

Clinical and Radiological Features of Seizures in Children Admitted in the PICU at a Tertiary Care Hospital in North-eastern India: A Retrospective Study

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ABSTRACT

Introduction: A seizure is a brief change in normal electrical brain activity resulting in alterations in awareness, perception, behaviour, or movement, which affect persons of all ages, but are particularly common in childhood. Seizure is a serious neurological symptom in the Paediatric Intensive Care Unit (PICU), yet data on the clinical spectrum of seizures occurring in the PICU setting in India are scarce.

Aim: To determine the aetiology, clinical and radiological features of seizures in critically ill children admitted to PICU at a tertiary care hospital.

Materials and Methods: This retrospective study was conducted at Gauhati Medical College and Hospital, Guwahati, Assam, India, from April 2017 to September 2018. A total of 253 children aged between 29 days to 12 years, admitted to PICU with seizures were enrolled in the study. Data regarding demographics, diagnosis, clinical seizures, associated diagnosis,

Electroencephalogram (EEG) features, imaging, length of stay in PICU, and in-hospital mortality were collected. Data was presented in frequencies, mean, standard deviation.

Results: In present study, male to female ratio was 1.5:1 with mean age of 48.9±44.5 months. The most common causes of seizures in PICU setting were acute symptomatic in 185 (73.1%) and epileptic in 68 (26.9%) patients. Central Nervous System (CNS) infections constituted 15.8% of the PICU admissions following seizures. Most frequent co-existent diagnosis at admission was infectious diseases in 96 (38%) patients, followed by pulmonary diseases in 28 (11%) and cardiologic diseases in 14 (5.5%).

Conclusion: The CNS infections are the most common cause of acute symptomatic seizure, while non infectious diseases such as metabolic disorders, epilepsy and immune disorders also contribute to seizure occurrence in PICU. Identification of common seizure aetiologies in PICU is important step for a prompt and effective treatment.

Keywords: Epileptic encephalopathy, Neurological disorders, Paediatric intensive care unit, Status epilepticus

INTRODUCTION

The burden of acute neurological conditions in paediatric population is high and contributes to 16.2% of the total admissions to PICU globally [1]. Incidence of seizure in critically ill children is only 0.5%, which was much lower than adults, ranging from 0.8-3.3% with vascular, metabolic, and drug withdrawal, being the most common cause [2,3].

In a retrospective review, of a total of 550 consecutive children in PICUs, who underwent EEG monitoring showed electrographic seizures in 30% children and multivariate logistic regression model showed that independent risk factors for electrographic seizures included younger age, clinical seizures prior to EEG monitoring, an abnormal initial EEG background, interictal epileptiform discharges, and a diagnosis of epilepsy [4].

Despite the fact that some of the earlier studies showed the incidence and aetiologies of acute symptomatic seizures in intensive care units in adults [5-8], but the features of seizures occurring in children in the PICU setting still remain insufficient. The topic of seizures in the PICU has not been previously addressed properly, as limited studies are conducted on seizures in critically ill children admitted in PICU [3,9,10]. Moreover, data on clinical spectrum of seizure disorders from India particularly from North-east India is scarce. Hence, present study was undertaken to study the aetiology, clinical and radiological features of seizures in critically ill children admitted to PICU.

MATERIALS AND METHODS

This retrospective study was conducted at Gauhati Medical College and Hospital, Guwahati, Assam, India, which is an academic

Government Institution providing tertiary care to the people of North-eastern region of India. Data were collected from April 2017 to September 2018 and were analysed from December 2018 to May 2019, after obtaining approval from Institutional Ethics Committee (IEC) of Gauhati Medical College and Hospital, Guwahati (Reference No MC/190/2007/Pt-11/Dec-18/11).

Inclusion criteria: Children with a known history of seizures and epilepsy, aged between 29 days to 12 years of age, admitted to PICU with complete patient information along with the investigation reports available in the medical records, were included in the study.

