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The clinical, electrographic, and laboratory findings of patients with seizure followed-up in the pediatric intensive care unit, and their effect on prognosis

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ABSTRACT

Aim: To investigate the clinical characteristics of seizures, treatment options, and electroencephalographic, laboratory findings and factors affecting the prognosis of children admitted to the pediatric intensive care unit (PICU).

Method: The demographic, clinical, electrophysiological, and laboratory findings of patients under follow-up due to seizures in the PICU between January and December 2020 were investigated retrospectively.

Results: One hundred fifty-two patients, 90 (60%) of whom were boys, were included in the study. The patients' mean age was 45.08±40.40 months (range 1-208 months), the mean length of stay was 2.29±2.09 days, and 83 (53.5%) presented due to seizures and were diagnosed with epilepsy. Sixty-nine (44.5%) patients presented with first seizures. Etiological factors were idiopathic in 67 cases (43.3%), constitutional seizures in 37 cases (23.9%), fever and infection in 31 cases (24.5%), autoimmune encephalitis in 4 cases (2.6%), and post-traumatic in 16 cases (10.3%). Complete seizure control was achieved in 89 (57.4%) patients and partial control in 62 (40%), while mortality occurred in one case (0.7%). Cranial magnetic resonance imaging was performed on 54 patients, of whom 50 (32.8%) exhibited pathological findings. Neuromotor developmental delay was present in 47 (30.3%) patients. Sixteen (10.3%) were diagnosed with cerebral palsy, 17 (11%) with neuropsychiatric disease, and 12 (7.7%) with structural brain malformation (Dandy Walker syndrome, chromosomal disease, and neurogenetic syndromes). A comparison of the patients in whom complete and partial seizure control was achieved revealed that seizure control was more difficult in cases with accompanying cerebral malformation, with chronic disease, with neuromotor developmental delay, with histories of admission to the neonatal ICU, and with histories of perinatal asphyxia, and this was found to be statistically significant ($p<0.018$, $p<0.008$, $p<0.017$, *and* $p<0.001$, respectively).

Conclusion: Rapid and effective interventions can be planned by identifying the clinical characteristics and etiologies of patients followed-up in the PICU due to seizures, and by considering that seizures may be prolonged, difficult to control, and recurring in patients with accompanying factors that adversely affect seizure prognosis.

Keywords: Childhood, seizure, EEG, etiology, pediatric intensive care unit.

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1. Introduction

Patients presenting with seizures or who experience these while being followed-up due to critical disease represent a large propoartion

of individuals admitted to the pediatric intensive care unit (PICU), and the clinical characteristics of these seizures in children have been well defined [1].

Studies of the incidence and clinical characteristics of seizures in adult ICUs have determined a figure of 0.8-3% and that the etiologies involve stroke, trauma, encephalitis, and anoxia developing in association with cardiovascular diseases [2].

However, although there has been no research on the incidence of cases followed-up due to seizures in the PICU, a limited numbers of studies on their clinical characteristics have reported that the etiology of seizures largely consists of acute symptomatic seizures [2].

Identifying the clinical characteristics and etiologies in patients followed-up due to seizures in the PICU will in all probability lead to more effective and rapid treatment. Consultation with the pediatric neurology department and electroencephalography (EEG) evaluation are exceedingly important in helping to exclude seizure etiologies other than epilepsy [3,4].

Although some previous adult studies have reported incidences and etiologies for patients followed-up due to seizures in the ICU, the numbers of studies concerning the seizure etiologies and clinical characteristics and prognoses of patients in the PICU are still insufficient [3,4].

Improved seizure control and decreases in mortality and morbidity depend on early and effective treatment [5-7]. However, studies of seizures in critically ill children are exceedingly scarce and have generally focused on status epilepticus [8,9].

The aim of this study was to investigate the clinical characteristics of seizures, their etiologies, treatment choices, and electroencephalographic and laboratory findings and factors affecting prognosis in children admitted to the PICU.

