Discharge

In this section, the feelings that parents had when they first learned that they would be discharged are discussed. In this theme, care-related inadequacy anxiety, worry, fear, uneasiness, helplessness, burnout, lack of self-confidence, hope and joy/happiness codes exist (Figure 1). The subcode hierarchical map of parents' feelings about discharge has been given in Figure 1.

Some of the parents stated that they experienced anxiety about being inadequate especially regarding the care of the child. *"It was very terrible. At first, I couldn't even aspirate, my spouse did."*(K4). More than half of the parents declared that they felt fear, anxiety and uneasiness when they learned that their child would be discharged. *"Since I saw it for the first time, I felt bad at first. I was thinking about what to expect and how to do it. I was worried"* (K17). Some other parent added *"We had questions about whether we would have problems with the electricity. What would we do if it's gone? I was very afraid about intervening. If something would happen."* (K12). One other parent said, *"The ventilator made us quite nervous"* (K8).

Some of the parents reported that they experienced helplessness and burnout. *"... when the doctor says, let's*

Table 2. Preparations for home care at discharge		
Characteristics	n	%
<b>Getting home from the hospital</b>		
By themselves	5	22.7
Support of the home health services center	1	4.6
112 ambulance	15	68.1
Municipal ambulance	1	4.6
<b>Being ready to be discharged</b>		
Yes	18	81.8
No	4	18.2
<b>Home support systems*</b>		
Tracheostomy	22	100
Household mechanical ventilator	21	95.4
Gastrostomy	8	36.3
Nasogastric/orogastric	13	59.0
<b>Re-hospitalization after discharge</b>		
Yes	13	59.0
No	9	41.0
<b>Number of re-hospitalizations after discharge (n=13)</b>		
1 time	6	46.2
2 times	3	23.0
3 or more times	4	30.8

\*: The patient has more than one support system

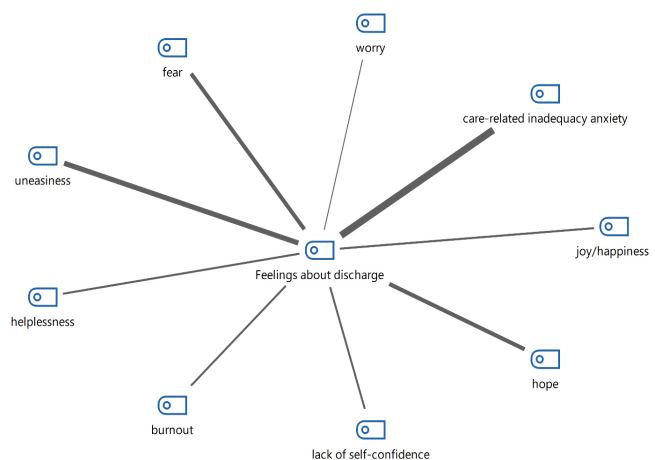


Figure 1. Feelings about discharge code-subcode sections model

discharge you, you can get out now; my direct thought was, okay, there was nothing left to do, you could go. He thought there was nothing left to do" (K3). One of the parents reported having lack of self-confidence regarding the care. "There are things we see for the first time. There were a lot of devices, a lot of things I had to do. I thought I couldn't be able to..." (K22).

Two of the parents stated that they felt hope and joy/happiness when they found out that their child would be discharged. "He had a tracheostomy and we were going to go out with a ventilator. After all this was also a step forward and we could go home. It was about the recovery process" (K6). Another parent said, "I was so glad. I felt on top of the world. Going home made me have great joy. We would be more comfortable at home ..." (K15).

One parent added, "I could rest at home and have a better time with my children. I could provide better opportunities for my children." (K18).

## Theme 2. Physical Conditions for Home Care

This theme includes the physical conditions of the parents whose children were taken care of at home. This theme consists of special room reservation, staying in the same room and cleaning/hygiene increasing codes. (Figure 2). The subcode hierarchical map of the parents' physical conditions for home care is demonstrated in Figure 2.

Some of the parents stated that they reserved a private room for their children. "We tried to provide a room. We were using it as a cellar, we prepared the room for him first" (K11). The vast majority of parents declared that they were more careful about the hygiene of their houses after their children were discharged. "We don't even let anyone else into my child's room except the two of us. We have quarantined. We keep everything clean." (K5).

Several parents reported that they had to stay in the same room with their children. "He still sleeps with us because I

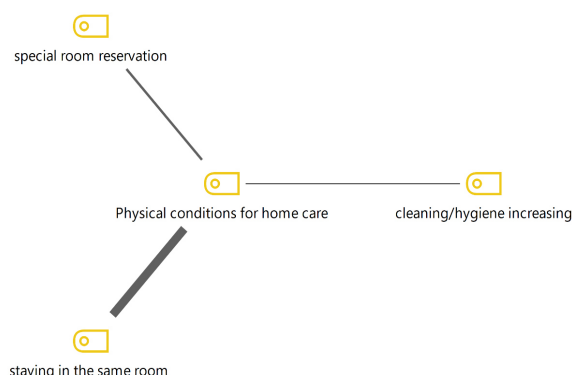


Figure 2. Physical condition for home care code-subcode sections model

feel the need to take care of him 24/7, we are always in the same room." (K14).

## Theme 3. Family Relationships

This theme includes the experience of the parents in the family relationship during the home care process. This theme consists of the codes to protect family integrity, difficulty in communication with family members, mother-centered care, taking time for oneself, touching and communicating with the child (Figure 3). The subcode hierarchical map of the family relationship of parents is given in Figure 3.

Almost all of the parents stated that they had difficulties in communicating and spending time with their family members. "We can't go anywhere together. When I go to my hometown, my wife stays at home. When she leaves, I stay. We can't spend time together" (K10). A parent mentioned that they had difficulty in maintaining family integrity due to the child's need for care. "I had to leave my other child to my mother or my older sister. This made me careless. I could not spend time with my spouse." (K19).

The majority of parents reported that they or their spouses had the responsibility of taking care of their children. "No one could take care of the way I did. I could leave her for an hour or two out of necessity and come quickly only when we went to the hospital. I took care of everything" (K7).

One of the parents mentioned that she was able to take time for herself because she took care of her child at home. "When I was at home, at least I could leave her to my husband and distract myself on Sunday. I could eat, buy clothes or something" (K20). Another parent stated that she could spend more time with her child because she took care of her child at home. "I used to leave the house in the morning and come back in the evening just to see my child for half an hour a day. All my time was spent in the traffic jam of Istanbul.

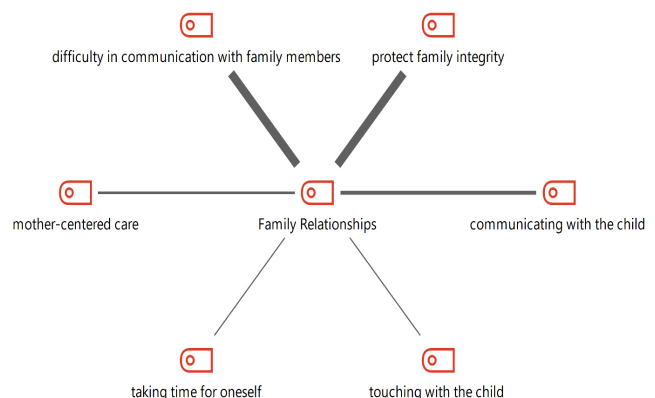


Figure 3. Family relationships code-subcode sections model

*At home, I could touch my child more and spend more time" (P16).*

**Theme 4. Social Relationship**

This theme includes the experience of the parents about their social relationship during the home care process. This theme consists of codes of loneliness, exclusion, child-centered life and visitor restriction (Figure 4). The subcode hierarchical map of the social relationship of parents is given in Figure 4.

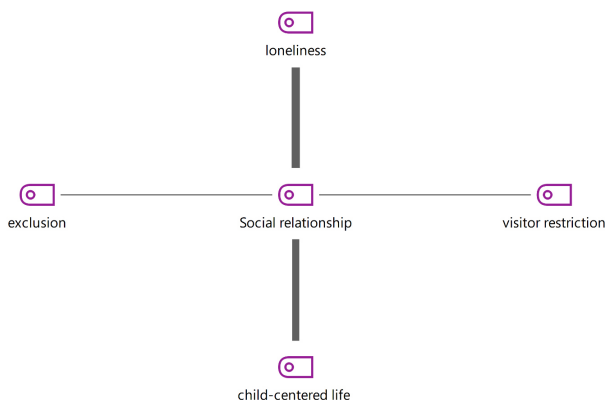
The majority of parents stated that their children felt lonely and excluded during the home care process. *"My social life was restricted. People were coming over, bu I could not go to them. In other words, my mother has been two streets away, but sometimes I couldn't visit them for two or three months" (P1).* Another parent said, *"When I started going out with my child recently, many families did not let their children be with my kid" (K4).*

Some parents confessed that their social life was restricted. *"You know, if A. had not been like this, maybe I would have been in Thailand with A. today" (K13).* Another parent added *"... at first, I did not let people into her room so that my child would not get infected" (K12).*

**Theme 5. Difficulty in Physical Care**

This theme includes statements about the parents' experiences in the physical care of their children. This theme consists of the codes of difficulty in feeding the child, difficulty in daily life activities, insomnia and difficulty in accessing health care services (Figure 5). The subcode hierarchical map of the parents' difficulty in physical care is shown in Figure 5.

Some parents stated that they had difficulties in feeding their children and performing activities of daily living. *"I did not know how to feed my child with those hoses, it was very difficult at first" (K2).* Another parent added, *"It was hard to carry him due to his weight. ...especially when it is shower time..." (K18).*



**Figure 4.** Social relationship code-subcode sections model

Almost half of the parents stated that they had insomnia due to the high care burden of their children. *"I was getting nervous every night, I waited by her side all the time in case something happens. Of course, I took medicine for 3 years ... now I only take it to sleep" (K9).* One of the parents reported that their child had difficulty in accessing health services. *"The concentrator (oxygen concentrator) broke down at night. My spouse called Ministry of Health. What they told us was there was nothing they could do. They said there was no machine in the institution if ours was broken down and we could take it back when it opens" (K20).*

**Theme 6. Inadequacy in Support Systems**

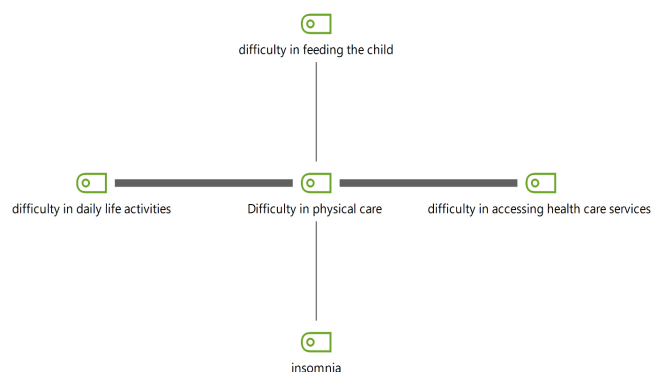
This theme includes inadequacy in support systems that the parents experience. This theme consists of insufficient social support, healthcare worker support, and spiritual support codes (Figure 6). The subcode hierarchical map of inadequacy in parents' support systems is demonstrated in Figure 6.

Some parents stated that the social support they received from their spouses, family, neighbors, relatives and health workers was insufficient. *"I have no spouse, no one but us" (K3).* Another parent added, *"We have been the only ones to take care and support. There has been no one to provide such support. If we had a very urgent job, we had to hire a paid nurse." (K8).*

One parent stated that spiritual support was useful for them. *"...I don't know, I pray a lot. You know, a lot. I'm reading the Quran. My support has always been spiritual." (K21).*

**Theme 7. Financial Difficulties**

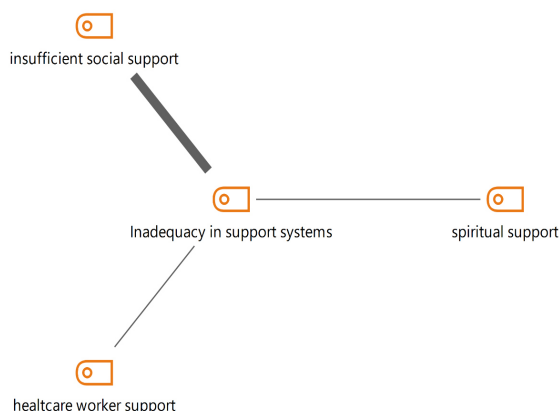
This theme includes financial difficulties that the parents experience. This theme consists of support codes for difficulty in obtaining medical supplies, power outage/lack of generator, one of the parents quitting job and care costs (Figure 7). The economic status subcode hierarchical map of the parents is shown in Figure 7.



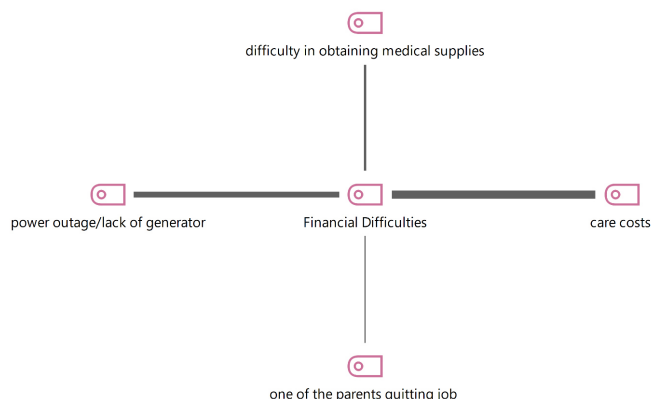
**Figure 5.** Difficulty in physical relationship code-subcode sections model

Two of the parents stated that their children had difficulty in obtaining medical supplies. *"First of all, we had a lot of financial problems. We had to pay for them since most of our materials were not covered by the report."* (K10). Another parent stated that she had difficulty due to a power cut/lack of generator. *"When there is an emergency, for instance when our electricity is cut-off, the machines did not have batteries ... I had to grab everything, look for people to help me. I called my nephew; he was somewhere else. Other people had things to do. This time the child turns purple, I call the ambulance, I have no money"* (K13).

One of the parents stated that he had to quit his job and had financial difficulties in caring for his child. *"I had my own company, you know what happens, it obviously bankrupted. When you don't care about your company, it fails. We had to shut it down. I'm not working now"* (K1). Another parent stated that they had financial difficulties due to high care costs. *"Unfortunately, children like S., how to say it, it is very sad to say but if you have money these children will live. There are a lot of maintenance costs. They can't live if you don't have money, that's all"* (K15).



**Figure 6.** Inadequacy in support systems code-subcode sections model



**Figure 7.** Financial difficulties code-subcode sections model

## Discussion

In order to use the limited intensive care capacity more efficiently, provide moral support when the patient goes back to the family environment, reduce the complications that increase the length of stay, and maintain and increase the quality of life; it is highly recommended to take care of the stable intensive care patients, whose vital functions have improved, at home.<sup>6</sup> Taking care of the children who need home care is more difficult than the others. The parents usually have difficulties in the care of these children in many aspects.<sup>22</sup> The findings obtained in this study, which was conducted to determine the difficulties experienced by the parents in the home care of the children discharged from the intensive care unit, were compared and discussed in accordance with the literature.

In this study, parents stated that they experienced many complex emotions when they found out that their child would be discharged. They reported that most of their feelings included being inadequate in the care of the child, anxiety, worry, fear, uneasiness, helplessness, burnout and lack of self-confidence. Children who are discharged from the intensive care unit and need home care should be fed with tracheostomy, ventilator support, gastrostomy and nasogastric tube. Parents who do not have the necessary skills to care for their child are known to be anxious. Teaching parents how to practice medical practices might reduce anxiety and stress levels.<sup>20,23</sup> In addition, two parents in the study group stated that they were hopeful and happy when they found out that their child would be discharged. In the literature, it was reported that parents usually prefer taking care of their children at home rather than the hospital.<sup>9</sup> Taking care of children with long-term care needs at home may be preferred to provide comfort to the child and family. However, technology-dependent children should be supported by home care teams considering possible risks at home.

In order to maintain a safe environment at home to the children discharged from intensive care, the home must be physically prepared. In addition, intensive care conditions should be made at home and security measures should be taken against all possible risks that may be encountered at home to increase the comfort of the child and family.<sup>24</sup> Some parents reported that they prepared a room in the house for their child before their children were discharged, whereas the others mentioned sleeping in the same room with their children. The vast majority of parents declared that they pay more attention to the hygiene of the house after the discharge. For at home care of children on mechanical ventilators, having a clean environment, optimal temperature and clean ventilation can reduce the risk of infection. Home care may need to be individualized in order to best meet

the complex requirements of children with special health care needs and their families. The physical conditions of the child at home should be arranged within the scope of family-centered care.<sup>9,24</sup>

In this study, all of the mothers stated that they or their spouses were primarily responsible for the care of their children, and they had difficulties in family relations, maintaining family integrity and communicating with family members. Similarly, previous studies demonstrated that the care burden of mothers was quite high.<sup>25-28</sup> It has been stated that it is not easy for parents to transfer their responsibilities to someone else.<sup>27</sup> Home care teams and social support systems should be well coordinated in order to support the family and the home care needs of children who are dependent on medical technology. When home care services and social support systems are insufficient, families continue their lives with individual solutions. However, the best results for all parties can be achieved with a family-centered, systematic and comprehensive care approach.<sup>9</sup>

Parents of children with home care needs often spend most of the day caring for their children. Therefore, social relations of parents are negatively affected.<sup>19,29</sup> In this study, parents stated that they lead a child-centered life because their children need home care. They also stated that they do not let people in when they want to come to their homes due to infection concerns, and they feel lonely and excluded. In the literature, it was declared that the parents think that people in their social circle do not understand the health status of their children and themselves. Parents are emotionally affected and feel socially excluded.<sup>27,30</sup>

In the study, parents reported that they had difficulties in feeding the child and performing daily life activities. These parents mentioned that they encountered problems in accessing health services. In a similar study, parents of children with tracheostomy connected to mechanical ventilator at home reported that the child had problems in feeding, positioning, and bathing.<sup>31</sup>

Similar to our findings, parents reported that they had problems in accessing health care. Studies showed that families who had difficulty in accessing health services feel safer in the hospital and prefer staying at the hospital.<sup>27</sup> In our country, technology-dependent patients, especially, have problems in accessing home care services.