Exclusion criteria: Children admitted for a change in mental status after seizures or seizures occurring only outside of the unit, were excluded in the present study. Patients with psychogenic nonepileptic seizures (defined as altered movement, sensation or experience, similar to epilepsy, but caused by a psychological process [11], diagnosed by the clinical description and neurophysiologic studies during the episodes and children with incomplete medical records were excluded from the present study.

All diagnoses were reviewed to confirm that the events corresponded to seizures. A total of 314 patients were admitted to PICU with seizures, within the study duration. A total of 61 patients were excluded due to incomplete data and the remaining 253 patients were analysed.

Study Procedure

Data were collected including the aetiology of the seizures, associated diagnosis, antiepileptic drugs used to treat the seizures and Computed Tomography (CT) Scan of brain, Magnetic

Resonance Imaging (MRI) Brain, laboratory and EEG data, length of stay in PICU, and in-hospital mortality. Seizures were sorted based on the classification of epileptic seizures and epilepsy from the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE), 2017 [12]. The patients with epilepsy were grouped based on the same classification as either having symptomatic, probably symptomatic or idiopathic epilepsy [13]. Status epilepticus were defined as seizures lasting ≥30 minutes or two or a series of seizures, without full return to baseline lasting ≥30 minutes [14].

Operational Definitions

Seizure: A seizure is defined as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain [15].

Convulsion: The term “convulsion” is a popular, ambiguous, and unofficial term used to mean substantial motor activity during a seizure. Such activity might be tonic, clonic, myoclonic, or tonic-clonic [15].

Epilepsy: Epilepsy is a disorder of the brain characterised by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure [15].

Infantile spasm: The term infantile spasms remain suitable to describe a seizure type, the most common form of epileptic spasms occurring in infancy [13].

Status epilepticus: Status epilepticus had previously been defined as continuous seizure activity lasting greater than five minutes. Recently, the ILAE redefined status epilepticus as ongoing seizure activity due to failure of mechanisms responsible for seizure termination or initiation of mechanisms provoking ongoing seizures causing prolonged seizures after timepoint t1, and which can have long-term consequences after timepoint t2, with t1 and t2 being 5 minutes and 30 minutes, respectively for convulsive status epilepticus, 10 minutes and 60 minutes for focal status epilepticus with impaired consciousness, and 10-15 minutes and unknown for absence status epilepticus [14].

Patients were divided into two groups, acute symptomatic seizure and epileptic seizures. Acute symptomatic seizures were further subgrouped into the following categories: CNS infection, Sepsis, metabolic, CNS inflammation or autoimmune disorders, stroke, unknown, tumour/oncologic, hypoxic-ischaemic encephalopathy and toxin etc. Diagnoses were made based on recorded clinical and laboratory data and verified with standard reference. Co-existent diagnosis were noted for both groups of children with seizures at the time of admission or during stay in PICU.

STATISTICAL ANALYSIS

Data was collected, entered in Microsoft excel sheet and analysed using Statistical Package for Social Science (SPSS, Chicago) software version 20.0. Data was presented in frequencies, mean, standard deviation.

RESULTS

In the present study, out of 253 patients, 153 male and 100 female patients were included, with a mean age of 48.9±44.5 months. Generalised tonic clonic seizure was the most common type of seizure in the cohort (66%) followed by focal seizure (25%). A 27 (10.6%) children presented with status epilepticus out of which, four had history of fever prior to and during presentation. Demographic characteristics, types of seizures, and EEG features are demonstrated in [Table/Fig-1].

The most common causes of seizures in present study, were acute symptomatic in 185 (73.1%) and epileptic in 68 (26.9%) patients. A total of 211 (83.4%) patients had co-existent diseases,