2. Materials and methods

This retrospective study included 152 pediatric patients aged 1 month to 18 years who were admitted to the PICU with seizures between January and December 2020. Ethical approval for our study was granted by the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University on 06/12/2022, with decision number 2022/308. Inclusion criteria were: (1) presentation with seizures or development of seizures during PICU stay due to critical illness, and (2) availability of at least one year of clinical follow-up. Exclusion criteria included neonatal patients and individuals over 18 years old. Acute symptomatic seizures were distinguished from idiopathic epilepsy using clinical history, EEG findings, neuroimaging (MRI), and laboratory results. Acute symptomatic seizures were associated with identifiable provoking factors such as fever, CNS infections, metabolic disturbances, trauma, or autoimmune encephalitis. Idiopathic epilepsy was diagnosed in patients with unprovoked seizures and no identifiable structural or metabolic cause. Antiseizure medications used included intravenous midazolam or diazepam as first-line agents, followed by levetiracetam or phenytoin based on clinical response. EEG recordings were evaluated and categorized as normal, focal/multifocal epileptic discharges, or generalized epileptic activity, following standard electroencephalographic classification systems.

Patients with seizures may present to the emergency department and be admitted to intensive care, or else may experience seizures when already in intensive are due to critical diseases. Both types were included in the

present study. Their ages ranged from two months to 18 years. The pediatric risk of mortality score III and Glasgow coma scale were used to estimate disease severity [10].

Medical histories, and clinical and laboratory findings were retrieved retrospectively from the hospital data system. The patients' age, sex, seizure type (focal or generalized), and seizure duration (<5 min, 5-15 min, and >15 min) were recorded. Patients with a known diagnosis of epilepsy and complaints of seizures, and patients with first epileptic seizures and normal/abnormal EEGs were also evaluated. There were also patients developing seizures in association with acute symptomatic causes (febrile seizures, intracranial infections (meningitis, encephalitis, cranial tumors, metabolic disorders, or autoimmune encephalitis). Seizures were initially treated with intravenous (i.v.) midazolam/diazepam, and secondarily with iv levetiracetam/phenytoin. EEG findings (focal or generalized), magnetic resonance imaging (MRI) findings, prognosis (complete seizure control, partial seizure control, or exitus), history findings (perinatal history, neuromotor development, and accompanying diseases), and length of stay in the PICU were retrieved retrospectively from the patient files.

Inclusion criteria were 1) age between one month and 18 years, 2) presentation due to seizure and follow-up in the PICU, or else may experience seizures when already in intensive are due to critical diseases, and 3) attendance of regular follow-ups for one year.

Neonates and patients over 18 were excluded from the study.

2.1. Statistical analysis

Continuous data were expressed as mean±SD (min–max), and categorical variables as frequency and percentage for each group. A range of statistical tests was applied, depending on the normality of data distribution. The Kolmogorov–Smirnov test was used to determine the normality of distribution of the variables. The independent sample t-test was applied to normally distributed variables, while Pearson's chi-square test and Fisher's exact test were applied to categorical variables. A *p*-value < 0.05 was considered statistically significant, and < 0.001 was accepted as highly significant. All results were presented with 95% confidence intervals.

3. Results

One hundred fifty-two patients admitted to the PICU due to seizure over a one-year period were included in the study. Ninety (60%) of these were boys and 62 (40%) were girls. The patients' mean age was 45.08±40.40 months (range 1-208 months). The mean length of stay in the PICU was 2.29±2.09 days. Twenty-four (15.5%) patients were followed-up due to status epilepticus. Eighty-three (53.5%) patients were diagnosed with epilepsy and presented due to seizures, 69 (44.5%) with first seizure. Sixty-seven (43.3%) cases were idiopathic, while seizures triggered by fever and infection were present in 31 (24.5%) patients, autoimmune encephalitis in four (2.6%), and post-traumatic etiology in 16 (10.3%). Ohtahara syndrome, West syndrome, and progressive myoclonic epilepsy were diagnosed in one patient each (Table 1).

The first drugs used in treatment were midazolam in 38 (24.5%) patients and diazepam in 13 (8.4%), while in the second stage phenytoin was used in 19 (12.3%) cases and levetiracetam in 27 (17.4%). Fifty-five (35.5%) patients used multiple drugs. Complete seizure control was achieved in 89 (57.4%) patients and partial control in 62 (40%), while mortality occurred in one case (0.7%), (Table 1).

Table 1. Patient and seizure characteristics.

Parameters	n (%) or mean (min-max)
Patients admitted to the PICU with seizure	152
Age (month)	45±40(1-208)
Gender	
F	62(40)
M	90(60)
PICU hospitalization duration	2.29±2.09
Diagnosed with epilepsy	83(53.5)
Etiology	
Idiopathic	67(43.3)
Structural	37(23.9)
Infectious	31(24.5)
Autoimmune encephalitis	4(2.6)
Trauma	16(10.3)
Drugs used in treatment	
Midazolam	38(24.5)
Diazepam	13(8.4)
Phenytoin	19(12.3)
Levetiracetam	27(17.4)
Multiple seizure-preventing drug use	55(35.5)
Prognosis	
Complete seizure	89(57.4)
Partial seizure	62(40)
Exitus	1(0.7)

Data expressed as mean±SD for continuous variables or n (%) for categorical variables. F: female, M: male, PICU: pediatric intensive care unit.