Social support has been identified as one of the most common and effective strategies for coping with stress and maintaining psychological/physical well-being.<sup>32</sup> Although parents receive support from their spouses or families, social support seems to be insufficient for many parents. Family and friends have difficulties in understanding the situation of the child and the

parents.<sup>29,30,33</sup> Park<sup>34</sup> demonstrated that the care burden of parents with social support has been low. In a study of Boyden et al.<sup>28</sup>, social support was shown to reduce the burden of care. Similarly, Park and Lee<sup>35</sup> concluded that there was a positive relationship between social support and parental care burden. In this study, it was determined that parents need the support of health professionals for the care of their children. The support of the healthcare team is important to provide safety and comfort to the child and parents.<sup>23</sup>

Economic difficulties due to conditions that require long-term care, treatment and frequent hospitalization are a universal problem, especially for families with low socio-economic status.<sup>13,21</sup> Parents in the study group stated that their children had economic difficulties due to the cost of care. In similar studies, it has been observed that families of children who need home care have financial difficulties.<sup>28,33,36,37</sup> In addition, the work life of the parents of the child who needed home care has been negatively affected, which caused economic problems.<sup>33</sup> The impact of economic difficulties should be considered when coordinating home care services.

### Study Limitations

It was challenging to support the cases if the in-depth interviews were unstable in the home setting because the targeted patients resided in various İstanbul neighborhoods. Analysis of the independent variables' similarity was not possible.

### Conclusion

Children who are discharged from the intensive care unit and are dependent on mechanical ventilator are most likely taken care of by their families. The results of this study revealed that there were difficulties in terms of feelings about discharge, physical conditions for home care, family relationship, social relationship, difficulty in physical care, inadequacy in support systems and financial status. Children dependent on ventilators should be supported by home care personnel to avoid potential risks. Supporting families emotionally, socially and economically are highly recommended.

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### Ethics

**Ethics Committee Approval:** Ethical permissions were obtained from the public İstanbul University, İstanbul Faculty of Medicine Ethics Committee in order to conduct the study (23.12.2017, no: 48).

**Informed Consent:** Approval was obtained from the family of the participants.

### Authorship Contributions

Concept: G.B., D.S.D., G.U., Design: G.B., D.S.D., G.U., T.Y., Data Collection or Processing: G.B., D.S.D., T.Y., Analysis or Interpretation: G.U., A.K., Literature Search: G.B., D.S.D., G.U., A.K., Writing: G.B., D.S.D., G.U., A.K.

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

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# Thiamine Therapy During Refractory Lactic Acidosis in Critically Ill Children

## Kritik Hasta Çocuklarda Dirençli Laktik Asidoz Sırasında Tiamin Tedavisi

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### Abstract

**Introduction:** Thiamin deficiency, which is an overlooked but important cause of lactic acidosis, can lead to several clinical symptoms, including neuropathy, cardiogenic shock, and death, even though it can be easily treated in critically ill children.

**Methods:** A single-center, retrospective cohort study conducted between March 2020 and March 2022.

**Results:** Twenty-two patients were included in the study. The mean age was 26.5 (range, 1-214) months. The median thiamin dose was 50 (range, 3-100) milligrams and the mean thiamin treatment duration was 4 (range, 1-16) days. The mean length of PICU when thiamin treatment was started was 8 (range, 2-177) days. Thiamin treatment was administered on the 2<sup>nd</sup> (1-5) day of lactic acidosis. The mean lactate values after thiamin treatment was 5.5 (range, 5-17) mmol/L at the 6<sup>th</sup> hour, 4.1 (range, 1.5-17) mmol/L at the 12<sup>th</sup> hour, 3.1 (1.4-20) mmol/L at the 24<sup>th</sup> hour, and 2.7 (range, 0.15-17) mmol/L at 48<sup>th</sup> hour. Eleven (50%) patients' lactate levels decreased below 4 mmol/L at the 12<sup>th</sup> hour of thiamin treatment. Blood gas values before thiamin treatment, lactate decrease trends, thiamin treatments' duration, and form, and patients' risk factors were not statistically significant in the two groups by 28-day mortality.

**Conclusion:** We believe that in patients with lactic acidosis not directly related to a circulatory disorder, low clinical suspicion and early thiamin treatment of lactic acidosis is the right approach in the absence of specific diagnostic tests.

**Keywords:** Thiamin, lactic acidosis, children, pediatric intensive care unit

### Öz

**Giriş:** Laktik asidozun gözden kaçan ancak önemli bir nedeni olan tiamin eksikliği, kritik hasta çocuklarda kolaylıkla tedavi edilebilmesine rağmen nöropati, kardiyojenik şok ve ölüm gibi çok çeşitli klinik spektrumlara yol açabilmektedir.

**Yöntemler:** Mart 2020 ile Mart 2022 arasında tek merkezli, geriye dönük bir kohort çalışmasıdır.

**Bulgular:** Yirmi iki hasta çalışmaya dahil edildi. Ortalama yaş 26,5 (1-214) aydı. Ortanca tiamin dozu 50 (3-100) miligram ve ortalama tiamin tedavi süresi 4 (1-16) gündü. Tiamin tedavisine başlandığında hastaların ortalama çocuk yoğun bakım ünite süresi 8 (2-177) gündü. Laktik asidozun 2. (1-5) gününde tiamin tedavisi başlandı. Tiamin tedavisi sonrası ortalama laktat değerleri 6. saatte 5,5 (5-17) mmol/L, 12. saatte 4,1 (1,5-17) mmol/L, 24. saatte 3,1 (1,4-20) mmol/L olarak ve 48. saatte 2,7 (aralık, 0,15-17) mmol/L olarak belirlendi. Tiamin tedavisinin 12. saatinde 11 (%50) hastanın laktat düzeyi 4 mmol/L'nin altına düştü. Tiamin tedavisi öncesi kan gazı değerleri, laktat düşüş eğilimleri, tiamin tedavilerinin süresi, şekli ve hasta risk faktörleri her iki grupta da 28 günlük mortalite açısından istatistiksel olarak anlamlı değildi.

**Sonuç:** Dolaşım bozukluğu ile doğrudan ilişkili olmayan laktik asidozlu hastalarda, özgül tanı testlerinin yokluğunda düşük klinik şüphe ve laktik asidozun erken tiamin tedavisinin doğru yaklaşım olduğunu düşünüyoruz.

**Anahtar Kelimeler:** Tiamin, laktik asidoz, çocuklar, çocuk yoğun bakım ünitesi

### Introduction

High or increasing lactate levels in the blood usually mean inadequate oxygen delivery or cellular hypoxia in pediatric

intensive care units (PICUs). Generally, mortality risk increases when blood lactate levels are the highest or lactate normalization times are increased.<sup>1</sup> Hyperlactatemia refers to lactate levels above 2 mmol/L, and lactic acidosis refers

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to serum lactate concentration above 4 mmol/L. Arterial pH levels decrease when lactic acidosis emerges as an acid-base disorder. At the same time, other coexisting disorders may increase pH levels to the normal range or higher levels. Lactic acidosis occurs when lactic acid production exceeds lactic acid clearance.<sup>2</sup> Children with thiamin deficiency who are incapable of oral feeding and receive total parenteral nutrition (TPN) need age-appropriate thiamin support.<sup>3</sup>

It has been shown in the medical literature that thiamin deficiency contributes to mortality in critically ill children who have shock and lactic acidosis. Thiamin is mostly absorbed in the duodenum and ileum. Oral and intravenous thiamin treatments have similar effects on recovering lactic acidosis.<sup>1</sup> Irreversible neurological deficits can occur in untreated thiamin deficiency.<sup>4</sup> In this study, we aimed to investigate the relationship between thiamin and the related status of patients with lactic acidosis who received thiamin treatment. Also, to investigate patients' demographic data, the outcomes of those who were diagnosed as having thiamin deficiency during diagnosis and treatment, and thiamin's effects on mortality.

## Materials and Methods

### Setting

This study was conducted in the PICU of a university hospital. In our PICU, intensive care services are provided to patients in non-surgical and surgical departments, and approximately 700 patients are followed up annually. Our PICU is a combined unit offering both pediatric and cardiac critical care. Written permission was obtained from the Local Ethics Committee of Ankara University Hospital for this study (ethics committee number: İ09-566-22). Our study was conducted in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association.

### Study Population and Protocol

This study was conducted retrospectively by scanning patients between 2020 and 2022 who had refractory (>24 hours) lactate rise (<2 mmol/L) and lactic acidosis (>4 mmol/L) and received thiamin treatment. Thiamin was given 3-100 mg orally, intravenously (IV), or intramuscularly (IM). Treatment was continued for 5 days if there was a positive treatment response or for 10 days if thiamin levels were monitored and a low level was detected. We mostly prefer the IM form of thiamin even though the available form of thiamin in our hospital pharmacy affects our choice. The inclusion criteria were lactate rise or lactic acidosis lasting 24 h or more and no recently developed hemodynamic problems or an oxygenation problem that explained lactic acidosis. The exclusion criteria

were acute hepatic failure, mitochondrial diseases, or cardiac arrest.

### Follow-up

The data of 22 patients who met the inclusion criteria including age, weight, thiamin dosage, thiamin form, thiamin treatment duration, thiamin levels if possible, respiratory distress, inotrope usage, anemia existence, abnormal liver function tests, abnormal renal function tests, history of metabolic diseases, history of abdominal surgery, accompanying malignancy, the existence of oral or enteral feeding when lactic acidosis was identified, TPN treatment, imaging in suspected thiamin deficient patients, ICU length of stay, and 28-day mortality were recorded. Blood gas (pH, pCO<sub>2</sub>, HCO<sub>3</sub>, lactate) before thiamin treatment and lactate levels at 6, 12, 24, 48, and 72 h after thiamin treatments were recorded.

### Definitions

Lactate rise and lactic acidosis: A lactate rise above 4 mmol/L regardless of whether the pH level is low, normal, or high.<sup>2</sup> Refractory lactate rise: A lactate rise persisting for 24 h or more and cannot be explained by any other reason. VIS: Vasoactive inotrope score.<sup>5</sup>

### Statistical Analysis

The data were analyzed using SPSS version 26.0 software (IBM Corp, Armonk, NY). The mean, standard deviation, median, frequency distribution, and percentage values were determined as descriptive statistics of the variables. Mean values were used in parametric tests and median values in non-parametric tests. Pearson's chi-square test and Fisher's Exact test were used to analyze categorical variables. The data were tested for normal distribution using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). The independent samples t-test was used to analyze differences in normally distributed variables between the two independent groups. The Mann-Whitney U test was used to analyze the differences between the median values of non-normally distributed variables. P-values of <0.05 were considered statistically significant.

## Results

We enrolled 22 patients who had refractory lactate rise or lactic acidosis and received thiamin treatment. These 22 patients met the inclusion criteria, had refractory lactate rise or lactic acidosis, and received thiamin treatment in the 2-year study period.

### Patient Demographic Data (22 Patients)

Twenty-two patients were included in the study. The mean age was 26.5 (range, 1-214) months. The median thiamin dose

was 50 (3-100) milligrams and the median thiamin treatment duration was 4 (range, 1-16) days. The patients' mean length of PICU stay when thiamin treatment was initiated was 8 (range, 2-177) days. Thiamin treatment was administered on the 2<sup>nd</sup> (range, 1-5) day of lactic acidosis. Thiamin treatment was administered IV to two (9%), IM to 15 (68%) patients, and orally to five (23%) patients. Thiamin levels were obtained in 2 of 22 (9%) patients. Six patients had malignancies [ganglioneuroblastoma, T-cell acute lymphoblastic leukemia (T-ALL), hemophagocytic lymphohistiocytosis (HLH), B-cell acute lymphoblastic leukemia (B-ALL), acute myeloid leukemia, craniopharyngioma). Two (9.2%) patients had metabolic disease [fatty acid oxidation defect, methylmalonic acidemia (MMA)], five patients had respiratory distress and respiratory failure (viral pneumonia n=4, Coronavirus disease-2019 pneumonia n=1), five had cardiac disease (Fallot tetralogy; cardiac arrest due to food aspiration in a patient who was post-op for pulmonary artery binding surgery and had heart failure secondary to anemia), and four (18.2%) patients had other etiologies (convulsion n=3, arteriovenous malformation n=1) and were followed up in our PICU.

### Post-thiamin Treatment Lactate Trend

Seventeen of the 22 patients had a significant lactate decrease after thiamin treatment. The mean lactate values after thiamin treatment were 5.5 (5-17) mmol/L at the 6<sup>th</sup> hour, 4.1 (1.5-17) mmol/L at the 12<sup>th</sup> hour, 3.1 (1.4-20) mmol/L at the 24<sup>th</sup> hour, and 2.7 (0.15-17) mmol/L at the 48<sup>th</sup> hour. Eleven patients (50%), lactate levels decreased below 4 mmol/L at the 12<sup>th</sup> hour of thiamin treatment (Figure 1). Patient characteristics and thiamin treatment outcomes are shown in Figure 2. Patient characteristics and incidence of 28-day mortality

When patients were analyzed in two groups by 28-day mortality (survivor and non-survivor); age, weight, and length of stay in the PICU were statistically significant ( $p=0.04$ ,  $p=0.02$ , and  $p=0.01$ , respectively). Thiamin treatment start days were found to be statistically significant between the living and deceased groups ( $p=0.02$ ). Blood gas values before thiamin treatment, lactate decrease trends, thiamin treatments' duration, and form, and patients' risk factors were not statistically significant in either group (Table 1, Figure 3).

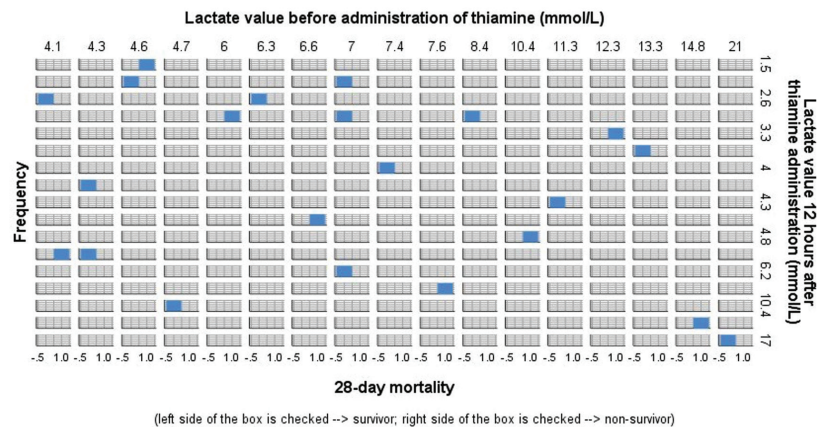


Figure 1. Post-thiamin treatment lactate trend

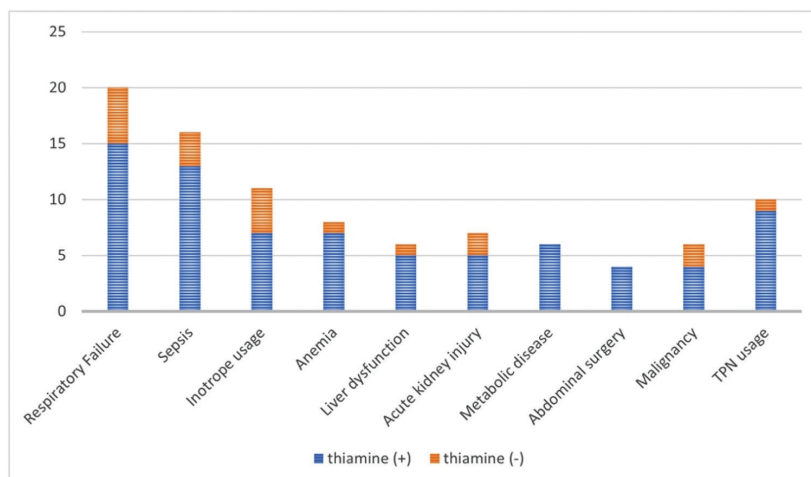
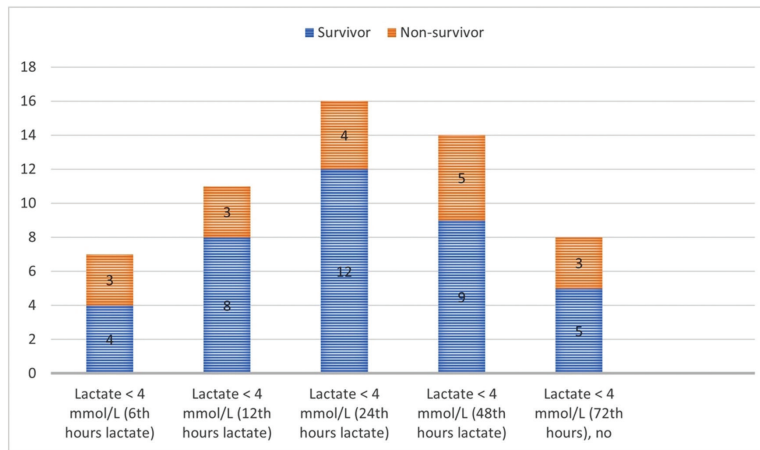