Demographic characteristics	N=253 (%)
Age (in months) Mean±SD	48.9±44.5
Gender	
Male	153 (60.4)
Female	100 (39.6)
Glasgow Coma Scale (GCS) (Mean±SD)	
Prematurity	42 (16.6)
Perinatal asphyxia	31 (12.2)
History of admission to neonatal intensive care unit	34 (13.4)
Developmental delay	46 (18.1)
Mental retardation	37 (14.6)
Mechanical ventilation	69 (27.2)
Duration of mechanical ventilation (days) Mean±SD	
Length of stay in PICU (days) Mean±SD	
Prior epilepsy diagnosis	68 (26.8)
Prior epileptic encephalopathy diagnosis	50 (19.7)
Prior neurological disorder	68 (26.8)
Type of seizures	
Generalised Tonic-clonic Seizure (GTCS)	167 (66)
Focal	63 (25)
Unclassified	23 (9)
Status epilepticus	27 (10.7)
Clinical seizures prior to EEG	132 (52.1)
EEG characteristics	
Normal/Sleep	99 (46)
Electrographic seizure	113 (52.6%)
Neuroimaging	
CT scan brain alone	110 (47.8)
MRI brain alone	100 (43.5)
CT scan brain and MRI brain both	20 (8.7)

[Table/Fig-1]: Demographic characteristics of the patients (N=253).

34 children in the epileptic group and 177 children in acute symptomatic group. The three most common co-existent diagnosis with seizures observed were infectious diseases (38%), pulmonary diseases (11%), cardiologic diseases (5.5%). Other causes of acute symptomatic seizures included children in postoperative care with Ventriculoperitoneal (VP) shunt, craniotomy and brain abscess drainage procedures. The other underlying co-existent diagnoses in the cohort are illustrated in the [Table/Fig-2].

Co-existent diagnoses	n (%)
Epileptic group (n=68)	
Cardiologic diseases	Tetralogy of Fallot, Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), and Patent Ductus Arteriosus (PDA), acute rheumatic fever, viral myocarditis, dilated cardiomyopathy 14 (5.5)
Brain malformation	Corpus callosal agenesis, cortical dysplasia, schizencephaly, Arnold-Chiari malformation 12 (4.7)
Endocrinologic disorders	Hypothyroidism, diabetes insipidus, Type 1 diabetes mellitus 6 (2.3)
Syndromes	Down syndrome, Leigh disease 2 (0.7)
Acute symptomatic group (n=185)	
Infectious diseases	Pneumonia, sepsis, infective endocarditis, urinary tract infection 96 (38)
Pulmonary diseases	Pneumothorax, chronic lung disease, bronchial asthma, respiratory failure 28 (11)
Stroke	Embolic stroke, spontaneous intracerebral haemorrhage, cerebral venous sinus thrombosis 14 (5.5)
Tumour/ oncologic	Acute leukaemia, Wilm’s tumour, Hodgkin’s lymphoma, glioblastoma multiforme 14 (5.5)

Postoperative care	Post VP shunt, postcraniotomy, postbrain abscess drainage.	11 (4.3)
Gastroenterologic diseases	Chronic liver disease with upper gastrointestinal bleeding	6 (2.3)
Others	Acute renal failure, aplastic anaemia, poisoning, unexplained encephalopathy, Acute post <i>Streptococcal</i> glomerulonephritis, CNS inflammation or autoimmune disorder	18 (7.1)

[Table/Fig-2]: Co-existent diagnosis at admission in PICU.

*Subjects could have more than one diagnosis

*Normal EEG counting may not match the total number of EEG done as each patient may have multiple diagnoses

In symptomatic seizures group, common aetiologies was CNS infection (29.7%), metabolic (16.2%), sepsis (14.1%) and hypoxic ischaemic encephalopathy (9.2%). Ten patients were classified under unknown aetiology as further evaluation of these cases remained incomplete. Relationship between various aetiologies and electrographic seizure are depicted in the [Table/Fig-3].

Diagnosis (n)	Electrographic seizures present, %	Electrographic seizures absent*, %
CNS infection (55)	16 (29)	39 (71)
Acute viral meningoencephalitis (36)	8 (22.2)	28 (77.8)
Bacterial meningitis (9)	3 (33.3)	6 (66.7)
Tubercular meningitis (3)	2 (66.7)	1 (33.3)
Brain abscess (3)	1 (33.3)	2 (66.7)
Cerebral malaria (2)	0	2 (100)
Rickettsial meningoencephalitis (1)	0	1 (100)
Neurocysticercosis (1)	1 (100)	0
Metabolic (30)	9 (30)	21 (70)
Sepsis (26)	16 (61.5)	10 (38.5)
Hypoxic-ischaemic encephalopathy (17)	4 (23.5)	13 (76.4)
Tumour/oncologic (14)	3 (21.4)	11 (78.6)
Stroke (14)	3 (21.4)	11 (78.6)
CNS inflammation or autoimmune disorders (11)	4 (36.4)	7 (63.6)
Unknown (10)	2 (20)	8 (80)
Toxin (8)	1 (12.5)	7 (87.5)