EEG findings were normal in 62 (40%) patients, while focal or multifocal epileptic disorder was present in 69 (44.5%) and generalized epileptic disorder in 13 (8.4%). EEG could not be performed in eight (5.2%) cases (Table 1).

Cranial magnetic resonance imaging was performed on 54 patients, of whom 50 (32.8%) exhibited pathological findings. Periventricular leukomalacia, multicystic porencephaly, and encephalomalacia were determined in nine, cerebral atrophy in five, partial agenesis of the corpus callosum in three and total agenesis in two, hydrocephalus in three, delayed myelination in one, cortical dysplasia in four, pachygyria, agyria, and heterotopia in three, subdural effusion in five, cephalohematoma in five, Sturge Weber findings in one, intracranial mass in a patient diagnosed with type 1 neurofibromatosis, a frontotemporal mass with cystic and solid components in one, and non-specific signal changes in eight. Cranial diffusion MRI was indicated in 54 patients, of whom three (5.5%) exhibited pathological diffusion restriction.

A history of prematurity was present in 28 (18.1%) patients, of perinatal asphyxia in 17 (11%), and of admission to the neonatal intensive care unit in 27 (17.4%). Neuromotor developmental delay was present in 47 (30.3%) patients. Sixteen (10.3%) had diagnoses of cerebral palsy, 17 (11%) of neuropsychiatric diseases such as autism spectrum disorder and attention deficit hyperactivity disorder, and 12 (7.7%) of structural brain malformation (Dandy Walker syndrome, chromosomal disease, and neurogenetic syndromes). White blood cell elevation was present in 18 (11.6%) patients, lymphopenia in one, liver function test elevation in nine (5.8%), and acidosis in 36 (23.2%).

A comparison of the patients in whom complete and partial seizure control was achieved revealed that seizure control was more difficult in cases with accompanying cerebral malformation, with chronic disease, with neuromotor developmental delay, with histories of admission to the neonatal ICU, and with histories of perinatal asphyxia, and this was found to be statistically significant ($p<0.018$, $p<0.008$, $p<0.017$, and $p<0.001$, respectively), (Table 2).

Table 2. Factors affecting prognosis.

Paramater	**Complete seizure control**	**Partial seizure control**	***p***
Gender			0.28
M	50	40	
F	39	22	
Seizure type			0.27
Focal	5	2	
Generalized	30	12	
Other	54	49	
Etiology			**0.018**
Idiopathic	44	20	
Structural	12	24	
Infection	20	11	
Autoimmune	4	0	
Trauma	9	7	
EEG			0.78
Focal/multifocal	39	29	
Generalized	6	7	
Normal	38	24	
None	6	2	
History of prematurity			0.72
Present	15	13	
Absent	74	49	
History of Asphyxia			**0.008**
Present	7	9	
Absent	82	53	
History of NICU admission			**0.017**
Present	11	15	
Absent	78	47	
Neuromotor developmental delay			**0.001**
Present	16	30	
Absent	72	32	
Accompanying disease			**0.001**
Absent	70	26	
Cerebral palsy	3	13	
Neurogenetic	5	6	
Neuropsychiatric	7	10	
Other	3	8	

Data expressed as mean±SD for continuous variables or n (%) for categorical variables. Continuous variables were compared using an Independent samples t-test. Categorical variables are presented as frequency (percent) and compared using a Chi-square test. F: female, M: male, EEG: electroencephalography, NICU: neonatal intensive care unit.

4. Discussion

This study examined the clinical and electrophysiological characteristics, etiological findings, response to treatment rates, and factors associated with prognosis of pediatric patients admitted to the PICU due to seizures. It is one of the rare studies investigating patients admitted to the PICU due to seizures in the pediatric population.

The mean age in this study, 45 months (3.75 years), was similar to that in previous studies, in which mean ages under five years have generally been reported. Almost all studies have reported that since the seizure threshold declines as age decreases, seizures associated with an acute symptomatic etiology in particular may be seen at younger ages [1,11-13].