Figure 2. Patients' characteristics and thiamin treatment outcomes

<b>Table 1. The patient characteristics and outcomes according to the 28-day mortality</b>				
<b>Parameters</b>	<b>All patients (n=22)</b>	<b>28-day mortality, survivor (n=14)</b>	<b>28-day mortality, non-survivor (n=8)</b>	<b>p-value</b>
Age (months)	26.5 (1-214)	57.0 (2-191)	5.7 (1-214)	<b>0.04*</b>
Weight (kg)	14 (2.7-50)	23.0 (4.6-50)	5.3 (2.7-40)	<b>0.02*</b>
Thiamine dose (mg)	50 (3-100)	50.0 (3-100)	50.0 (13-100)	0.71*
Thiamine, days	4 (1-16)	5.0 (1-16)	2.0 (1-9)	0.57*
Enteral nutrition, no, days (until LA)	4 (0-45)	3.5 (0-45)	5.5 (0-11)	0.97*
PRISM III score	9±5.6	7.9±5.6	10.8±5.3	0.24**
PELOD 2 score	15.6±9.4	14.9±9.5	17±9.8	0.63**
VIS score	2.5 (0-92)	0 (0-35)	12.5 (0-92)	0.18*
CRRT, yes	5 (100%)	3 (21%)	2 (25%)	0.84***
PEX, yes	6 (100%)	4 (28%)	2 (25%)	0.85***
ECMO, yes	3 (100%)	1 (7%)	2 (25%)	0.24***
Duration of lactic acidosis (until treatment)	2 (1-5)	2 (1-4)	2 (1-5)	0.97*
Thiamine treatment day	8 (2-177)	4 (2-83)	14.5 (4-177)	<b>0.02*</b>
<b>Pre-thiamine treatment laboratory values</b>				
pH	7.39±0.05	7.39±0.04	7.39±0.07	0.96**
pCO <sub>2</sub>	37.5 (17-58)	37.2 (17-43.5)	40.2 (27-58)	0.19*
HCO <sub>3</sub>	23.0±5.7	21.7±4.0	25.4±7.6	0.15**
Lactate (mmol/L)	7 (4-21)	7.0 (4-21)	7.1 (4.1-14.8)	0.70*
<b>Post-thiamine treatment lactate values</b>				
6 <sup>th</sup> hours lactate (mmol/L)	5.5 (5-17)	5.4 (1-17)	5.3 (0.5-13.2)	0.83*
12 <sup>th</sup> hours lactate (mmol/L)	4.1 (1.5-17)	3.7 (2-17)	4.6 (1.5-13.2)	0.47*
24 <sup>th</sup> hours lactate (mmol/L)	3.1 (1.4-20)	2.9 (1.4-20)	3.9 (2.6-14.3)	0.11*
48 <sup>th</sup> hours lactate (mmol/L)	2.7 (0.5-17)	2.3 (0.5-17)	2.9 (1.2-17)	0.63*
<b>Post-thiamine treatment lactate trends</b>				
Lactate <4 mmol/L (12 <sup>th</sup> hours), yes	11 (100%)	8 (57.1%)	3 (37.5%)	0.37***
Lactate <4 mmol/L (48 <sup>th</sup> hours), yes	17 (100%)	11 (78.5%)	6 (75.0%)	0.84***
<b>Thiamine administration (iv, oral, im)</b>				
Intravenous	2 (100%)	1 (87.5%)	1 (12.5%)	0.66***
Intramuscular	15 (100%)	9 (64.2%)	6 (75.0%)	
Oral	5 (100%)	4 (28.5%)	1 (12.5%)	
<b>Patients characteristics</b>				
Respiratory failure, yes	19 (100%)	11 (78.5%)	8 (100%)	0.15***
Sepsis, yes	16 (100%)	10 (71.4%)	6 (75%)	0.85***
Inotrope usage, yes	11 (100%)	6 (42.8%)	5 (62.5%)	0.37***
Anemia, yes	8 (100%)	6 (42.8%)	2 (25.0%)	0.40***
Liver dysfunction, yes	6 (100%)	2 (14.2%)	4 (50%)	0.07***
Acute kidney injury, yes	7 (100%)	5 (35.7%)	2 (25.0%)	0.60***
Abdominal surgery, yes	4 (100%)	3 (21.4%)	1 (12.5%)	0.60***
Malignancy, yes	6 (100%)	5 (35.7%)	1 (12.5%)	0.24***
TPN usage, yes	10 (100%)	7 (50.0%)	3 (37.5%)	0.57***
PICU length of stay, days	17 (3-242)	10.5 (3-116)	35.0 (15-242)	<b>0.01*</b>
ECMO: Extracorporeal membrane oxygenation, VIS: Vasoactive inotropic score, PRISM III: Pediatric Risk of mortality, PELOD 2: Pediatric logistic organ dysfunction, CRRT: Continuous renal replacement therapy, PEX: Plasma exchange, TPN: Total parenteral nutrition, PICU: Pediatric intensive care unit, LA: Lactic acidosis, *: Mann-Whitney U test, ** Independent samples t-test, ***: chi-square test				



**Figure 3.** Lactate trends and 28-day mortality outcomes

### Patient Characteristics and 24<sup>th</sup>-hour Lactate Levels

When patients were analyzed in two groups by whether lactate levels at the 24<sup>th</sup> hour were below 4 mmol/L, bicarbonate values were found to be statistically significant ( $p=0.01$ ). Lactate levels at the 24<sup>th</sup> hour of thiamin treatment were found to be statistically significant in both groups ( $p=0.02$ ). Blood gas levels except for bicarbonate level, lactate decrease trend, thiamin treatments' duration, and form, and patients' risk factors except for acute kidney injury were not statistically significant in either group (Table 2).

### Characteristics of Patients Unresponsive to Thiamin Therapy (n=8)

Four of eight patients (50%) for whom thiamin treatment was unsuccessful died in the PICU. The patients' diagnoses were HLH (n=1, 12.5%), MMA (n=1, 12.5%), T-ALL (n=1, 12.5%), EBV-related lymphoma (n=1, 12.5%), pneumonia (n=2, 12.5%), arteriovenous malformation (n=1, 12.5%), and postoperative pulmonary binding surgery (n=1, 12.5%).

### Discussion

Thiamin deficiency is an important cause of lactic acidosis, and a wide clinical spectrum, including neuropathy and cardiogenic shock, is observed. Thiamin deficiency may be fatal for critically ill children in the PICU. We aimed to assess the relationship between thiamin and the related status of patients with lactic acidosis who received thiamin treatment. In our study, we investigated patient characteristics and the effects of thiamin treatment on patients.

Fourteen (63.6%) patients' lactate levels who were given thiamin treatment decreased below 4 mmol/L after 24 h of treatment. Thiamin dosage, treatment form, blood gas levels before treatment, patients' risk factors, and lactate decrease trend were not found to be statistically significant between

the two groups that were responsive to thiamin treatment. When patients were evaluated by 28-day mortality, there was no statistical significance between lactate levels before thiamin treatment and mortality.

There is a strong relationship between mortality, morbidity, tissue hypoxia, hypoperfusion, and lactate levels in both shock models and clinical studies.<sup>6</sup> The higher the lactate levels, the longer the time of normalization, and the greater the risk of death. Vincent et al.'s<sup>7</sup> study, which evaluated lactate clearance in 96 patients from different disease groups, showed a correlation between steady lactate decrease and lower mortality rate in all disease groups. Abbas et al.'s<sup>8</sup> single-variable retrospective study on 202 patients showed a correlation between lactate rise, multiple organ dysfunction syndrome (MODS) development, and mortality. Lactate rise and MODS development were correlated with mortality in multivariate logistic regression analysis, and hyperlactatemia was correlated with poor prognosis in PICU stay.<sup>8</sup> Hatherill et al.'s<sup>9</sup> study, which evaluated 24-h lactate trends after PICU admission, found a correlation between hyperlactatemia and high mortality in children. Sachdev et al.'s<sup>10</sup> logistic regression analysis study on 172 patients admitted to a PICU for dengue fever stated that 24<sup>th</sup>-hour mortality was an important indicator. Thiamin deficiency was not associated with mortality in our study. Due to the design of our study, we believe that the diagnosis of thiamin deficiency depending on whether the treatment works or not. We concluded that there was no association between thiamin deficiency and 28-day mortality, primarily because we did not consider thiamin deficiency in clinically unstable patients.

Vincent et al.'s<sup>7</sup> study on patients' lactate clearance in different disease groups (sepsis, septic shock, cardiogenic shock, and respiratory failure in the general surgery ICU, general ICU, and cardiac ICU) detected similar results in lactate clearance and kinetics of different patient groups. Most

studies found a significant difference in the lactate trend at 6, 12, and 24-h or shorter intervals.<sup>7</sup> Teagarden et al.<sup>11</sup> showed lactate normalization in 30 h of a newborn who received extracorporeal membrane oxygenation (ECMO) support for respiratory failure, and Ramsi et al.<sup>12</sup> reported a 16-year-old

patient's notable decrease in lactate levels and recovery of metabolic acidosis after one dose of thiamin treatment whose lactate levels increased up to 35 mmol/L after inotrope support for MODS.<sup>11,12</sup> Lerner et al.<sup>13</sup> found that after thiamin treatment in two patients aged 4 and 10 years with refractory

**Table 2. The patient characteristics and outcomes according to the 24<sup>th</sup>-hour lactate level**

Parameters	All (n=22)	Lactate <4 mmol/L (24 <sup>th</sup> hours), yes (n=14)	Lactate <4 mmol/L (24 <sup>th</sup> hours), no (n=8)	p-value
Age (months)	26.5 (1-214)	18 (2-214)	37 (1-191)	0.73*
Weight (kg)	14 (2.7-50)	12 (2.7-50)	15 (3.5-41)	0.94*
Thiamine dose (mg)	50 (3-100)	50 (3-100)	50 (10-100)	0.35*
Thiamine, days	4 (1-16)	3 (1-16)	6 (1-9)	0.36*
Enteral nutrition, no, days (until LA)	4 (0-45)	3.5 (0-20)	5 (0-45)	0.58*
PRISM III score	9±5.6	12.6±4.2	6.9±5.2	0.13**
PELOD 2 score	15.6±9.4	17.1±11.1	14.8±8.6	0.59**
VIS score	2.5 (0-92)	20 (0-92)	0 (0-35)	0.17*
CRRT, yes	5 (100%)	3 (21%)	2 (25%)	0.84***
PEX, yes	6 (100%)	3 (21%)	3 (37.5%)	0.41***
ECMO, yes	3 (100%)	1 (7%)	2 (25%)	0.24***
Duration of lactic acidosis (until treatment)	2 (1-5)	2 (1-5)	2 (1-4)	0.97*
Thiamine treatment day	8 (2-177)	12.5 (2-177)	6 (2-83)	<b>0.02*</b>
<b>Pre-thiamine treatment laboratory values</b>				
pH	7.39±0.05	7.40±0.05	7.37±0.05	0.18**
pCO <sub>2</sub>	36.9±9.8	38.4±10.7	34.3±7.8	0.31**
HCO <sub>3</sub>	23.0±5.7	25.1±5.8	19.4±3.7	<b>0.01**</b>
Lactate (mmol/L)	8.0±4.3	7.31±2.7	9.2±6.2	0.42**
<b>Post-thiamine treatment lactate values</b>				
6 <sup>th</sup> hours lactate (mmol/L)	6.0±3.9	5.26±2.7	7.3±5.3	0.34**
12 <sup>th</sup> hours lactate (mmol/L)	4.1 (1.5-17)	3.2 (1.5-10.4)	4.7 (2.6-17)	0.12*
48 <sup>th</sup> hours lactate (mmol/L)	2.7 (0.5-17)	2.3 (0.5-6)	4.8 (1.2-17)	0.14*
<b>Patients characteristics</b>				
Respiratory failure, yes	19 (100%)	12 (85.7%)	7 (87.5%)	0.90***
Sepsis, yes	16 (100%)	10 (71.5%)	6 (75%)	0.85***
Inotrope usage, yes	11 (100%)	5 (35.7%)	6 (75%)	0.07***
Anemia, yes	8 (100%)	6 (42.8%)	2 (25%)	0.4***
Liver dysfunction, yes	6 (100%)	4 (28.5%)	2 (25%)	0.85***
Acute kidney injury, yes	7 (100%)	4 (28.5%)	3 (37.5%)	0.66***
Metabolic disease, yes	2 (100%)	2 (14.2%)	0 (0%)	0.26***
Abdominal surgery, yes	4 (100%)	3 (21.4%)	1 (12.5%)	0.6***
Malignancy, yes	6 (100%)	4 (28.5%)	2 (25%)	0.85***
TPN usage, yes	10 (100%)	7 (50%)	3 (37.5%)	0.57***
PICU length of stay, days	17 (3-242)	15.5 (3-116)	20.5 (6-242)	0.49*
28-day mortality	8 (100%)	4 (28.5%)	4 (50%)	0.31***
ECMO: Extracorporeal membrane oxygenation, VIS: Vasoactive inotropic score, PRISM III: Pediatric Risk of mortality, PELOD 2: Pediatric logistic organ dysfunction, CRRT: Continuous renal replacement therapy, PEX: Plasma exchange, TPN: Total parenteral nutrition, PICU: Pediatric intensive care unit, LA: Lactic acidosis, *: Mann-Whitney U test, **: Independent samples t-test, ***: chi-square test				

lactic acidosis and hematologic malignancy, the lactate value decreased to the normal range within 2 h in the 4-year-old patient and approximately 6 h in the 10-year-old patient. Similar to studies in the literature, we evaluated 6-12-24 and the 48-hour lactate trends in our clinical study. Twelve (50%) patients' lactate levels decreased below 4 mmol/L at the 12<sup>th</sup> hour, and 14 (63.6%) patients' lactate levels decreased below 4 mmol/L at the 24<sup>th</sup> hour. Only three (12.5%) patients' thiamin levels were obtained and found to be low. The greatest obstacle to obtaining thiamin levels for the patients was the availability of the necessary kit in our clinical center and the obligation to transport blood in optimal conditions to a private laboratory. Thiamin treatment decision times were the greatest obstacles to obtaining necessary blood samples and transportation to the available laboratory because 11 (45.8%) were on weekdays after working hours and 6 (25%) were on weekends. Given the results of other related studies, if a patient had not shown a response to thiamin treatment after 24 h, we did not consider a diagnosis of thiamin deficiency in the patient. Akkuzu et al.'s<sup>14</sup> prospective study researched thiamin deficiency prevalence and duration in 476 pediatric patients in three PICUs, including our clinical center and detected the thiamin deficiency prevalence as 11.1%. Thiamin deficiency risk is increased in patients undergoing solid organ transplantation, gastrointestinal surgery, malignancy, systemic diseases in PICUs, and TPN.

Thiamin is a water-soluble vitamin that has a significant role in energy metabolism; therefore, a wide spectrum of metabolic, neurologic, cardiovascular, respiratory, gastrointestinal, and musculoskeletal problems are observed in its deficiency.<sup>15</sup> Our clinical center participated in Akkuzu et al.'s<sup>14</sup> study, which included 24 patients whose treatment was over 2 years. During that period, we predicted that 155 patients with thiamin deficiency were admitted to our clinical center; 700 patients were admitted during the same period. Because the inclusion and exclusion criteria were applied similarly to patients with refractory lactic acidosis and lactate rise in the last 2 years, thiamin deficiency was not considered in some symptomatic patients whose thiamin deficiency contributed to clinical worsening or in patients on TPN who received thiamin supplements unknowingly because TPN includes a thiamin supplement. We concluded that patients' features that could create a risk factor for thiamin deficiency did not affect 28-day mortality.

In summary, there is no proven treatment regime for thiamin deficiency specific to infants and children, and every clinical center empirically decides its dosage and form of treatment. The lowest thiamin dose in our study was 3 mg, and it was administered to a patient who had undergone a solid organ transplant whose lactate levels increased up to 11.9 mmol/L

on the 21<sup>st</sup> follow-up day of cardiac arrest after the glucose infusion rate was increased from 3 mg/kg/minutes to 7 mg/kg/minutes. Oral thiamin (2.5 mg) was administered to the patient because they had intestinal perforation and were on TPN without thiamin supplements. Lactic acidosis quickly resolved after thiamin treatment. Lactate levels decreased to 0.9 mmol/L in 24 h. We have seen a dramatic response to thiamin treatment even at low doses.

### Study Limitations

The greatest limitations of this study were that it was a retrospective study, the study was conducted in a relatively small patient group, and thiamin levels could not be obtained from most of the patients. In our study, thiamin deficiency was not associated with mortality. In our study, we believe that one of the reasons for the no relationship detected between thiamin deficiency and 28<sup>th</sup>-day mortality was not diagnosed thiamin deficiency in clinically unstable patients.

### Conclusion

Thiamin is not an uncommon cause of lactic acidosis and lactate rise in patients in PICUs. It can contribute to current comorbidities because of its relationship with energy metabolism. When patients were analyzed in two groups by whether lactate levels were below 4 mmol/L at the 24<sup>th</sup> hour and if there was 28-day mortality, blood gas values before thiamin treatment, lactate decrease trends, thiamin treatments' duration, and form, and patients' risk factors were not statistically significant. We believe that in patients with lactic acidosis not directly related to a circulatory disorder, low clinical suspicion, and in the absence of specific diagnostic tests, early thiamin treatment of lactic acidosis is the right approach.

### Ethics

**Ethics Committee Approval:** Written permission was obtained from the Local Ethics Committee of Ankara University Hospital for this study (ethics committee number: İ09-566-22). Our study was conducted in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association.

**Informed Consent:** Written informed consent was obtained from all patients' relatives or legal authorities when necessary.

### Authorship Contributions

Concept: F.K., İ.F., Design: F.K., H.Ö., M.H., Data Collection or Processing: M.K.C., H.U., A.G., B.B., Analysis or Interpretation: F.K., T.K., Literature Search: F.K., Writing: F.K., T.K.

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# Where Should the Transition of Newborns Who are Technology Dependent and in Need of Support to Home Care in Turkey?

Türkiye’de Teknoloji Bağımlı ve Destek İhtiyacı Olan Yenidoğanların Evde Bakıma Geçişi Neresi Olmalıdır?

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## Abstract

**Introduction:** The discharge rates of newborns dependent on medical technology and in need of palliative care have increased. Specialized care units aimed to reduce patient load in neonatal intensive care units (NICU), and increase the quality of home care. In our country, there are few specialized care units for these patients. This study aimed to determine the characteristics of patients who were hospitalized in NICU and transferred to pediatric intensive care unit (PICU) due to continuing care.

**Methods:** The data of patients who were hospitalized in NICU between January 1, 2008 and July 31, 2022 and transferred to PICU were analyzed.

**Results:** Twenty (51%) of 39 patients were male, 46% had congenital anomaly(s), 33% had neurometabolic diseases. Forty-nine percent (n=19) of patients died during PICU stay, 2.6% (n=1) died after discharge. Demographic findings of died and survived patients were similar. Ninety percent of patients received invasive respiratory support (IRS) for a median of 43 days during NICU, 97% received IRS for a median of 31 days during PICU. Percutaneous endoscopic gastrostomy (PEG) and tracheostomy were performed 31%, and 51% of patients, respectively. The median length of stay in NICU and PICU were 55 days and 37 days, respectively. The discharged patients had a higher rate of PEG or tracheostomy (p<0.05).

**Conclusion:** Establishment of specialized care units is important to provide comprehensive, family-centered care to newborns who need palliative care, to reduce the burden on NICUs and PICUs. This study, which is first in our country, will lead to future studies for establishment of specialized care units.

**Keywords:** Pediatric intensive care, palliative care, neonatal intensive care

## Öz

**Giriş:** Neonatoloji alanındaki gelişmelerle birlikte tıbbi teknolojiye bağımlı ve palyatif bakım ihtiyacı olan yenidoğanların sayısı ve bu hastaların taburculuk oranları artmaktadır. Taburculuğa hazırlık için kurulan donanımlı bakım ekipleriyle yenidoğan yoğun bakım ünitelerindeki (YYBÜ) hasta yükünün azaltılması, hasta ve ailelerine multidisipliner bakım hizmetleri verilerek evde bakım kalitesinin artırılması amaçlanmaktadır. Ülkemizde, bu hastalara yönelik özelleşmiş bakım birimlerinin sayısı çok azdır. Çalışmamızda, YYBÜ’ne yatırılmış, tıbbi teknoloji bağımlılığı veya palyatif bakım ihtiyacı devam ettiği için çocuk yoğun bakım ünitesine (ÇYBÜ) devredilen hastaların özelliklerinin belirlenmesi amaçlanmıştır.