[Table/Fig-3]: Relationship between acute symptomatic group and electrographic seizure.

In the present study, 36 (14.2%) patients had hyponatraemia, 14 (5.5%) had hypoglycaemia, 20 (7.9%) had hypokalaemia, 23 (9%) had hypophosphataemia and 38 (15%) had hypocalcaemia. Laboratory test results are summarised in [Table/Fig-4].

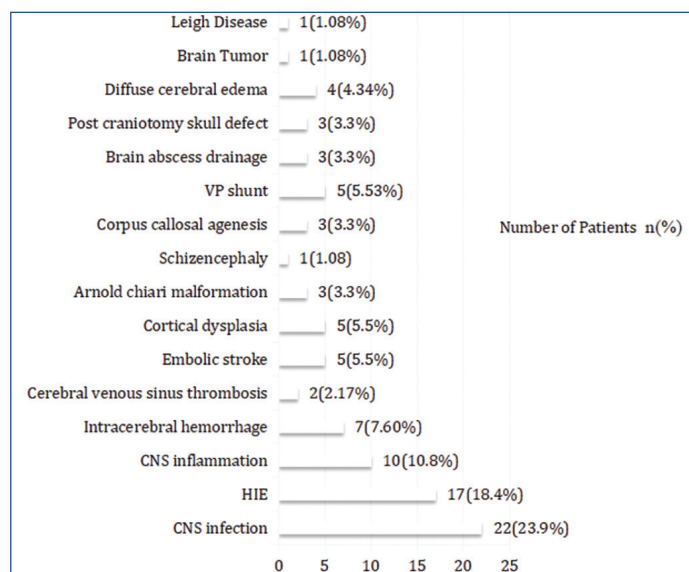
Laboratory test	Low n (%)	Normal n (%)	High n (%)
White blood cell count	28 (11)	124 (49)	101 (39.9)
Haemoglobin	140 (55.3)	111 (43.8)	2 (0.7)
Liver enzymes	0	190 (75)	63 (25)
BUN, creatinine	0	232 (91.6)	21 (8.3)
Glucose	14 (5.5)	178 (70.3)	61 (24.1)
Sodium	36 (14.2)	202 (79.8)	15 (5.9)
Potassium	20 (7.9)	215 (84.9)	18 (7.1)
Phosphate	23 (9)	187 (73.9)	43 (16.9)
Calcium	38 (15.1)	215 (84.9)	0

[Table/Fig-4]: Laboratory test results of patients with seizures.

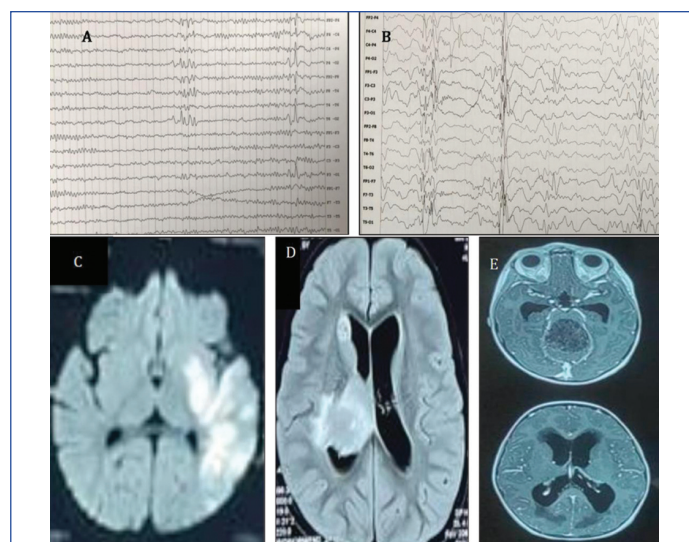
*Blood Urea Nitrogen (BUN)