The short mean length of stay of two days in this study may be attributable to the seizures being idiopathic or triggered by fever or infection. It may also be due rapid circulation due to our unit's small patient capacity.

Idiopathic causes were most frequently involved in our patients' seizure etiologies. Data concerning etiology in previous studies are inconsistent. While some studies have reported that acute symptomatic seizures are frequently determined in the etiology [1,11], others have reported that symptomatic epilepsy and post-craniotomy-related seizures are often involved [12]. Inconsistent results concerning etiological causes have been reported from different countries and regions. In a study from the UK by Hussain et al. [13] 34% of patients had prolonged febrile seizure, 28% had remote symptomatic seizure, 11% had acute exacerbation of a pre-existing idiopathic epilepsy, and only 18% had acute symptomatic seizures. A systematic review reported that 1% to 12% of cases from countries in the developed world presenting with SE have infectious causes, compared to 28.6% observed in another study [14]. An eight-year review of PICU admissions in a hospital in South Africa determined an infectious cause in 43% of cases [15], whereas a study from Bihar in India reported a figure of 38.5% of cases [16], and Amonkar et al. reported that 64% children had acute symptomatic seizures, with central nervous system infections constituting the majority of these [11]. The prevalence of acute symptomatic seizures in the present study was 24.5%. Since the majority of acute symptomatic causes result from diseases that can be prevented by vaccination, this can vary by country and region.

Pre-existing epilepsy was present in 53.5% patients in the present research, compared to 25.7% [16] and 21% in two similar studies from India [11], 36% in a study from the UK [13], 69.7% in a five-year retrospective study conducted in a PICU in the USA [17], and 46.6% in a similar study from Delhi, India [18]. Approximately half our patients presented due to seizures, the most common type being generalized tonic clonic. Electrophysiologically, focal and multifocal epileptic anomaly was most frequently detected. Seizures lasted between 30 min and 24 hours in 15.5% of patients. None of our patients experienced seizures exceeding 24 hours in duration.

A systematic review of 63 studies conducted worldwide determined a mortality rate of 5-8% among children admitted to the PICU with status epilepticus [19]. Studies from India have reported higher rates of 16.7% [20], 30% [18], and 31.4% [16], while another study reported a mortality rate of 8.9% [11]. Our mortality rate, 0.7%, was considerably lower than that in the previous literature. This low figure may be attributable to our prompt and appropriate

intervention, patients being quickly transferred to our center, and physicians working in the periphery and emergency health service personal being trained on the approach to and treatment of seizures. It was more difficult to achieve complete seizure control in patients with structural brain lesions, histories of perinatal asphyxia, neuromotor developmental delay, abnormalities at neurological examination, and accompanying diseases, and seizures were prolonged in such cases.

Our study observed a notably lower mortality rate (0.7%) compared to prior literature, where mortality in pediatric patients with seizures admitted to the PICU typically ranges from 5–8% or higher. Several factors may have contributed to this favorable outcome. Firstly, prompt and standardized seizure management protocols were applied in our unit, with first-line treatment initiated quickly in the emergency setting. Secondly, our center acts as a regional referral unit with close coordination between emergency teams and pediatric neurology, allowing early EEG monitoring and tailored interventions. Additionally, many patients had idiopathic or febrile seizure etiologies, which are associated with better outcomes.

In comparison with recent studies from various countries, our results align with the lower end of reported mortality rates. For instance, a recent Italian study by Bonardi et al. [5] found that early EEG monitoring and care standardization helped reduce adverse outcomes. Conversely, studies from India and South Africa reported higher mortality due to delays in intervention and a higher incidence of CNS infections and status epilepticus. This suggests that access to timely and protocol-driven care plays a key role in improving seizure-related outcomes in PICU settings [4,6,7].

These findings reinforce the importance of early recognition, standardized treatment pathways, and multidisciplinary coordination in improving outcomes for critically ill children with seizures.

The limitations of this study include its employment of retrospective patient data, the PICU's low bed capacity, and ours being a peripheral center.

In conclusion, our findings showed that the type of seizure, antiseizure medications used, and patient characteristics such as age and gender have no effect on seizure control/prognosis in critically ill children, but that the presence of accompanying cerebral malformation, concomitant diseases, neuromotor developmental delay, and neurological examination abnormalities impact adversely on seizure control. Rapid and effective interventions may usefully be based on the consideration that seizures may be prolonged and recurrent and control may be difficult in such patients.

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