**Yöntemler:** Çalışmamızda 1 Ocak 2008-31 Temmuz 2022 arasında YYBÜ’nde yatan ve tıbbi teknoloji bağımlılığı veya palyatif bakım ihtiyacı devam ettiği için ÇYBÜ’ne devredilen hastaların verileri, geriye dönük olarak incelenmiştir.

**Bulgular:** Otuz dokuz hastanın 20’si (%51) erkek olup, %46’sında doğuştan anomali(ler), %33’ünde nörometabolik hastalık tanıları mevcuttu. Hastaların %49’u (n=19) ÇYBÜ takibindeyken, %2,6’sı (n=1) taburculuk sonrasında kaybedilmiştir. Kaybedilen ve taburcu olan hastaların demografik ve tanılal özellikleri benzerdi. Hastaların %90’ı YYBÜ yatış sürecinde ortalama 43 gün invaziv solunum desteği (İSD) almışken, ÇYBÜ yatış sürecinde %97’si ortalama 31 gün İSD almıştı. Hastaların %31’ine YYBÜ veya ÇYBÜ yatışı sürecinde perkütan endoskopik gastrostomi (PEG), %51’ine trakeostomi açılmıştı. YYBÜ ve sonrasında ÇYBÜ yatış süreleri ortalama sırasıyla 55 gün ve 37 gündü. PEG ya da trakeostomili olma durumu, taburcu olanlarda kaybedilenlere göre daha fazlaydı (p<0,05).

**Sonuç:** Tıbbi teknoloji bağımlılığı olan yenidoğanlara kapsamlı ve aile merkezli bakımın sağlanabilmesi, YYBÜ ve ÇYBÜ’ler üzerindeki yükün azaltılabilmesi için kompleks bakım birimlerinin kurulması önemlidir. Ülkemizde bu alanla ilgili bir ilk olan çalışmamızın gelecek çalışmalara ve kompleks tıbbi bakım ve palyatif birimlerinin kurulmasına öncülük edeceğini düşünmekteyiz.

**Anahtar Kelimeler:** Çocuk yoğun bakım, palyatif bakım, yenidoğan yoğun bakım

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## Introduction

Globally, 2.4 million infants died in the first month of life in 2020, and neonatal mortality accounts for almost half (47%) of all deaths in children under 5 years of age. Most neonatal deaths (75%) occur in the first week of life and are most commonly caused by prematurity, birth-related complications (such as birth asphyxia) and congenital anomalies.<sup>1</sup> However, in recent years, with the developments in the field of neonatology, the number of extremely premature newborns and newborns with chronic diseases and the life expectancy for those having diseases such as hypoxic ischemic encephalopathy and severe congenital anomalies, who were previously lost in the early stages of life, have been gradually increasing.<sup>2,5</sup>

These changes in the field have created the need for two important patient groups and associated definitions. Medical technology-dependent neonates are defined as infants who are dependent on a medical device such as invasive or non-invasive mechanical ventilation with tracheostomy, nasogastric catheter feeding, parenteral nutrition, cardiovascular monitoring, airway care and aspiration.<sup>6,7</sup> Palliative care is defined as the organization of end-of-life care and refers to an active and holistic approach to meet the physical, emotional, social and spiritual needs of the patient and family.<sup>8</sup> In newborns, almost all patients with life-limiting diseases who need palliative care are also dependent on medical technology. In many centers around the world, equipped care teams and units are established to meet the care needs of these babies, and it is aimed to increase the quality of home care and reduce hospitalizations after discharge by providing more comprehensive, family-centered, specialized and multidisciplinary care services to patients and their families.<sup>9-11</sup> In a survey conducted in 2022 with pediatricians in four major cities in our country, it was found that 19.1% of the centers had a pediatric palliative care unit.<sup>12</sup>

Since the number of specialized teams and centers for both technology-dependent supportive patients and palliative care patients is insufficient in our country, these patients are transferred to pediatric intensive care units (PICUs) in many centers for the continuation of their treatment and follow-up after completing the neonatal period. This situation increases infections due to chronic patient follow-up in PICUs, leads to loss of workforce and motivation of the team, decreases bed turnover rate, causes bed occupancy and problems in the admission of real intensive care patients. In this study, we aimed to evaluate the characteristics of patients who were transferred to PICU after NICU follow-up in our hospital due to medical technology dependency and palliative care need and lack of palliative care unit.

## Materials and Methods

Patients who were hospitalized in Ankara University Faculty of Medicine NICU between January 1, 2008 and July 31, 2022 and who were transferred to the PICU after completing the neonatal period due to medical technology dependence or continued need for palliative care were included in the study. Demographic data, hospitalization diagnosis, duration of invasive respiratory support (IRS), percutaneous endoscopic gastrostomy (PEG) and tracheostomy interventions, and survival status of the patients were retrospectively recorded from their files. Data of lost and discharged patients were compared. Tracheostomy opening on day  $\geq 14$  in a patient who received IRS was defined as late tracheostomy.<sup>13</sup>

Between January 2008 and February 2014, Ankara University Faculty of Medicine NICU served as a tertiary intensive care unit with 24 beds and PICU served as a secondary intensive care unit with 6 beds. As of February 2014, the NICU continues to serve as a tertiary intensive care unit with 30 beds and PICU continues to serve as a tertiary intensive care unit with 20 beds.

The study was approved by the Ankara University Faculty of Medicine Clinical Research Ethics Committee (103-126-23).

## Statistical Analysis

Statistical analyses were performed using standard statistical software (IBM SPSS 22). Continuous variables were expressed as mean and standard deviation or median [interquartile range (IQR) (25-75%)]. Categorical variables were expressed as numbers and percentages. The chi-square test was used to compare nominal variables and the Mann-Whitney U test was used to compare means. In all analyses,  $p < 0.05$  was used to indicate statistical significance.

## Results

During the study period, 39 (0.4%) of a total of 9242 patients admitted to the NICU were transferred to the PICU. Of the 39 patients, 20 (51%) were male, the median gestational week was 37.6 weeks (IQR: 34.1-38.5 weeks) and the mean birth weight was  $2422 \pm 632$  g. The comorbidities in the patients were congenital anomalies (46%) and neurometabolic disease (33%) in order of frequency. Table 1 shows the demographic and diagnostic characteristics of the patients.

Of the patients, 49% (n=19) died during PICU follow-up and 2.6% (n=1) died during post-discharge follow-up. Demographic and diagnostic characteristics of the discharged and deceased patients were similar (Table 1). Eight (42%) patients died due to cardiac arrest, 7 (37%) due to septic shock and 4 (21%) due to respiratory failure.

90% of the patients received IRS for a median of 43 days (IQR: 9-53 days) during NICU hospitalization and 97% of the patients received IRS for a median of 31 days (IQR: 11-47 days) during PICU hospitalization. PEG was opened in 23% of patients in the NICU and 8% in the PICU, while tracheostomy was opened in 15% of patients in the NICU and 36% in the PICU.

The median lengths of NICU and then PICU stay were 55 days (IQR: 43-77 days) and 37 days (IQR: 14-62 days), respectively. The rate of PEG or tracheostomy was higher in those who were discharged compared to those who were lost ( $p < 0.05$ ) (Table 2).

When the calculation was made according to the bed capacity used during the study period, it was found that infants who were dependent on medical technology and needed palliative care used 3% of the NICU capacity and 3.9% of the PICU capacity.

## Discussion

In recent years, medical technology dependency of extremely premature infants, whose survival and discharge rates have increased with advances in neonatology and medicine, has been increasing, and some of these infants can be discharged home with respiratory and nutritional support. Similarly, newborns with complex chronic diseases that limit life expectancy can be discharged home with medical devices. Education and preparation for discharge of these two vulnerable groups of patients and their families are a difficult and long process.<sup>3-5</sup> This group of patients who are followed up in the NICU of our hospital are transferred to the PICU if the need for intensive care continues after completing the neonatal period, as in most of the centers in our country. In this study, in which the characteristics of patients who were transferred to the PICU after NICU follow-up due to medical technology dependence and palliative care need were

evaluated, it was found that 39 patients hospitalized in the NICU were transferred to the PICU in a 15-year period.

The majority of newborns who are dependent on medical technology are extremely premature infants and infants with congenital anomalies, neurometabolic diseases or genetic and chromosomal anomalies.<sup>9</sup> In a study by Kieran et al.,<sup>9</sup> it was found that 48% of the patients were diagnosed with genetic/chromosomal diseases, 26% with extremely premature, 12% with neurometabolic disease and 11% with congenital anomaly. In our study, 46% of the patients who were transferred to the PICU due to continued dependence on medical technology had a diagnosis of congenital anomaly and 33% had a diagnosis of neurometabolic disease.

In a study of neonates in need of complex care, it was reported that 58% of patients were discharged with tracheostomy and 69% with PEG,<sup>14</sup> while another study showed that 40% had technology dependency (tracheostomy, PEG, cardiorespiratory monitoring, supplemental oxygen) at discharge.<sup>15</sup> A study by Kieran et al.<sup>9</sup> showed that 91% had technology dependency (tracheostomy, supplemental oxygen, PEG, nasogastric catheter, total parenteral nutrition, central venous catheter, ventriculoperitoneal shunt, cardiorespiratory monitoring) at discharge. In our patients, 90% received IRS during NICU hospitalization and 97% during PICU hospitalization; PEG was opened in 31% and tracheostomy in 51% of the patients during NICU or PICU hospitalization.

It has been reported that neonates in need of complex medical care should be given care by specialized multidisciplinary teams.<sup>16,17</sup> These practices have been shown to improve care coordination and family education, facilitate the transition of newborns to home and/or community and shorten the duration of hospitalization.<sup>9,15</sup> Identifying patients in need of complex medical care during their hospitalization allows the development of innovative complex care models that focus on the needs of patients and families. The transition from hospital to community care is a very difficult process,

**Table 1. Demographic and diagnostic characteristics of patients**

	Total number of patients (n=39)	Deceased patients (n=20)	Discharged patients (n=19)	p
Gestational age, <34 weeks, n (%)	7 (17.9)	5 (25)	2 (10.5)	0.239
≥34 weeks, n (%)	32 (82.1)	15 (75)	17 (89.5)	
Sex (male), n (%)	20 (51.3)	13 (65)	7 (37)	0.079
Delivery method (CS), n (%)	29 (74.4)	14 (70)	15 (78.9)	0.522
<b>Distribution of diagnosis, n (%)</b>				
Congenital anomaly(s)	18 (46.2)	11 (55)	7 (36.8)	0.170
Neurometabolic disease	13 (33.2)	5 (25)	8 (42.1)	
Acquired brain injury	5 (12.8)	1 (5)	4 (21.1)	
Multiple organ failure	1 (2.6)	1 (5)	0	
Genetic disease	2 (5.1)	2 (10)	0	
CS: Caesarean section				

**Table 2. Duration of treatment and hospitalization length of discharged and deceased patients**

	Total (n=39)	Deceased (n=20)	Discharged (n=19)	p
With PEG, n (%)	12 (30.8)	3 (15)	9 (47.4)	0.029*
With tracheostomy, n (%)	20 (51.3)	3 (15)	17 (89.5)	<0.001*
Duration of NICU hospitalization (day)*	55 (43-77)	49.5 (42.25-74.5)	66 (46-86)	0.411^
Duration of PICU hospitalization (day)*	37 (14-62)	36.5 (12.5-54)	41 (18-65)	0.461^
Total duration of MV (day)*	72 (31-115)	66.5 (26.5-102.25)	79 (43-147)	0.411^
Total hospitalization length	99 (72-142)	95 (67.5-125)	107 (79-181)	0.411^

\*: Median (IQR), †: Chi-square test, ^: Mann-Whitney U test, PICU: Pediatric intensive care unit, MV: Mechanical ventilation, PEG: Percutaneous endoscopic gastrostomy, NICU: Neonatal intensive care unit, IQR: Interquartile range

especially for families of infants with chronic care needs. The most appropriate approach is to establish complex care units and teams to improve parenting skills and thus improve outcomes for infants and their families, and to involve families in the care of their infants as soon as possible in these care units.

In our country, infants continue to be hospitalized in NICUs or transferred to PICUs after completing the neonatal period due to the lack of specialized units and palliative care centers that play a role in the transition of newborns with complex medical care needs and ongoing technology dependency to home care. Similar to the hospitalization durations reported in the literature,<sup>9</sup> the median durations of both NICU and PICU hospitalization were 55 days (IQR: 43-77 days) and 37 days (IQR: 14-62 days), respectively. When the bed capacity used during the study period was calculated, it was found that infants who were dependent on medical technology and needed palliative care used 3% of the NICU capacity and 3.9% of the PICU capacity. Considering that only 39 patients were followed up in our hospital for medical technology dependency and palliative care needs in the 15-year period covering the study period, it can be said that this patient group used a significant portion of the intensive care unit beds due to their long hospitalization periods. In our country with a high birth rate, very long hospitalization periods make it difficult to admit new patients to NICUs. PICUs accept patients between 0-18 years of age for many reasons, such as the need for advanced cardiorespiratory support, major traumas, poisonings, renal replacement therapies and complex postoperative care after major surgeries. In addition to the limited capacity of PICU beds to provide these services in our country, the

number of PICU specialists is far below the needs of our country. Although the critical intensive care process does not continue, the continued long-term hospitalization of infants in the PICU due to the need for complex care and technology dependency makes it difficult to admit patients who need advanced intensive care and specialized treatments, and prevents the use of the workforce of healthcare personnel such as physicians and nurses in necessary areas. Pediatric palliative care is a new field for our country and there are very few centers providing pediatric palliative care. On the other hand, while a child in need of palliative care should be handled with a family-centered, holistic approach in all aspects of physical, mental and spiritual life, these needs can only be partially met in dynamic NICUs and PICUs where the patient cycle is faster. The difficulties in the establishment of these care units include the need for the training of competent and experienced personnel, the need for team formation and the necessity to plan cost-effectiveness studies.<sup>9,18</sup>

### Study Limitations

The limitations of our study include the small number of patients, the lack of objective clinical scoring that can express the severity of the patients, its being a descriptive, single-center and retrospective study in which different practices were not compared, and the lack of cost-effectiveness analysis. We think that our study is important in terms of taking steps towards the establishment of complex medical care and palliative units, which we think is an important need in our country.

Under the conditions of our country, the patient density, which is quite high according to the limited bed capacity and insufficient number of specialist physicians, can only be overcome with the proper use of trained and experienced manpower. We believe that establishing complex medical care and palliative care centers in each province, taking into account the number of neonatal and intensive care patients, and using these centers as an intermediate step before discharge for patients dependent on medical technology can provide a more effective service without disrupting NICU and PICU services.

### Conclusion

In conclusion, NICUs and PICUs are units where patient turnover is rapid and treatment and care services are provided to a large number of infants with limited bed capacity. Neonates with medical technology dependence constitute a significant proportion of total intensive care unit hospitalizations due to prolonged hospitalization. It is important to establish complex care units to provide comprehensive and family-centered care to this patient group after the neonatal period in order to

reduce the burden on both NICUs and PICUs. These units should aim to counsel parents, plan health care resources, shorten length of stay in intensive care units and plan post-discharge care coordination interventions.

### Ethics

**Ethics Committee Approval:** The study was approved by the Ankara University Faculty of Medicine Clinical Research Ethics Committee (103-126-23).

**Informed Consent:** Retrospective study.

### Authorship Contributions

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

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

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# Postoperative Intensive Care Requirements of Pediatric Surgery Patients

## Pediatric Cerrahi Hastalarının Postoperatif Yoğun Bakım İhtiyacı

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### Abstract

**Introduction:** To evaluate the duration of pediatric intensive care stay, hospitalization and the factors affecting mortality in patients who were operated by pediatric surgery and followed up in pediatric intensive care unit (PICU) in the postoperative period.

**Methods:** One hundred forty-three patients who were operated between September 2018 and January 2020 and hospitalized in the PICU for post-operative follow-up were included in the study.

**Results:** The median age of the 143 patients included in the study was 31.00 (1-205) months, and 76 (53.1%) were male. Ninety-six patients had no comorbidity, 47 patients had at least one comorbidity. The most frequent developed post-operative complications were sepsis (n=7) and intra-abdominal hypertension (n=7). The presence of sepsis extended the intensive care unit stay by 4.46 days, the need for inotropes by 3.61 days, the development of intra-abdominal hypertension by 3.33 days, and the presence of comorbidity by 0.86 days. The presence of sepsis extended the hospitalization period 28.04 days, the need for respiratory support 21.78 days, and the presence of malnutrition 14.42 days.

**Conclusion:** It would be more appropriate to follow-up patients, who are operated by pediatric surgery, especially those with comorbidity and malnutrition, who need intraoperative blood products or who have the risk of developing complications in the postoperative period in PICUs.

**Keywords:** Post-operative, intensive care, children

### Öz

**Giriş:** Bu çalışmada çocuk cerrahisi tarafından opere edilen ve çocuk yoğun bakım ünitesinde (ÇYBÜ) takip edilen hastaların klinik özelliklerinin çocuk yoğun bakım yatış süresi, hastane yatış süresi ve mortaliteye olan etkileri değerlendirilmesi amaçlandı.

**Yöntemler:** Eylül 2018 ve Ocak 2020 arasında ÇYBÜ'de postoperatif takip edilen 143 hasta çalışmaya dahil edildi.

**Bulgular:** Çalışmaya dahil edilen 143 hastanın ortanca yaşı 31,00 (1-205) ay ve 76'sı (%53,1) erkek idi. Çalışmamızda 96 hastanın hiçbir komorbitesi olmayıp 47 hastanın en az 1 komorbitesi mevcuttu. Post-operatif en sık gelişen komplikasyonlar sepsis (n=7) ve intraabdominal hipertansiyondur (n=7). Postoperatif sadece bir (%0,7) hastada ölüm gerçekleşti. Çoğul lineer regresyon analizinde yoğun bakım yatış süresini sepsis varlığının 4,46 gün, inotrop ihtiyacı olmasının 3,61 gün, intra-abdominal hipertansiyon gelişmesinin 3,33 gün, komorbidite varlığının 0,86 gün uzattığı saptandı. Hastane yatış süresini; sepsis varlığının 28,04 gün, solunum desteği ihtiyacının 21,78 gün, malnütrisyon varlığının 14,42 gün uzattığı saptandı.