The EEG was performed during hospital stay in 215 (84.9%) patients and 113 (52.6%) patients had abnormal recordings, 73 (64.6%) in acute symptomatic group and 40 (34.5%) in epileptic group. Neuroimaging was performed in 230 (90.9%) patients, out of which 92 (40%) showed abnormality. MRI brain was done in 120 (52.2%) patients; CT scan brain in 130 (56.5%) patients and

20 patients underwent CT followed by MRI. Neuroradiological features are described in the [Table/Fig-5]. EEG and neuroimaging findings of few representative cases are shown in [Table/Fig-6].

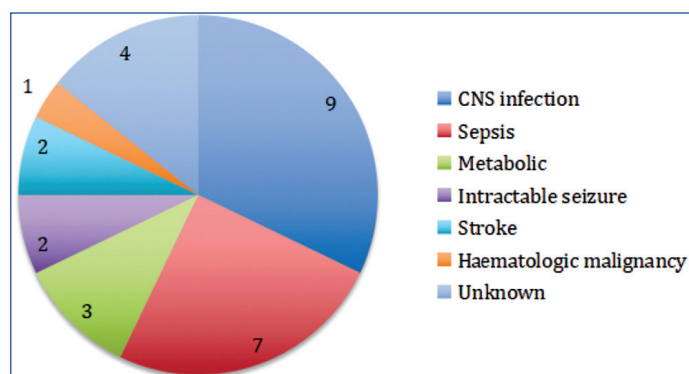


[Table/Fig-5]: Neuroimaging characteristics in the study.



[Table/Fig-6]: Electroencephalography (EEG) of a 4-year-old patient admitted after treatment of status epilepticus showing (A) onset of a right frontal seizure (B) A 7-year-old child showing frequent, generalised spike-polyspike seizure discharges. EEG speed 10 s/page, sensitivity 7.5 uV/mm, and 50 Hz filter on. Acute ischaemic stroke-Diffusion weighted image showing diffusion restriction in the left middle cerebral arterial territory in a 4-year-old child (C), FLAIR image showing a large right thalamic tumour in a 5-year-old patient (D), Contrast enhanced T1 weighted MRI showing medulloblastoma with hydrocephalus in a 2-year-old patient (E). *Fluid attenuated inversion recovery (FLAIR)

Out of the 253, 28 (11%) patients admitted with seizures died during stay in PICU as compared to an average all-cause mortality rate of 30% in our PICU. Common causes of death were CNS infection, sepsis and metabolic causes [Table/Fig-7].



[Table/Fig-7]: Causes of death in the study population.

S. No.	Authors	Study period, type of study	Number of patients	Age	Seizure frequency	Aetiological risk factors	Mortality
1	Amonkar P and Gavhane J, 2020 [10]	March 2015 to February 2018, retrospective study	157	4 y	GTCS-104 (66.2%) Focal 39 (24.8%) Unknown 14 (8.9)	Viral meningoencephalitis 26 (25.7%) Tubercular meningitis 10 (9.9%) Traumatic brain injury 13 (12.8) Metabolic disorder 12 (11.8%)	14 (8.9%)
2	Kumar M et al., 2014 [18]	April 2008 to March 2009, prospective study	70	5.94±3.152 y	GTCS 91.4% Partial SE 8.6%	Viral encephalitis 11 (33.3%) Pyogenic meningitis 7 (21.2%) Tubercular meningitis 5 (15.1%) Cerebral malaria 4 (12.1%) Hepatic encephalopathy 3 (9%)	22 (31.4%)
3	Narayanan JT and Murthy J, 2007 [8]	January 2003 to April 2005, prospective study	66	49.07±20.2 y	GTCS 36 (55%) Focal 30 (45%) SE 4 (6%)	CNS infections (32%), Metabolic disorders (32%) Cerebrovascular diseases (21%).	2 (3.03%)
4	Present study	April 2017 to September 2018, retrospective study	253	48.9±44.5 months	GTCS 167 (66%) Focal 63 (25%) Unknown 23 (9%)	CNS infection 55 (29.7%) Metabolic 30 (16.2%) Sepsis-26 (14.05%) Hypoxic-ischaemic encephalopathy 17 (9.18%)	28 (11.06%)

[Table/Fig-8]: Comparative studies of seizure in children and adults [8,10,18].