**Sonuç:** Çocuk cerrahi tarafından opere edilen, özellikle komorbidite ve malnütrisyonu olan, intraoperatif kan ürün desteği yapılan ve postoperatif komplikasyon gelişme riski olan hastalarının ÇYBÜ'lerinde takip edilmeleri uygundur.

**Anahtar Kelimeler:** Postoperatif, yoğun bakım, çocuk

\*One of the authors of this article (D.Y.) is a member of the Editorial Board of this journal. He was completely blinded to the peer review process of the article.

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## Introduction

Today, the frequency of perioperative mortality has decreased because of developments in the fields of anesthesia and intensive care, blood product support, and provision of parental nutrition.<sup>1,2</sup> However, emergency operations, comorbidities, reoperation, sepsis, postoperative bleeding, a lack of experienced staff, and financial difficulties (specifically in low- and middle-income countries) can still cause an increase in morbidity and mortality.<sup>3,4</sup> Early detection and intervention of complications occurring during the follow-up of postoperative pediatric patients, infection control, and adequate nutrition at the appropriate time are important.

Follow-up of postoperative pediatric surgery patients with a multidisciplinary approach including anesthesia, pediatric intensive care, and the pediatric surgery team will reduce perioperative morbidity and mortality. During the postoperative period, close follow-up of patients with a high risk of developing perioperative morbidity and mortality in the pediatric intensive care unit (PICU) can improve survival. However, when we investigated the literature, we found that the number of studies evaluating the factors affecting the duration of intensive care and hospital stay of patients followed up in the PICU in the postoperative period was limited.

This study was conducted retrospectively to investigate the duration of pediatric intensive care stay, hospitalization, and factors affecting mortality in patients who underwent pediatric surgery and were followed up in the PICU in the postoperative period.

## Materials and Methods

This retrospective observational study was performed at a tertiary medical-surgical PICU. A total of 143 patients who underwent surgery at Çukurova University Faculty of Medicine, Department of Pediatric Surgery, between September 2018 and January 2020 and were hospitalized in the PICU for postoperative follow-up were included in the study. We do not have a written protocol on which patients will be followed in the PICU in the postoperative period; however, patients with comorbidities, unplanned operations, all those who underwent bronchoscopy for suspected foreign body aspiration, those with perioperative complications, and sometimes with the surgeon's foresight are followed up in pediatric intensive care. Approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Çukurova University Faculty of Medicine (2019/94).

Sepsis was defined as a proven or clinically suspected infection along with systemic inflammatory response syndrome.<sup>5</sup> Intra-abdominal pressure was measured using the gold standard

method, the trans-bladder technique. As previously described; sustained or repeated pathological elevation in intra-abdominal pressure >10 mmHg was accepted as intra-abdominal hypertension (IAH). The development of at least one organ failure or worsening of existing organ failure in addition to IAH was considered abdominal compartment syndrome.<sup>6</sup> In our study, patients with weight-for-age (measured weight/median weight) measurements <90% were considered as malnutrition,<sup>7</sup> and patients with body mass index >95p were considered obese.<sup>8</sup>

Demographic information of patients, primary cause of operation, comorbidity, PRISM-III score, blood product support during and after the operation, mechanical ventilation and inotrope need, intra-abdominal pressure measurements, length of the PICU, and hospital stay were recorded.

## Statistical Analysis

Descriptive analyses were conducted to characterize the study cohort. Categorical measurements are summarized as numbers and percentages, whereas numerical measurements are summarized as median (minimum-maximum) values. We used the chi-square test or Fisher's Exact test, whichever was appropriate, to compare categorical variables. In the comparison of numerical measurements performed on the same individual at two different times, the t-test was used in dependent groups, and the Wilcoxon test was used when the differences did not show a normal distribution. The IBM SPSS Statistics Version 20.0 package program was used for statistical analysis of the data. The level of statistical significance was set as 0.05 in all tests. Multiple linear regression analysis was used for data analysis of the patients.

## Results

The median age of the patients was 31.0 (1-205) months, 76 of them (53.1%) were male, and the median PRISM-III score was 2.0 (0-25).

The most frequent operations were abdominal surgery in 68 (47.6%) patients and bronchoscopy in 60 (42%) patients with suspicion of foreign body aspiration. In our study, 96 patients had no comorbidity, and 47 patients had at least one comorbidity. The most frequent comorbidities were neurological in 19 (13.2%) and cardiac in 12 (8.3%) patients. The primary diseases of the patients, the accompanying diseases, and the operations performed are given in Table 1 in detail. Thirty-two (22.4%) of the patients had malnutrition, and seven (4.9%) had obesity. An elective operation was performed on 136 (95.1%) of the patients, and an emergency operation was performed on 7 (4.9%) of them.

Nineteen (13.3%) patients received blood product support in the intraoperative period, and these supports were only

**Table 1. Characteristics of the patients**

	<b>Mean ± SD Median (25p-75p)</b>
Age (months)	55.0±54.7 31.00 (15-85)
Male n (%)	76 (53.1)
Malnutrition n (%)	32 (22.4)
Obesity	7 (4.9)
<b>Primary diseases n (%)</b>	
Respiratory	69 (48.3)
Gastrointestinal	36 (25.2)
Hemato/oncological	28 (19.6)
Genitourinary	5 (3.5)
Trauma	3 (2.1)
Infection	2 (1.4)
<b>Comorbidity n (%)</b>	
None	96 (67.1)
Neurological	19 (13.2)
Cardiac	12 (8.3)
Endocrinological	10 (6.9)
Respiratory	10 (6.9)
Genetics	9 (6.3)
Others	10 (7.1)
Elective surgery	136 (95.1)
Intraoperative blood product support	19 (13.3)
Postoperative blood product support	14 (9.8)
PRISM-III	3.8±4.64 2.0 (0-6)
<b>Postoperative respiratory support</b>	
None	46 (32.2)
Oxygen with a non-rebreather mask	82 (57.3)
Invasive ventilation	11 (7.7)
HFNC	4 (2.8)
<b>Post-operative complications</b>	
Sepsis	7 (4.9)
Intra-abdominal hypertension	7 (4.9)
Abdominal compartment syndrome	2 (1.4)
Length of PICU stay	2.1±2.3 1.0 (1-2)
Length of hospital stay	12.9±19.5 7.0 (3-16)
Death	1 (0.7)

HFNC: High-flow nasal cannula oxygen therapy, PICU: Pediatric intensive care unit, SD: Standard deviation

erythrocyte suspension (ES) or ES + fresh frozen plasma support. The PRISM-III score of patients who received intraoperative blood products was higher than that of patients who did not (7.4 vs. 3.3, respectively,  $p=0.005$ ). Ten of these 19 patients needed blood product support during their PICU stay. Inotrope support was provided to three (2.1%) patients during the postoperative period. The most frequent postoperative complications were sepsis ( $n=7$ ) and IAH ( $n=7$ ). Three (42.8%) patients who developed sepsis were malnourished, and one (14.3%) was obese. IAH was present in 2 (28.6%) of 7 patients with sepsis and in only 5 (3.7%) of 136 patients without sepsis ( $p=0.003$ ). In our study, a patient with neurometabolic disease who was

hospitalized for postoperative follow-up after tracheostomy and gastrostomy underwent emergency surgery because of gastrostomy leakage. This patient developed intra-abdominal sepsis and abdominal compartment syndrome during follow-up and died. No patient required intensive care again after being transferred to the pediatric surgery ward.

Factors affecting the duration of PICU and hospital stay were evaluated (Table 2). Patients who needed intraoperative blood products, respiratory support, and postoperative inotrope and who developed IAH and sepsis had a longer hospitalization period in pediatric intensive care ( $p<0.05$ ). Multiple linear regression analysis was performed to determine the factors affecting the duration of PICU stay (Table 3). It was determined that sepsis extended the duration of intensive care by 4.46 days, the need for inotrope by 3.61 days, the development of IAH by 3.33 days, and the presence of comorbidity by 0.86 days. The duration of hospital stay was longer in patients with intraoperative blood product support, IAH, sepsis, comorbidity, lactate elevation, and those who needed respiratory support during postoperative follow-up. Multiple linear regression analysis demonstrated that the presence of sepsis prolonged the duration of hospital stay by 28.04 days, the need for respiratory support by 21.78 days, and the presence of malnutrition by 14.42 days (Table 4).

## Discussion

In our study, postoperative complications during the PICU stay, factors affecting the length of the PICU and hospital stay, and mortality rates were evaluated. The length of the PICU and hospital stays were 2.1 and 12.9 days, respectively. In a retrospective study, Altintas et al.<sup>9</sup> reported similar findings (2.0 and 13.0 days) to our study. The most common postoperative complications were sepsis and IAH. We found that comorbidity, postoperative need for inotrope, and IAH prolonged the duration of pediatric intensive care stay, and the presence of malnutrition and respiratory support prolonged the duration of hospital stay, whereas the presence of sepsis prolonged both PICU and hospital stays.

Postoperative sepsis remains a problem because it increases the risk of morbidity and mortality. Children with severe injury, comorbidity, and debilitating conditions are at risk of developing sepsis.<sup>5</sup> Studies conducted in children have demonstrated that postoperative sepsis increases the duration of PICU and hospital stays.<sup>10-12</sup> In a multicenter study by Kronman et al.,<sup>12</sup> postoperative sepsis was reported to prolong hospital stays by 23.5 days. We also found that the development of sepsis in the postoperative period extended the duration of the PICU stay by 4.4 days and the duration of hospitalization by 28 days. In a large-scale retrospective study conducted with adults, it was reported that death occurred in

**Table 2. Comparison of length of pediatric intensive care unit and hospital stay of the patients with regard to some factors**

	Length of PICU stay Mean ± SD Median (25p-75p)	Length of hospital stay Mean ± SD Median (25p-75p)
<b>Comorbidity</b>		
Yes (n=47)	2.8±3.5 1 (1-3)	19.0±23.5 10 (4-26)
No (n=96)	1.7±1.4 1 (1-2)	10.0±16.5 5 (2-15)
p	0.056	0.006
<b>Malnutrition</b>		
Yes (n=32)	2.2±2.2 1 (1-2)	26.5±33.1 15 (8-27)
No (n=111)	2.1±2.4 1 (1-2)	9.1±10.6 5 (2-11)
p	0.956	<0.001
<b>Obesity</b>		
Yes (n=7)	1.7±1.5 1 (1-2)	11.7±6.9 11 (6-19)
No (n=136)	2.1±2.3 1 (1-2)	13.0±19.9 7 (2-16)
p	0.570	0.295
<b>Emergency operation</b>		
Yes (n=7)	7.6±6.6 5 (3-12)	29.8±22.9 25 (8-43)
No (n=136)	1.8±1.6 1 (1-2)	12.1±19.0 6 (2-15)
p	p<0.001	p=0.007
<b>Intraoperative blood product support</b>		
Yes (n=19)	3.9±4.3 3 (2-5)	19.2±15.5 16 (10-19)
No (n=124)	1.8±1.7 1 (1-2)	12.0±19.9 5 (2-13)
p	<0.001	<0.001
<b>Postoperative respiratory support</b>		
Yes (n=97)	2.4±2.7 1 (1-2.5)	15.1±22.5 8 (3-16)
No (n=46)	1.4±1.0 1 (1-1)	8.4±9.6 4 (2-15)
p	0.002	0.011
<b>Intra-abdominal hypertension</b>		
Yes (n=7)	6.7±6.2 5 (2-8)	22.1±10.2 19 (19-25)
No (n=136)	1.9±1.7 1 (1-2)	12.5±19.8 6 (2-15)
p	<0.001	0.004
<b>Sepsis</b>		
Yes (n=7)	8.3±6.2 7.0 (5-12)	47.1±35.1 37 (19-80)
No (n=136)	1.8±1.4 1.0 (1-2)	11.2±16.8 6 (5-15)
p	<0.001	<0.001

**Table 2. Continued**

	Length of PICU stay Mean ± SD Median (25p-75p)	Length of hospital stay Mean ± SD Median (25p-75p)
<b>Inotropic support</b>		
Yes (n=3)	9.3±9.3 5 (3-20)	24.7±15.9 16 (15-43)
No (n=140)	1.9±1.8 1 (1-2)	12.7±19.5 6 (2-16)
p	0.004	0.062
<b>Lactate</b>		
<2 mmol/L (n=56)	2.0±1.9 1 (1-2)	9.8±16.2 4.5 (2-10)
≥2 mmol/L (n=87)	2.2±2.6 1 (1-2)	15.0±21.2 8 (3-19)
p	0.379	0.011

PICU: Pediatric intensive care unit, SD: Standard deviation

**Table 3. Impact of associated factors on the length of pediatric intensive care unit stay**

Length of PICU stay (adjusted R <sup>2</sup> =0.34)	p	Regression coefficient (Beta)	95% CI for beta	
			Lower	Upper
Sepsis	<0.001	4.46	3.07	5.86
Intra-abdominal hypertension	<0.001	3.33	2.05	4.61
Comorbidity	0.004	0.86	0.29	1.43
Inotrope support	0.001	3.61	1.56	5.67
Invariable	<0.001	1.35	1.02	1.68

PICU: Pediatric intensive care unit, CI: Confidence interval

**Table 4. Impact of associated factors on the length of hospital stay**

Length of hospital stay (adjusted R <sup>2</sup> =0.34)	p	Regression coefficient (Beta)	95% CI for beta	
			Lower	Upper
Sepsis	<0.001	28.04	15.67	40.41
Malnutrition	<0.001	14.52	8.19	20.85
Respiratory support	<0.001	21.78	11.78	31.78
Invariable	<0.001	6.66	3.61	9.71

PICU: Pediatric intensive care unit, CI: Confidence interval

14.4% of patients who developed postoperative sepsis. Based on these data, a model was created to predict postoperative sepsis-associated mortality.<sup>13</sup> There are no large-scale recent studies evaluating the development of postoperative sepsis and mortality in children. In our study, death occurred in 1 (14.2%) of 7 patients who developed postoperative sepsis. Prolonged intensive care unit and hospital stays and mortality due to postoperative sepsis were similar to those reported in previous studies.<sup>10-12</sup>

Although the prevalence of malnutrition in hospitalized children varies according to the development level of the countries, this rate varies between 6% and 31%.<sup>14,15</sup> It has been



shown in many studies that the preoperative nutritional status of pediatric patients is related to postoperative morbidity and mortality as well as the duration of hospital stay.<sup>15-18</sup> In a large-scale study evaluating non-cardiac pediatric surgery patients, it was reported that the extreme weight percentile (<5<sup>th</sup>, >95<sup>th</sup>) increased the incidence of postoperative complications.<sup>18</sup> In our study, patients with malnutrition or obesity had a higher rate of sepsis than those who did not (of the patients who developed sepsis were 42.8% of malnourished and 14.2% were obese), and the hospitalization periods of these patients were longer.

IAH is another condition that should be followed up specifically in pediatric patients who have undergone abdominal surgery. Complications that may decrease abdominal wall compliance or an increase in postoperative intra-abdominal content can cause IAH. The association of IAH and abdominal compartment syndrome with organ failure and mortality has been demonstrated in previous studies.<sup>19-21</sup> In a multicenter study conducted by Horoz et al.,<sup>21</sup> it was reported that the frequency of IAH in patients who underwent abdominal surgery may increase up to 48%. In our study, IAH developed in seven (14.3%) of 49 patients who were followed up because of the risk of developing IAH in the postoperative period, and abdominal compartment syndrome developed in two (4.1%) of them. We believe that the frequency of IAH may vary depending on the type of operation performed, intraoperative or postoperative complications, and excessive fluid resuscitation.

It is expected that patients in the PICU with comorbidities will stay longer. In the study by Tobi and Amadasun,<sup>22</sup> it was stated that comorbidities may be associated with prolonged intensive care stays. In our study, we found that the presence of comorbidity was associated with prolonged hospital stays rather than with pediatric intensive care stays.

It has been determined that emergency operations are associated with prolonged PICU and hospital stays. In the retrospective study of Talabi et al.,<sup>3</sup> in which they analyzed 10-year perioperative mortality, it was found that emergency surgery increased the mortality rate by 90 times. In another study, the mortality rate was reported to be 12% in pediatric patients undergoing emergency surgery.<sup>23</sup> Considering the risk of developing complications in the follow-up of patients who have been urgently operated and need perioperative blood product support and comorbidity, it may be more appropriate to be followed up in PICUs in the postoperative period. In our study, one patient was urgently operated after gastrostomy operation because of gastrostomy leakage. Intra-abdominal sepsis and abdominal compartment syndrome occurred during follow-up.

## Study Limitations

Our findings should be interpreted in light of some limitations. Because the study was conducted in a single center, it is not appropriate to generalize it to PICUs where different patient groups are followed. Surgical complications that occurred during the operation and could lead to a prolonged PICU stay were not recorded.

## Conclusion

We believe that it would be more appropriate to follow-up patients who are operated on by pediatric surgery, especially those with comorbidity and malnutrition, who need intraoperative blood products, or who have the risk of developing complications in the postoperative period, in PICUs. In the postoperative follow-up of children, the clinician should be alert to the possibility of developing sepsis and IAH because both are associated with mortality and morbidity. According to our study, the presence of sepsis prolonged both PICU and hospital stays.

## Ethics

**Ethics Committee Approval:** Approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Çukurova University Faculty of Medicine (2019/94).

**Informed Consent:** Informed consent was obtained from the patients' parents for their anonymized information to be published in this article.

## Authorship Contributions

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

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# A Forgotten Disease in Children: Lemierre Syndrome

## Çocuklarda Unutulan Bir Hastalık: Lemierre Sendromu

© Zekiye Aybüke Şen Ersöz<sup>1</sup>, © Nazan Ülgen Tekerek<sup>2</sup>, © Alper Köker<sup>2</sup>, © Oğuz Dursun<sup>2</sup>, © Tuğçe Tural Kara<sup>3</sup>, © Nilgün Erkek<sup>4</sup>

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### Abstract

Lemierre's syndrome is a life-threatening disease following oropharyngeal infections. A thirteen-year-old female patient presented with fatigue, facial edema, and shortness of breath. In the computerized tomographic examination, an abscessed area extends from the left temporal region to the bilateral submandibular area and the submental area from the para calvarial area. The right jugular vein calibration was thin and there was an intraluminal thrombus in the right innominate vein. The patient, who developed respiratory failure and whose mouth opening could not be achieved due to the abscess, was admitted to the pediatric intensive care unit after an emergency tracheostomy was performed. Thoracostomy and pericardiectomy were performed due to pleural and pericardial effusion. Lemierre's syndrome was diagnosed because of this clinical picture, which includes sepsis and jugular vein thrombosis after oropharyngeal infection. Early diagnosis, initiation of appropriate antibiotics and abscess drainage are important for Lemierre syndrome. A timely and multidisciplinary approach will be lifesaving.