DISCUSSION

To authors' knowledge, the present study is the first study evaluating seizures in a PICU setting at a tertiary care hospital in North-east India. The purpose of the present study was to determine the aetiology and characteristics of seizures in children admitted in PICU. In the present study, the mean age was 48.9±44.5 months. Studies conducted in developing, as well as, developed countries have shown similar results having younger age at presentation [1, 16, 17]. This may be attributable to the low threshold for seizures in young children and their vulnerability to acquired disorders involving the CNS. A study conducted by Shinnar S et al., found a strong effect of age on cause of status epilepticus, where febrile and other acute symptomatic aetiologies were more common in less than two years of age and unknown and remote symptomatic aetiologies were more common in the older children [16].

A total of 26.8% patients in the present study had pre-existing epilepsy as compared to 69.7% in a five-year retrospective study conducted in PICU in USA [2], 36% in a similar study conducted in UK [17], 46.6% in study conducted in Delhi, India and 25.7% in a study in Bihar, India [1, 18]. The GTCS were the most common type seen in the present study and type of seizure did not have any association with underlying aetiology or outcome.

The CNS infections (15.8%) were the most common cause in the symptomatic seizure category in the present series. Among CNS infections, viral meningoencephalitis (65.5%) was the most common aetiology followed by bacterial meningitis (16.4%). Twenty-seven (10.6%) patient presented with status epilepticus. Only four out of 253 (0.01%) children had refractory status epilepticus, which was likely due to infectious aetiology, since all of them had fever prior or during the illness. The EEG could be performed in 215 (85%) cases out of which 113 (52.6%) had abnormal recordings. Interictal discharges were the most common EEG abnormality noted followed closely by electrographic seizures and slow background activity.

In the current study, among the metabolic causes hypocalcaemia (15%) was the most frequent metabolic abnormality observed followed by hyponatraemia (14.2%) and hypoglycaemia (14.2%). This condition may not be associated directly with the development of seizures, but our opinion is that these are worth mentioning because they might precipitate seizures, and in these patients, administration of supportive treatment was required. In a previous study of children presenting to the emergency room with unprovoked seizures, the authors stated that hyponatraemia was a rare cause of seizures unless suggested by the history [19].

Twenty-eight (11%) patients in the present study died during their PICU stay. CNS infection was found to be the most common cause of all the aetiologies. Comparison between studies on seizures in intensive care units in children and adults from India are depicted

in [Table/Fig-8] [8,10,18]. By far, the present study has shown a number of uncommon co-existing medical conditions associated with acute symptomatic seizure. Though a causative effect couldn't be ascertained from the present study, the identification of factors predicting poor outcome will help in early risk stratification for optimal management.

Limitation(s)

The evaluation of clinical spectrum of seizures in present study was retrospective and was based on documentation of GCS score and deficits detected on physical examination. The presence of cognitive or behavioural deficits may have been over looked in the absence of formal methods of assessment.

CONCLUSION(S)

The most common causes of seizures in PICU were acute symptomatic followed by epileptic seizures. But uncommon causes like hypertensive encephalopathy, hypoxic seizures, epileptic encephalopathy, and metabolic disorders such as hepatic encephalopathy, hypocalcaemic seizures, mitochondrial diseases, hypoglycaemic seizures and other inborn errors of metabolism are also being increasingly diagnosed. High indices of suspicion for these conditions are essential for prompt and effective treatment to reduce morbidity and mortality. The authors would like to recommend further large prospective studies in future, with emphasis on the awareness of the most common and emerging uncommon aetiologies in children admitted to PICU.

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