**Keywords:** Lemierre, children thrombus, abscess

### Öz

Lemierre sendromu, orofaringeal enfeksiyonları takiben gelişen hayatı tehdit eden bir hastalıktır. On üç yaşında kız hasta halsizlik, yüzde ödem ve nefes darlığı yakınmaları ile başvurdu. Bilgisayarlı tomografi incelemesinde sol temporal parakalvarial bölgeden başlayarak bilateral submandibular bölgeden submental bölgeye uzanan apse görünümü, sağ jugüler ven kalibrasyonu incelenmiş ve sağ innominat vende intraluminal trombüs mevcuttu. Solunum yetmezliği gelişen ve apse nedeniyle ağız açıklığı sağlanamayan hasta acil trakeostomi yapıldıktan sonra çocuk yoğun bakım ünitesine yatırıldı. Plevral ve perikardiyal efüzyon nedeniyle torasentez ve perikardiyosentez yapıldı. Orofaringeal enfeksiyon sonrası sepsis ve jugüler ven trombozunu içeren bu klinik tablo nedeniyle Lemierre sendromu tanısı konuldu. Lemierre sendromumu için erken tanı, uygun antibiyotik başlanması ve apse drenajı oldukça önemlidir. Zamanında ve multidisipliner bir yaklaşım hayat kurtarıcıdır.

**Anahtar Kelimeler:** Lemierre, çocuk trombüs, apse

### Introduction

Lemierre's syndrome is a life-threatening disease characterized by septicemia and internal jugular thrombosis with septic emboli, following oropharyngeal infections.<sup>1,2</sup> It was described by Andre Lemierre in 1936. Lemierre syndrome is also known as the "forgotten disease", because of its rarity. The incidence of this disease is 3.6 cases per million per year. The most common microorganism causing Lemierre's syndrome is the Gram-negative anaerobic rod

*Fusobacterium necrophorum*.<sup>3</sup> *Bacteroides*, *Streptococcus* group B and C, *Streptococcus oralis*, *Staphylococcus epidermitis*, *Enterococcus* and *Proteus mirabilis* may also be involved.<sup>4</sup> Today, morbidity and mortality have gradually decreased after the use of appropriate antibiotics.<sup>5</sup>

In this case report, we describe a patient who exhibited Lemierre's syndrome atypically with pericardial and pleural effusion after treatment for a dental abscess and was followed up in the intensive care unit by placing an emergency tracheostomy due to tracheal deviation is presented.

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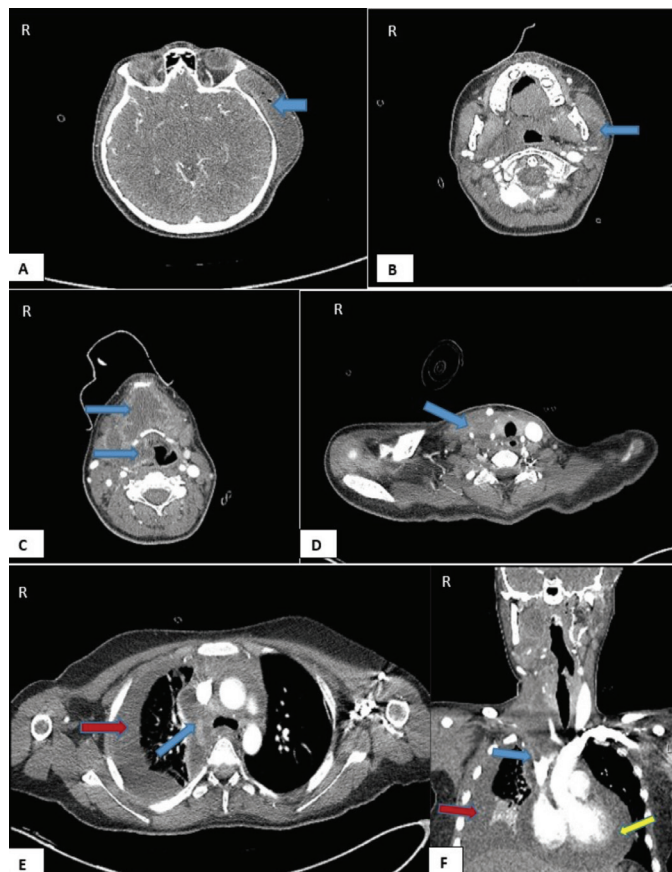
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## Case Report

A thirteen-year-old female patient presented with fatigue, facial edema, and shortness of breath. She had been treated with intravenous ceftriaxone and clindamycin for five days and had complained of pain in her left upper molar for ten days before admission.

On admission, the patient was in poor general condition, she had tachypnea (70/min) and left hemiface edema. Laboratory tests were: Hemoglobin 9.7 g/dL, leukocyte count 26,420/mm<sup>3</sup> (neutrophils 85%), platelet count 729,000/mm<sup>3</sup>, and C-reactive protein 191 mg/L. On computed tomography of the patient's brain, cervical spine, and chest, an abscessed area extended from the left temporal region to the bilateral submandibular area and the submental area from the paracalvarial area. The abscess has opened to the floor of the mouth and the right aryepiglottic fold was obliterated. The collection area extended inferiorly on the right, deviated the trachea to the left, and passed between the jugular vein and the carotid artery toward the mediastinal area (Figure 1). The calibration of the right jugular vein was thin and there was an intraluminal thrombus in the right innominate vein. There was a 2.5 cm pericardial effusion and a 6 cm pleural effusion in the right hemithorax with an associated atelectatic lung area. The patient, who developed respiratory failure and was unable to open his mouth due to the abscess, was admitted to the pediatric intensive care unit after an emergency tracheostomy was performed. An echocardiogram showed normal left ventricular ejection fraction and pericardial effusion. Empirical antibiotic therapy was a combination of piperacillin-tazobactam, vancomycin, and metronidazole. Intravenous immunoglobulin (IVIG) treatment was given for sepsis. Colchicine and non-steroidal anti-inflammatory drugs were initiated for pericardial effusion. Inotropic therapy (noradrenaline) was started for hypotension and discontinued during follow-up. Tube thoracostomy and tube pericardiotomy were performed due to pleural and pericardial effusion. The pleural fluid was exudate according to biochemical criteria. The patient was evaluated for mediastinitis and surgical abscess drainage was performed for the abscess in the mediasten. *Streptococcus mitis* and *Candida dubliniensis* were isolated from pleural fluid culture and treatment was revised as meropenem, vancomycin, metronidazole, and caspofungin. Lemierre's syndrome was diagnosed because of this clinical status, which includes sepsis and jugular vein thrombosis after oropharyngeal infection. She was anticoagulated with enoxaparin sodium. Immunoglobulin levels and lymphocyte subgroup analysis were normally concluded before IVIG treatment. Colchicine and non-steroidal anti-inflammatory drugs were initiated

for pericardial effusion. Inotropic therapy was started for hypotension and discontinued during follow-up. Tube thoracostomy and tube pericardiotomy were performed for pleural and pericardial effusion. The pleural fluid was evaluated as exudative according to biochemical criteria. The patient was evaluated for mediastinitis and surgical abscess drainage was performed for the mediastinal abscess. *Streptococcus mitis* and *Candida dubliniensis* were isolated from the pleural fluid culture and treatment was changed to meropenem, vancomycin, metronidazole, and caspofungin. Lemierre's syndrome was diagnosed based on this clinical status, which includes sepsis and jugular vein thrombosis after oropharyngeal infection. She was anticoagulated with enoxaparin sodium. Immunoglobulin levels and lymphocyte subgroup analysis were normally concluded before IVIG treatment.



**Figure 1.** Abscess localization and accompanying findings in computed tomography. Abscess obliterating the aryepiglottic fossa is seen in the left temporal region paracalvarial area (A; blue arrow), around the left mandibular ramus (B; blue arrow), and in the right parapharyngeal area. The collection area crosses the submental and submandibular areas in a horseshoe shape (C; blue arrows) and deviates the trachea slightly to the left on the right side (D; blue arrow). The abscess area extends to the mediastinal area between the jugular vein and the carotid artery on the right side (E; blue arrow). Compression-related thinning in the right jugular vein calibration, intraluminal thrombus image in the innominate vein (F; blue arrow). Pericardial effusion (F; yellow arrow), pleural effusion and atelectatic lung fields (E, F; red arrow) accompanying abscess

Clinical response was achieved after surgical intervention and antibiotic therapy. Thoracic and pericardial tubes were removed on day 6. She was decannulated and discharged from the hospital 28 days after admission. Control ultrasound was normal without thrombus.

## Discussion

Lemierre's syndrome is a condition in which an oropharyngeal infection progresses to thrombophlebitis of the internal jugular vein and septic embolization.<sup>6</sup> Lemierre primarily affects young adults. The primary source of infection may be odontogenic infection, mastoiditis, parotitis, sinusitis, otitis media, and skin or subcutaneous tissue infections.<sup>7,8</sup> Clinical findings include fever, cervical lymphadenopathy, pain, and stiffness of the neck from 4 to 5 days after the onset of pharyngitis. Edema and pain at the angle of the mandible and parallel to the sternocleidomastoid muscle indicate involvement of the parapharyngeal space. Septic embolism of the jugular vein mainly affects the lungs. Pulmonary involvement may present with severe chest pain, shortness of breath, and hemoptysis. Respiratory distress is present in the majority of cases.<sup>9-11</sup> The diagnosis was based on the following criteria: 1-primary oropharyngeal infection, 2-septicemia with at least one culture growth, 3-clinical or radiological evidence of cranial or cervical vein thrombosis and 4-secondary metastatic abscesses. In our case, Lemierre syndrome was diagnosed based on a history of dental infection, leukocytosis in laboratory tests, elevated C-reactive protein, abscess on computed tomography scan, a thrombus in the right jugular vein, and a pericardial and pleural effusion due to a mediastinal abscess.

Although causal bacteria are isolated in 80% of cases, many organisms including *Staphylococci*, *Streptococci*, *Fusobacterium* and anaerobic Gram-negative *Bacilli*, have been reported in etiology.<sup>12,13</sup>

The first line of treatment is intravenous antimicrobial therapy, with coverage for anaerobes, staphylococci, and streptococci.  $\beta$ -lactam/ $\beta$ -lactamase inhibitor, clindamycin, and metronidazole have been suggested for *Fusobacterium* species. Piperacillin-tazobactam and carbapenems are widely used in antibiotic treatment in cases with a severe clinical course.<sup>14</sup> In this case, *Streptococcus mitis* was isolated from a blood culture. Piperacillin-tazobactam, vancomycin, and metronidazole were started in our case who was followed up in the pediatric intensive care unit, and then piperacillin-tazobactam was revised as meropenem.

The routine use of anticoagulation in Lemierre's syndrome cannot be recommended because of limited data.<sup>11,15</sup> Our patient was anticoagulated with enoxaparin sodium.

## Conclusion

Considering the high mortality rate of Lemierre's syndrome, early diagnosis, initiation of appropriate antibiotics and abscess drainage are important. Prolonged oropharyngeal infection and worsening of symptoms in a young healthy adolescent should suggest Lemierre's syndrome and should be investigated for thrombosis and septic embolism. A timely and multidisciplinary approach to Lemierre's syndrome will be lifesaving.

## Ethics

**Informed Consent:** Informed consent was obtained from the patient's family.

## Authorship Contributions

Concept: Z.A.Ş.E., N.Ü.T., O.D., N.E., Design: N.Ü.T., O.D., Data Collection or Processing: Z.A.Ş.E., N.Ü.T., Analysis or Interpretation: Z.A.Ş.E., N.Ü.T., A.K., T.T.K., Literature Search: Z.A.Ş.E., N.Ü.T., Writing: Z.A.Ş.E., N.Ü.T.

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

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# A Didactic Case Report: FAST Examination Diagnosing Combined Bladder Rupture Following Blunt Abdominal Trauma

Öğretici Bir Olgu: Künt Abdominal Travma Sonrasında FAST Değerlendirilmesiyle Tanı Alan Kombine Mesane Rüptürü

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## Abstract

Bedside procedures can be a lifesaver for emergency pediatric trauma patients. The use of ultrasound in emergency pediatric trauma resuscitation may improve patient outcomes. A 15-year-old male patient was brought with the complaint of being stuck between the wall and the support leg of the crane. The patient, who was found to have abrasion and tenderness in the lower abdominal quadrants during emergency trauma examination, was evaluated with a focused assessment with sonography for trauma. The patient was examined with the preliminary diagnosis of bladder rupture. Surgery was planned for the patient, whose diagnosis was confirmed. The use of ultrasound in stable or unstable pediatric abdominal trauma patients can also detect bladder injuries. As a result, it is critical for emergency physicians to improve their ultrasonography abilities.

**Keywords:** FAST, bladder rupture, emergency medicine, pediatric trauma

## Öz

Hasta başı prosedürler acil çocuk travma hastaları için kurtarıcı olabilir. Acil çocuk travma resüsitasyonunda ultrason kullanımı hasta mortalite ve morbiditesini azaltabilir. On beş yaşındaki erkek hasta duvarla vincin destek ayağı arasına sıkışma şikayeti ile getirildi. Acil servis travma bakımında karın alt kadrantlarında abrazyon ve hassasiyet saptanan hasta, travmada sonografi ile odaklanmış değerlendirme ile değerlendirildi. Mesane rüptürü ön tanısı ile hastamız ileri incelemeye alındı. Tanısı kesinleştirilen hastaya ameliyat planlandı. Stabil veya anstabil çocuk abdominal travma hastalarında ultrason kullanımı mesane yaralanmalarını da tespit edebilir. Acil servislerde çalışan hekimlerin ultrason farkındalıklarını artırmaları önemlidir.

**Anahtar Kelimeler:** FAST, mesane rüptürü, acil servis, pediatrik travma

## Introduction

Due to their nature, 80% of paediatric abdominal injuries are blunt.<sup>1</sup> Although the most injured organ in these cases is the spleen, bladder injuries are rare compared to others. One of the most feared bladder injuries is rupture. Mortality in adults has been reported as 22%.<sup>2</sup> Choosing the right imaging is important for early diagnosis. Ultrasound is frequently preferred because it can be applied at the bedside, helps rapid diagnosis, is repeatable, cost-effective, and has no radiation. Although the sensitivity of focused assessment with sonography for trauma (FAST) is evaluated between 20-80%, its positivity may accelerate the detection of the patient's pathology.<sup>3</sup>

In this case, a patient diagnosed with combined bladder rupture who was admitted to the emergency department after blunt trauma is presented with FAST images.

## Case Report

A 15-year-old male patient presented to the emergency department with the complaint of being stuck between the wall and the support leg of the crane. The conscious patient had no complaints other than lower abdominal pain. He denied any significant past medical history. His vital signs were blood pressure 144/83 mmHg, heart rate 84/min, temperature 36.6 °C, respiratory rate 14/min, and oxygen saturation 99% in room air respectively. His Glasgow Coma score was 15. In

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the physical examination, there were ecchymosis and abrasions on the pelvic region (Figure 1). He described severe abdominal pain. The patient's abdominal visual analogue scale pain score was 9/10. There was no blood at the meatus. The patient's bedside FAST imaging revealed fluid around the bladder, coagulum inside, and irregularity in the lateral wall (Video 1). An indwelling foley catheter was placed, and gross hematuria was noted. Contrast-enhanced abdominal computed tomography (CT) was planned. Intraperitoneal and extraperitoneal bladder rupture was detected in late-phase images (Figure 2). Additionally, minimally displaced, and non-displaced fractures were observed in the left acetabulum, left superior and inferior pubic ramus. There were no clinically significant findings in blood tests. The stable patient was admitted by the pediatric surgeon and an operation plan was created.

## Discussion

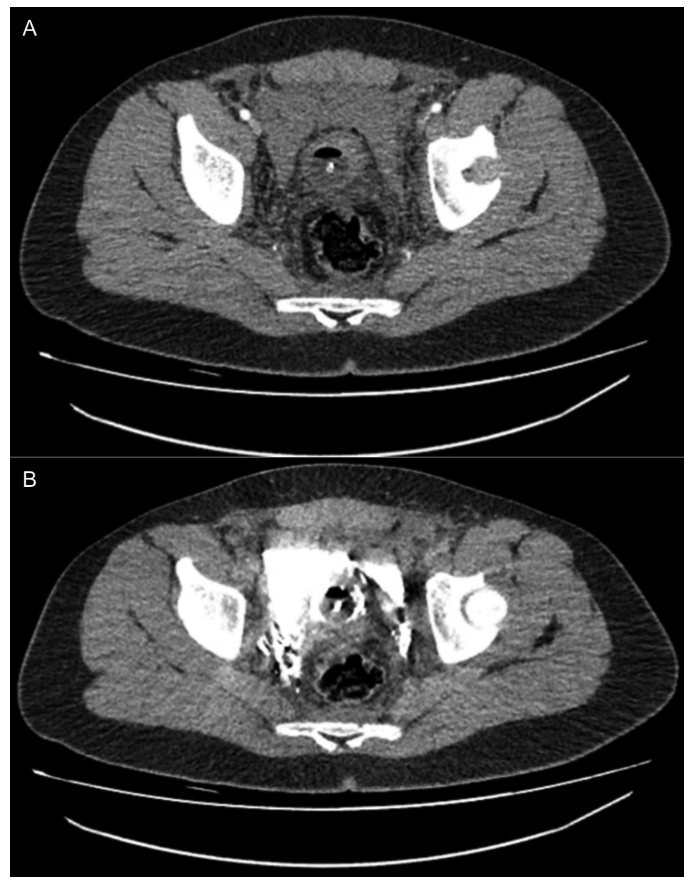
One of the most frequently used trauma procedures in emergency departments is FAST. It can be defined as searching for free fluid in four quadrants as right upper quadrant, left upper quadrant, subxiphoid region, and pelvis. With the addition of lungs, it is called e-FAST (extended-FAST). As in adults, it is evaluated in the primary survey in pediatric trauma resuscitation. Unfortunately, due to physiological reasons such as the type of pediatric traumas, the small surface area of the patients, and the large size of the organs compared to the body, free fluid in the abdomen can only be detected in 40% of the patients.<sup>4</sup> It may not detect solid organ lacerations, which are the most common pediatric intra-abdominal pathologies. In other words, negativity does not exclude intra-abdominal injury. The fact that it is an operator-dependent process also supports this difficulty. After our patient was evaluated with the classical ABCDE approach, intra-abdominal pathology was suspected and free fluid in the pelvis was detected with point-of-care ultrasound. In addition to the fact that this fluid is adjacent to the bladder, the presence of anechoic irregular shapes in it and the irregularity of the wall borders have increased the possibility of bladder injury.



**Figure 1.** Ecchymosis and abrasions (suprapubic area)

CT cystogram or X-ray cystogram is used as the standard diagnostic test to evaluate the bladder. Although both modalities have similar sensitivity, studies have shown that CT cystogram is superior because it provides a faster and more accurate diagnosis while requiring less labor.<sup>5</sup> In addition, CT can accurately detect other trauma-related pathologies. Contrast-enhanced abdominal CT was planned for the patient, who was subjected to a load of thousands of kilos between the crane legs and the wall, to detect pathologies other than bladder injury. Early-phase and late-phase (approximately 15 minutes later) images were obtained and evaluated.<sup>6,7</sup> Contrast material leakage from the bladder to the intraperitoneal and extraperitoneal areas was detected in late-phase images. It has been stated in the literature that this method may not be sufficient to exclude bladder perforation by passive distension of the bladder filled with contrast, even if the urinary catheter is clamped.<sup>4</sup> However, it has been stated that it can be used in high-energy traumas, especially in patients who cannot be catheterized.<sup>6</sup> No active bleeding, vascular pathology, or organ injury was detected except for pelvic fractures.

Bladder injuries are most common in children under 6 years of age. Because from this age onwards the bladder is protected by the pubic symphysis.<sup>5</sup> It is associated with 60-90% of pelvic fractures in older age groups. Although there are two types:



**Figure 2.** A) Early phase, B) Late phase



Extraperitoneal (most common 60%) and intraperitoneal, both conditions can be seen in the same patient in 10% of cases.<sup>8</sup> Pubic ramus fractures generally accompany extraperitoneal injuries. Intraperitoneal injuries often originate from the dome, the weakest area of the bladder. It is reported that a full bladder increases the possibility of injury, but our patient did not have such a description.<sup>5</sup> Extraperitoneal injuries are usually healed with a Foley catheter. Intraperitoneal injuries should be operated.<sup>5,9</sup> Our patient was diagnosed with a combined bladder rupture and underwent surgery. For pelvic fractures, orthopedics recommended bed rest and outpatient follow-up.

## Conclusion

Blunt abdominal traumas are challenging cases for physicians. Diseases with high mortality, such as bladder rupture, should be considered in the differential diagnosis. Point-of-care ultrasound may be important for definitive treatment.

## Ethics

**Informed Consent:** The written informed consent of the patient's father was taken.

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



Video 1: <https://www.youtube.com/watch?v=wapHNGgVQ-c>

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# A Diagnostic Dilemma: Job Syndrome Mimics Abusive Trauma

## Bir Tanı İkilemi: Fiziksel İstismarı Taklit Eden Job Sendromu

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### Abstract

In some cases, making of physical abuse diagnosis can be difficult if the findings were derived from an unusual disease or an unexpected finding of a common disease. A female infant was admitted to emergency department of our hospital, who was suffering from loss of consciousness. Examination and imaging methods revealed subarachnoid hemorrhage, old and new femur fractures, bilateral retinal hemorrhage. Performing genetic tests with multidisciplinary approach concluded that our case was found to have a mutation, DOCK8 (NM\_001190458; c.2071G>A; p.Val691Met), suggests to Job syndrome (JS). JS is not only an immunodeficiency syndrome but also can be manifested by skeletal and connective tissue disorders. The fractures were most likely due to JS. Physicians must be aware of these probabilities. On the other hand, though it was only reported in a heterozygous form in GenomAD (genome aggregation database) it has big value that it was homozygous in our case.

**Keywords:** Child abuse, Job syndrome, physical abuse

### Öz

Fiziksel istismar tanısı koymak, sık görülmeyen bir hastalığa ait bulguları ya da yaygın görülen bir hastalığın beklenmeyen bir bulgusunu içeriyorsa bazı olgularda zor olabilmektedir. Küçük bir kız bebek annesi tarafından hastanemizin acil servisine bilinç kaybı şikayetiyle getirilmiştir. Muayene ve görüntüleme tetkikleri subaraknoid kanama, yeni ve eski femur kırıkları, bilateral retinal kanamayı ortaya koymuştur. Multidisipliner yaklaşımla yapılan genetik testler sonucunda olgumuzun Job sendromu (JS) olduğunu ortaya koyan DOCK8 (NM\_001190458; c.2071G>A; p.Val691Met) mutasyonuna sahip olduğu belirlendi. JS sadece bir immün yetmezlik sendromu olmayıp aynı zamanda iskelet ve bağ dokusu bozukluklarıyla da ortaya çıkabilmektedir. Kırıklar büyük olasılıkla JS'ye bağlıydı. Hekimlerin bu olasılıkların farkında olması gerekir. Öte taraftan, daha önce sadece GenomAD'de (Genom Aggregation Database) heterozigot form rapor edilmesine karşın, olgumuzun homozigot formda olması oldukça değerlidir.

**Anahtar Kelimeler:** Çocuk istismarı, Job sendromu, fiziksel istismar

### Introduction

The responsibility of the physicians involves conducting the physical examination, recording the findings, and ultimately preparing an expert report.<sup>1</sup> Physical abuse is a significant variety of childhood maltreatment. Physicians are legally and ethically obliged to identify child maltreatment to prevent further abuse. Either they treat their patients or widely investigate the symptoms for differential diagnosis. In many cases, making a physical abuse diagnosis can be difficult if it depends only on physical examination. Especially the patient with suspicion of physical abuse, suffers from an illness that

has findings can make the physician's mind confuse. A wide variety of diseases can mimic abusive fracture findings, such as rickets, secondary hyperparathyroidism, osteoporosis, Menkes syndrome, leukemia, and hemophagocytic lymphohistiocytosis, in addition to birth and rescue traumas.<sup>2</sup>

Hyper-IgE syndrome, also known as Job syndrome (JS), is an immunodeficiency disease characterized by recurrent infections, high serum immunoglobulin E levels, staphylococcal abscess, eczema, and pulmonary tract infections.<sup>3</sup> JS is known as Hiob syndrome in Germany.<sup>2</sup> JS is heritable in two ways: Autosomal dominant and autosomal recessive (AR).<sup>3</sup> The

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OR form of JS can be manifested by dental, skeletal, and connective tissue disorders.<sup>3</sup> The AR form is quite rare; in fact, almost 200 cases have been reported.<sup>3</sup>

Aim of this case presentation was to draw attention to the importance of making a diagnosis of child physical abuse. Diagnosis of physical abuse is simply based on excluding irrelevant diseases. JS is one of the diseases that have findings mimicking a physical abuse as well as our case. On the other hand, the causes of physical child abuse and shaken baby syndrome should be considered.

## Case Report

The case was a 5-month-old female infant who was admitted by her mother to the pediatric emergency department suffering from loss of consciousness. She was 5200 g, 68 cm in length, and 39 cm in head circumference. Examination and imaging revealed subarachnoid hemorrhage, old and new femur fractures, and bilateral retinal hemorrhage.

Her mother was 21 years old when she gave birth. Our case is the first pregnancy of her mother. She was born in 830 g via c-section. Her first Apgar score was 6 or 7. The patient was premature and small for gestational age. After birth, she suffered from pulmonary hemorrhage, icterus of the newborn, patent ductus arteriosus, Patent foramen ovale, and retinopathy of prematurity (ROP). When she was 3 months old, she was treated because of cellulite on the left thigh. At the age of 4 months, she developed a central nervous system infection.

Once the pediatricians who examined her were in doubt about physical abuse such as Shaken baby syndrome due to the findings above. The case was referred to each department of ophthalmology, orthopedics, medical genetics, and forensic medicine. Either detailed physical examination or laboratory tests (Table 1) and imaging methods were performed.

Parameter	Amount
Alkaline phosphatase	351 U/L
Phosphorus	5.53 mg/dL
Calcium	8.97 mg/dL
Potassium	5.69 mg/dL
25 hydroxy vit D	28.35 ng/mL
Free T3	4.09 pg/mL
Parathyroid hormone	55.17 ng/dL
Free T4	1.42 ng/dL
Thyroid-stimulating hormone	4.94 uIU/mL
C-reactive protein	25.6 mg/L*
Eosinophil	0.05*
Neutrophil	1.77*
Lymphocytes	3.54 *
White blood cells	5.8 mcl*

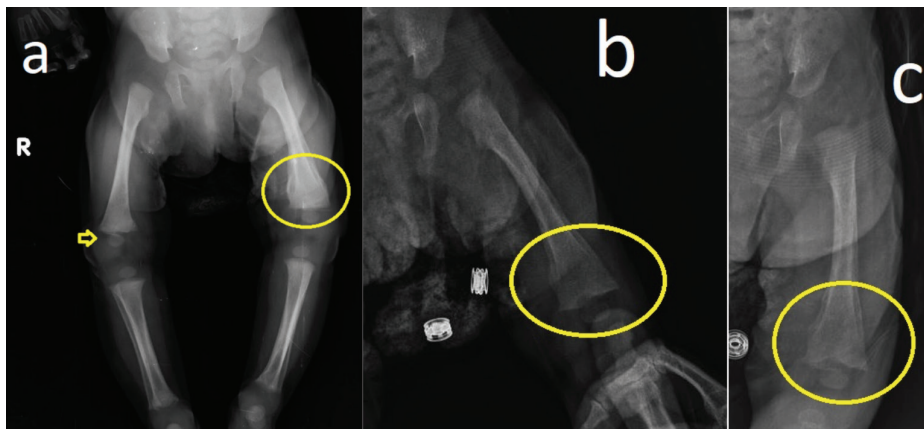
X-ray revealed a fracture line in the distal part of the right femur and callus tissue, which is a sign of an old fracture in the distal region of the left femur (Figure 1a-c). Magnetic resonance imaging of the brain revealed a common limitation of diffusion. Brain-CT showed a partial interventricular hemorrhage and subarachnoid hemorrhage in the left parietal lobe (Figure 2a-d). During the abdomen Ultrasound imaging, a thin septate cyst in the right adnexa was found, which was 15 mm in length, incidentally. During the physical examination, hyperextensibility, obvious forehead, small chin, and enlarged (15 mm) inter-alar width (Figure 3a) were noticed. The left foot was six-fingered (Figure 3b). However, asymmetric face, rough skin, and high or cleft palate were not observed. A homozygous variant (c.2071G>A; p. Val691Met) of *DOCK8* (NM\_001190458) was detected in the patient using a clinical exome sequencing kit (Sophia™, Saint Sulpice, Switzerland) on a next-generation sequencing platform (NextSeq 500® System, Illumina, USA). This is the variant AR form of JS. Due to suspicion of Shaken baby syndrome, social investigation was conducted by social service. Subsequently, custody was taken from her parents. Currently, the patient was discharged. She is still followed by ophthalmologists at proper intervals with in terms of ROP. It was determined that our patient's disease may have caused these allegations, involving physical abuse.

The social investigation report revealed that the parents of our case were poor people, but they were interested in their children. According to the information taken from their neighbors and impression from the behaviors of the parents of our case do not give rise to any doubt of harm to their children. The parents were found to have enough ability to raise their children by the social workers who prepared the report.

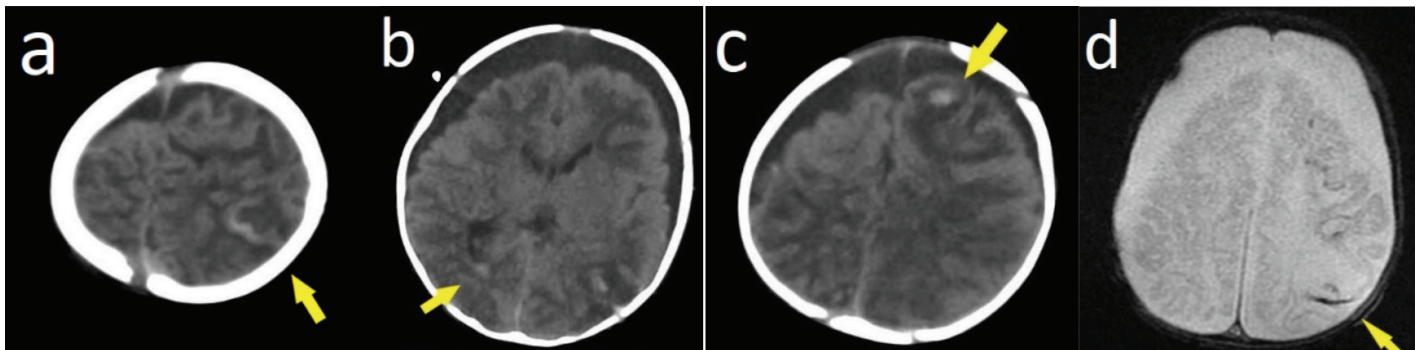
Informed voluntary consent form: The consent form was taken from the parents of the patient.

## Discussion

All physicians, especially pediatricians, forensic medicine, and emergency medicine specialists, can address child maltreatment at any time. At that moment, it is important that making a true diagnosis and declaring it to the legal authorities will prevent further traumas and even death. On the other hand, making an incorrect diagnosis of abuse may cause great injustice for the caregiver or parents of the child. At this point, the diagnosis of the physician is critical. Some cases, as well as ours, may manifest unusual findings that make the correct diagnosis harder. In these cases, a multidisciplinary approach is vital. A JS case very rarely seen was shared with the aim of drawing attention to colleagues on this topic. The purpose of our presentation was to remind and underline the skeletal findings of JS. It has been stated that JS can be due to



**Figure 1.** a) Fracture line in the right femur and callus tissue in left femur, b, c) callus tissue in left femur



**Figure 2.** a) Subarachnoid hemorrhage in the left parietal lobe, b) intraventricular hemorrhage and subdural effusion, c) parenchymal hematoma in the left frontal lobe, d) subarachnoid hemorrhage in the left parietal lobe



**Figure 3.** a) Dysmorphic findings, b) sixth finger in left foot

skeletal and connective tissue abnormalities.<sup>4</sup> Thus, physicians keep findings of those syndromes and diseases in their minds while making a diagnosis of physical abuse.

The etiology of femur shaft fractures in infants is fall accidents, fragility of the bone, and trauma without accident.<sup>5</sup> Femur shaft fracture in infants is very rare.<sup>5</sup> The

incidence of femur shaft fracture in children under one year of age is 0.016% per year in Sweden.<sup>5</sup> In a study based on the investigation of the etiology of long bone fractures in infants involving 187 infants, it was reported that two birth-related femur fracture cases were met and they were taken osteogenesis imperfecta diagnosis.<sup>5</sup> In the same study, three cases were rickets.<sup>5</sup> Some cases that were suspected of physical abuse were consulted to the register of children and young persons subjected to child welfare measure, but none of them were abused.<sup>5</sup> Femur shaft fractures can be linked with physical abuse in children under one year of age, underlining the significance of differential diagnostic consideration.<sup>5</sup> Von Heideken et al.<sup>5</sup> reported that the proportion of femur fractures in abuse cases was 9% among 287 cases in the study. Abulebda et al.<sup>6</sup> shared a case who was one and half years old and had bilateral femur, humeral, and tibia fractures. The case was drawn attention and searched by child protective services.

Although JS has many subtle features such as dysmorphic face and hyperlaxity of joints, these findings should raise the index of suspicion of JS. JS contains characteristic features such as asymmetric face, increasing inter-alar width, osteopenia, pathological fractures even if exposing a small trauma, hyperextensible joints, and vascular abnormalities. Our case also

had these abnormalities, so it has shown consistency with the literature.<sup>3</sup> Our case not only had interventricular hemorrhage but also subarachnoid hemorrhage.

Our case is the AR form of JS. It is likely benign according to American College of Medical Genetics and Genomics criteria and uncertain in significance according to ClinVar (www.ncbi.nlm.nih.gov/clinvar/). This variant was found to be heterozygous in two different patients previously diagnosed with common variable immunodeficiency in the literature.<sup>7</sup> Although it was only reported in a heterozygous form in GenomAD (genome aggregation database), it was important that it was homozygous in our case.

## Conclusion

JS has different components that cause confusion in the physician's mind to make a diagnosis only on the clinical aspect. It is clear that JS is difficult to diagnose without any genetic testing. During the evaluation of a child with trauma findings such as fractures, some diseases such as rickets, osteogenesis imperfecta, and JS should be considered before the diagnosis. Pediatricians, pediatric radiologists, forensic medicine specialists, and emergency physicians must be aware of these probabilities. This case was found to have a mutation, *DOCK8*, suggesting JS. Unfortunately, the levels of serum immunoglobulin E could not be tested because of the busy laboratory conditions of the pandemic. Nevertheless, common infections that our case met, eosinophilia, and decreasing lymphocyte and white blood cell levels may support our diagnosis. The fractures were most likely due to JS. Abandoning the misdiagnosis of abuse cases requires attention and an approach of multidisciplinary medical care.

**Information:** An abbreviated version of portions of this paper was presented at the 18. Adli Tıp Günleri Congress, Antalya, Türkiye, Oct 19, 2023.

## Ethics

**Informed Consent:** The consent form was taken from the parents of the patient.

## Authorship Contributions

Surgical and Medical Practices: S.K., A.O., O.G., A.M., Concept: S.K., A.O., O.G., Design: S.K., A.O., A.M., Data Collection or Processing: O.G., A.M., Analysis or Interpretation: S.K., A.O., O.G., A.M., Literature Search: S.K., A.O., Writing: S.K., A.O., O.G., A.M.

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# Diagnostic Challenges in a Nine-year-old Boy with ADEM and Longitudinal Extensive Transverse Myelitis

## ADEM ve Longitudinal Ekstensive Transvers Miyelitli Dokuz Yaşında Bir Erkek Çocukta Tanı Zorlukları

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### Abstract

Acute disseminated encephalomyelitis (ADEM), or postinfectious encephalomyelitis, is a demyelinating central nervous system disease that typically presents with multifocal neurologic symptoms and encephalopathy. Numerous pathogens have been associated with ADEM, and the implicated viruses include coronavirus, coxsackie, cytomegalovirus, Epstein-Barr, herpes simplex, hepatitis A, HIV, influenza, measles, rubella, varicella zoster, and adenovirus. Although severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection has been associated with ADEM, the incidence is quite low. We present the case of a 9-year-old boy with ADEM plus longitudinal extensive myelitis who had a SARS-CoV-2 infection history and acute adenovirus infection. We evaluated the diagnosis and treatment challenges. Although our patient had severe neurological respiratory failure requiring intubation and tetraplegic flaccid paralysis, he had a total recovery before hospital discharge.

**Keywords:** ADEM, adenovirus, COVID-19, transverse myelitis, children, rituximab

### Öz

Akut dissemine ensefalomyelit (ADEM) veya postenfeksiyöz ensefalomyelit, tipik olarak multifokal nörolojik semptomlar ve ensefalopati ile ortaya çıkan, demiyelinizan bir merkezi sinir sistemi hastalığıdır. Çok sayıda patojen ADEM ile ilişkilendirilmiştir ve ilişkili virüsler arasında koronavirüs, koksaki, sitomegalovirüs, Epstein-Barr, herpes simpleks, hepatit A, HIV, grip, kızamık, kızamıkçık, varicella zoster ve adenovirüs yer alır. Şiddetli akut solunum sendromu-koronavirüs-2 (SARS-CoV-2) enfeksiyonu ADEM ile ilişkilendirilse de görülme sıklığı oldukça düşüktür. SARS-CoV-2 enfeksiyon öyküsü ve akut adenovirüs enfeksiyonu olan, ADEM ve eşlik eden longitudinal yaygın transvers miyelitli 9 yaşında bir erkek hastayı sunduk. Tanı ve tedavi zorluklarını değerlendirdik. Hastamızda entübasyon gerektiren ciddi nörolojik solunum yetmezliği ve tetraplejik flask paralizi olmasına rağmen hastaneden taburcu olmadan tamamen iyileşti.

**Anahtar Kelimeler:** ADEM, adenovirüs, COVID-19, transverse myelit, rituksimab

### Introduction

Acute disseminated encephalomyelitis (ADEM), also known as postinfectious encephalomyelitis, is a demyelinating central nervous system disease that typically presents with multifocal neurologic symptoms and encephalopathy.<sup>1</sup> A febrile or viral infection precedes ADEM. Neurological complications following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Coronavirus disease-2019 (COVID-19) infection

have been reported in the literature, ranging from acute to weeks following infection with SARS-CoV-2.<sup>2</sup> There are only a few case reports in the literature about postvoid or COVID-related ADEM in children.<sup>3</sup> We know that adenoviral infection can also result in neurological dysfunction and ADEM.<sup>4</sup> Here, we present the case of a 9-year-old boy with ADEM plus longitudinal extensive transverse myelitis (LETM) and evaluate the diagnosis and treatment challenges.

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## Case Report

A nine-year-old previously healthy boy presented to the emergency room with a history of fever, nausea, vomiting, and diarrhea. He was unconscious; his Glasgow Coma scale (GCS) 8 (E:2, V:2, M:4), and his brain computed tomography and diffusion brain magnetic resonance imaging (MRI) were normal. His parents' COVID-19 tests were positive, and he lost his sense of smell 6 weeks ago. On admission to our pediatric intensive care unit (PICU), the patient was unconscious and there was no nuchal rigidity. His GCS was 8-10, pupils were bilaterally equal and reactive to light, deep tendon reflexes (DTR) were negative, and the Babinski sign was bilaterally positive. His basic laboratory markers (such as hemogram, electrolytes, liver function tests, and kidney function tests) were normal, but he had elevated inflammatory markers (such as C-reactive protein and sedimentation). His nasopharyngeal swap and stool analysis revealed an acute adenovirus infection. A summary of his autoimmunity and infection

laboratory results is shown in Table 1. His antinuclear antibody was positive. However, no other findings supported vasculitis or lupus.

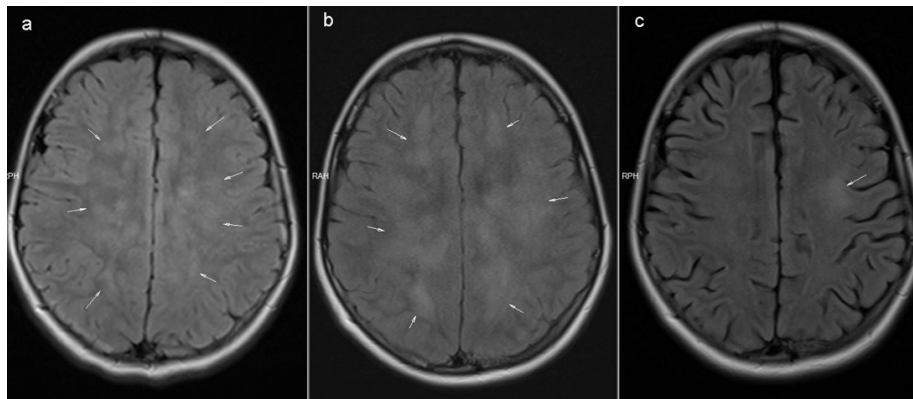
Empirical ceftriaxone and acyclovir treatment were started. His EEG showed a delta coma. Brain MRI revealed bilateral symmetric patchy and confluent white matter lesions in the centrum semiovale and periventricular region as well as in the brainstem compatible with ADEM (Figure 1a). The whole spinal MRI showed multiple patchy expansile T2 hyperintense intramedullary lesions predominantly involving the central part of the spinal cord, which tended to merge with each other and extend longitudinally, suggesting acute LETM (Figure 2).

We initially treated the patients with 1 g/kg/day intravenous immunoglobulin for 2 days and 30 mg/kg/day IV methylprednisolone for 5 days. We continued with IV methylprednisolone, starting on 1 mg/kg/day and tapered over 3 weeks. His symptoms continued progressively after his initial treatment, and we started total plasma exchange

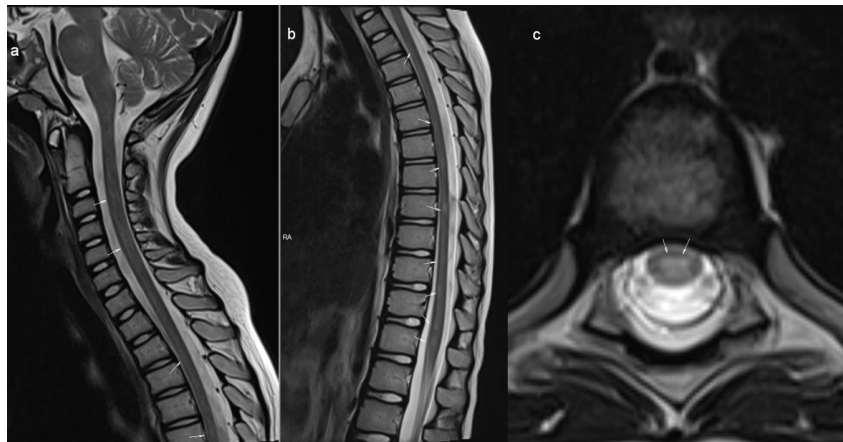
**Table 1. Summary of infections and autoimmunity laboratory findings**

Infections		Autoimmunity	
PCR SARS-CoV-2:	Negative	Anti-ds-DNA:	Negative
Anti-SARS-CoV-2 IgG:	Positive (986 U/mL)	ANA screening:	Positive
HIV 1/2:	Negative	Anti-SSA (anti-Ro):	Positive
HSV 1/2 IgG and IgM:	Negative	Anti-SSB (anti-La):	Negative
HTLV I/II:	Negative	C3 (N: 88-201 mg/dL):	98 mg/dL
CMV IgG and IgM:	Negative	C4 (N: 15-45 mg/dL):	13.5 mg/dL
EBV IgG, IgM, EBNA:	Negative	Anti-MPO and anti-PR3:	Negative
Blood cultures:	Negative	Anti-phospholipid antibodies:	Negative
Viral respiratory PCR panel:	Adenovirus positive	ESR (N: <15 mm/h):	42 mm/h
Cerebrospinal fluid		Cerebrospinal fluid	
Cells:	57/mm <sup>3</sup> (mononuclear)	Anti-MOG:	Negative
Proteins:	94 mg/dL	Anti-AQP4:	Negative
Glucose:	70 mg/dL	Oligoclonal bands:	Negative
PCR SARS-CoV-2:	Negative		
PCR multiple viral panels:	Negative		
Cultures (bacterial, fungal, mycobacterial):	Negative		

ANA: Antinuclear antibodies, AQP4: Aquaporin-4, C: Complement, CMV: Cytomegalovirus, EBV: Epstein-Barr virus, ESR: Erythrocyte sedimentation rate, HIV: Human immunodeficiency virus, HSV: Herpes simplex virus, HTLV: Human T-lymphotropic virus, MOG: Myelin oligodendrocyte glycoprotein, N: Normal range/value, PCR: Polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2



**Figure 1.** (a-c): Axial plane flair sequence of the patient on admission (a) demonstrates bilateral symmetric patchy and confluent white matter lesions in the centrum semiovale (arrows). One week later, the axial plane flair sequence of the follow-up MRI (b) shows that the white matter lesions coalesced over the 1-week period (arrows). One month later (c), the lesions substantially disappeared except for the left frontal cortical-subcortical lesion (arrow)  
MRI: Magnetic resonance imaging



**Figure 2.** (a-c): Sagittal plane T2-weighted images of the spinal cord (a, b) reveal multiple patchy expansile T2-hyperintense lesions that tend to merge with each other, compatible with longitudinally extensive spinal cord involvement (arrows). Note the extension into the brainstem. An axial plane T2-weighted image of the spinal cord (c) demonstrates the central involvement of the cord (arrows)

(PLEX) on the third day and continued for 6 consecutive days. On the fifth day of PICU admission, we intubated him because of neurogenic respiratory failure. On his 10<sup>th</sup> day of PICU admission, he was intubated, his four limb muscle strength was 1/5, and his DTRs were negative. We performed a new brain MRI and observed that his white matter lesions were extended (Figure 1b). We gave him rituximab on the 11<sup>th</sup> day of admission and continued it once a week for a total of four doses. We extubated him on his 14<sup>th</sup> day, and he started to eat orally and did not require respiratory support or oxygen on his 17<sup>th</sup> day of PICU admission. He received physiotherapy support in all his PICU days. We transferred him to the pediatric ward on his 18<sup>th</sup> day in the PICU. We performed a new brain and spinal MRI and observed that all his lesions regressed (Figure 1c). He was discharged on the 38<sup>th</sup> day of his hospital stay. His examination on discharge showed that his four limb muscle strength was 5/5, DTR was normoactive, Babinski's sign was negative, and he was able to eat and walk without support.

## Discussion

ADEM is an autoimmune disorder of the central nervous system that is triggered by environmental stimuli in genetically susceptible individuals.<sup>1</sup> Numerous pathogens have been associated with this disorder. Implicated viruses include coronavirus (and SARS-CoV-2 infection), coxsackie, cytomegalovirus, Epstein-Barr, herpes simplex, hepatitis A, HIV, influenza, measles, rubella, varicella zoster, and adenovirus.<sup>1</sup> Encephalopathy, the main characteristic feature of ADEM, develops within 7 days of prodromal symptoms. Neurological symptoms may include behavioral changes, confusion, irritability, restlessness, and coma.<sup>2</sup> Our patient had all these clinical features.

The pathophysiology of acute and post-acute neurologic manifestations of COVID-19 is likely multifactorial. Each of the following mechanistic pathways could interactively or independently cause disease: direct viral invasion and replication in the CNS, large vessel or microvascular insufficiency due to vasoconstriction or occlusion, non-specific effects of severe systemic COVID-19 illness or treatment, and immune system dysregulation and autoimmunity targeting cells, including myelin, neurons, axons, and oligodendrocytes.<sup>1,2</sup> The non-specific characteristic of COVID-19-related myelitis makes the diagnosis challenging, and it is mandatory to include several differential diagnoses, including other causes of infectious and metabolic syndromes.<sup>5</sup> Our case may have had immune system dysregulation due to COVID-19 and direct viral invasion due to adenovirus. However, our cerebrospinal fluid (CSF) examination did not show adenovirus in the patient's CSF.

Ismail II and Salama S reviewed the literature on COVID-19-related demyelinating diseases and found that 71/78 patients (90%) presented with encephalopathic clinical symptoms. There were 40 cases of transverse myelitis (TM), of which 24 were isolated TM and 16 were part of diffuse demyelinating processes. LETM was the most frequent feature of spinal involvement reported in 19 of 24 (72.5%) cases of isolated TM.<sup>6</sup> They evaluated 20 children with ADEM with a median age of 9 years and 5 of 20 patients with myelitis. Similar to adults, 4 of 5 patients with myelitis showed LETM in children.<sup>6</sup>

Our patients also had ADEM with LETM and an acute adenovirus infection. Adenoviral infection can also result in neurological dysfunction and ADEM, and the lack of adenovirus in the CSF does not exclude CNS involvement.<sup>4</sup>

MIS-C may cause neurologic dysfunction in children.<sup>7</sup> Our patient had a positive COVID-19 serologic test but did not completely meet the MIS-C criteria.



The treatments might be divided into two categories: treatments addressed to the cause and immunological treatments to reduce inflammation and exacerbate the immune response that causes myelitis. Antibiotics and antivirals can be used to treat primary causes. We used empirical ceftriaxone and discussed cidofovir; however, we did not administer it. Because cidofovir has many side effects, our patient was in the late period of his adenovirus infection, and we did not demonstrate it in CSF. The immunological treatments are corticosteroids, immunoglobulins, PLEX, and rituximab in severe cases.<sup>8</sup> Corticosteroids should be started as soon as possible after diagnosis (methylprednisolone 30 mg/kg/day up to 1 g for 3 to 7 days), and PLEX is indicated if corticosteroid treatment fails.<sup>8</sup> In severe cases, rituximab may be used if the other first-line treatment fails. We used rituximab for 4 weeks for our patient because the clinical situation worsened after primary treatment.

The outcome of the children population was favorable in 13/20 (65%) COVID-19-related TM patients.<sup>5</sup> Rodríguez de Antonio et al.<sup>4</sup> demonstrated that only 1/18 patients had total recovery. Although our patient had severe neurological respiratory failure requiring intubation and tetraplegic flaccid paralysis, he had a total recovery before hospital discharge.

In Conclusion, COVID-19-related demyelinating diseases are rare and life-threatening in children. Early diagnosis and appropriate treatment are critical for lifesaving outcomes.

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### Ethics

**Informed Consent:** Informed consent was obtained from our patient's family. However, written consent was not obtained because the publication was retrospective and did not show patient personal information.

### Authorship Contributions

Surgical and Medical Practices: E.A., M.U.Y., E.Az., Concept: E.A., M.U.Y., E.Az., T.H., Design: E.A., M.U.Y., E.Az., T.H., Data Collection or Processing: E.A., B.D., Analysis or Interpretation: E.A., B.D., H.T., Literature Search: E.A., M.U.Y., E.Az., T.H., Writing: E.A., M.U.Y., E.Az., T.H., B.D., H.T.

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# Can Bispectral Index be Used in the Diagnosis and Treatment of Non-convulsive Status Epilepticus in Children?

Bispektral İndeks Çocuklarda Non-konvülsif Statüs Epileptikusun Tanı ve Tedavisinde Kullanılabilir mi?

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## Dear Editor,

Bispectral index (BIS) which is used more in evaluating sedation deepness in anesthesia, can also be used in the evaluation of sedation deepness in pediatric intensive care units. Withholding a BIS level below 60, cognizance is reduced therefore patients would be monitored at safe intervals.<sup>1</sup> BIS analyses electroencephalographic (EEG) signals through algorithms to value patients' consciousness levels. BIS levels are between 0 to 100. "Zero" value means no brain activity, "0-20" levels mean burst suppression, "20-40" levels mean deep hypnotic state, "40-60" levels mean general anesthesia state, 60-80 levels mean sedation, and "100" value means awoken state. BIS pediatric sensors are available for measuring brain activity by detecting low-voltage EEG waves. Anesthetic agents, age, hypothermia, neurological disturbances, and interactions with medical devices can affect BIS evaluation.

A 7-year-old girl diagnosed with febrile infection-related epilepsy syndrome was put in a barbiturate coma because of refractory status epilepticus. In the patients' follow-up monitored by BIS, the patient's BIS levels are increased to around 90 while levels are around 20-30 even though the patient wasn't awakened and didn't have convulsion. When dormicum intravenous (IV) bolus (0.1 mg/kg) was given to the patient, levels decreased to around 70 levels, and after propofol IV bolus (3 mg/kg) and propofol infusion rate increased to 4 mg/kg/hr, BIS levels are decreased to around 25-30. Seizure patterns in EEG are seen consistent with BIS levels. This patient's non-convulsive seizures and treatment

efficiency and burst suppression competency are obtained by drug titration using BIS.

A 12-year-old patient who was receiving supportive treatments for earthquake related crush syndrome, sepsis and multiorgan failure developed refractory status epilepticus and sudden increasements were detected in the patient's BIS level from 30 to 90 during EEG monitorization. Readings in continuous EEG monitorization were consistent with seizures. Non-convulsive status epilepticus treatment is titrated by holding BIS levels below 40 when continuous EEG monitorization can't be done.

Kaisti et al.<sup>2</sup> saw consistency between sudden increasements in BIS levels and EEG waves during sevoflurane-induced anesthesia in 2 healthy patients when seizure activity is seen in EEG. Correlation between EEG and BIS was shown in 8 patients who were put in barbiturate coma in Prins et al.'s<sup>3</sup> study which emphasized the value of the usage of BIS for easy monitoring in a patient whose basal EEG was seen. BIS that can distinguish seizures can also be used to differentiate pseudo-seizure.<sup>4</sup> EEG signals are recorded 0.5-30 Hz frequency band while electromyogram (EMG) signals are recorded 30-300 Hz frequency band. BIS uses EEG signals up to 47 Hz. Hence, low-frequency EMG activity can overestimate BIS. This fact defined the patient as a temporary false negative. In these situations, muscle relaxants must be given. Thus, interpreting BIS results must be done carefully.<sup>5</sup>

In conclusion, in pediatric intensive care units where continuous EEG monitorization can't be done, BIS can be used in patients with non-convulsive status epilepticus follow-

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up and drug titration. We think BIS has a benefit in deciding EEG repeat, whether there is a burst suppression or else, and the treatment method and advice using BIS in non-convulsive status epilepticus follow-up. There is a need for more qualified studies on the use of BIS in non-convulsive status epilepticus in children.

**Keywords:** Bispectral index, children, non-convulsive status epilepticus, pediatric intensive care

**Anahtar Kelimeler:** Bispektral indeks, çocuk, non-konvülfik statüs epileptikus, çocuk yoğun bakım

### **Ethics**

### **Authorship Contributions**

Concept: F.K., Design: F.K., M.H., Data Collection or Processing: F.K., M.H., Analysis or Interpretation: F.K., T.K., Literature Search: F.K., Writing: F.K., Critical Review: T.K.

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