

Etiology, Clinical Profile and Outcome of Acute Seizure in Children Aged between 1 month to 12 years Admitted in a Tertiary Care Hospital in Eastern India

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Abstract

Background: Acute onset seizure is one of the common causes of childhood hospitalization with significant mortality and morbidity. There is limited data regarding acute seizures episodes and its outcome from developing countries. Current study aims to find the common etiology of seizure and classify seizure types in various age groups. It was also aimed to find outcome in relation to diagnosis, abnormal imaging, EEG and requirement of monotherapy or polytherapy.

Material and Method: This was a hospital based prospective study carried out in the department of Pediatrics, Calcutta National Medical College and Hospital from June 2016 to May 2017. Children aged 1 month to 12 years presented with acute onset seizure were enrolled. Variables collected were demographics, clinical presentation, laboratory tests, brain imaging, elect-roencephalography, diagnosis and therapy. The data was analysed using Statistical Package for the Social Sciences (SPSS) for Windows version 16.0 (SPSS Inc ; Chicago, IL, USA). **Results:** A total of 491 patients were admitted for acute onset seizure with 289(58.8%) males and 202(41%) females. Among these patient 280(57%) presented with fever and 55(10.9%) children presented with status epilepticus. Generalised onset tonic clonic was the most common seizure type, central nervous system infection was the most common etiology in all the age groups. Final outcome was made at the time of discharge as discharged without sequelae, discharged with sequelae and death. Patient with CNS infection had highest mortality. **Conclusion:** CNS infection and febrile seizure were common cause of seizure in fewer than 5 children. Group of children presenting with unprovoked seizure require long term follow up studies including neurophysiologic studies and neuroimaging for better understanding of childhood seizure disorder in developing countries.

Keywords: Seizure, central nervous system infections, children, developing country.

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INTRODUCTION

A seizure is a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain. Studies worldwide indicate that approximately 4 to 10% of children suffer at least one episode of seizure in the first 16 years of life [1]. Seizures contribute to about 1% of paediatric emergency visits and the incidence is highest in children less than 3 years of age, with decreasing frequency in older children [2]. Clinically epilepsy is defined as the occurrence of two or more unprovoked seizures in a time frame of longer than 24 hours. The prevalence rates of childhood epilepsy varies widely across different countries with most clustering around 4 to 6 per 1000 children [3,4].

Acute seizures are a common neurological symptom in sick children. In patients with fever, they include febrile seizure, acute symptomatic seizure (associated with meningitis, encephalitis) or may be the initial presentation in a child with epilepsy or epilepsy syndrome [5]. Worldwide data suggest that febrile seizures account for the most common type of seizures seen in children less than 5 years of age and overall have a good prognosis [6-8].

In the developing countries, central nervous system infections are the main cause of seizures and acquired epilepsy in paediatric population and the causes vary according to geographical variation [8, 9]. In case of acute seizures, the burden of mortality and morbidity including development of subsequent

epilepsy is considerably high [10-11]. However, among newly diagnosed childhood epilepsies, idiopathic epilepsy has a favourable outcome and a high rate of remission [12].

In resource poor developing countries, there is high concern regarding cost of investigation panel and management of acute seizures as well as epilepsy. An emergency paediatrician has to decide about the required investigations including infection screening and metabolic work up, electroencephalogram, neuroimaging when a child comes with first episode seizure. Better understanding of seizures in terms of clinical presentation as well as etiology is required not only to abort the acute attack but also for good long term control of epilepsy and to develop systems of care that move beyond the narrow level of individual treatment to a broad spectrum of implication of child's social, emotional and developmental wellbeing at a community level. With this in mind, we conducted this prospective study to analyse the prevalence of various etiologies, the clinical spectrum of seizure disorders and outcome of children admitted with seizure in the paediatric department of a tertiary care hospital in Eastern India.

MATERIAL AND METHOD

This was a descriptive prospective hospital based study conducted in the department of Paediatric Medicine, Calcutta National Medical College and Hospital, West Bengal. All admitted children, 1 month to 12 years of age admitted to paediatric emergency and paediatric ward presenting with seizure, both unprovoked and symptomatic (acute and remote) were enrolled over a period of one year from June 2016 to May 2017. The aim of the study was to evaluate the demographics, clinical seizure types, etiologies and outcome during the hospital stay of those children. Total 5564 children in this age group were admitted. Among these, 491 children (9%) with presenting complaint of seizure or those who developed seizure after admission were included in the study. Children below 1 month and above 12 years of age as well as those who refused to enrol or left the hospital without completing treatment were excluded from the study. The children were divided into 3 groups: 1 month -5 years, 6 - 9 years and 10 - 12 years. The medical records of patients were used to obtain the following data: age, sex, type of seizure, associated symptoms like fever, headache, vomiting, meningeal irritation, unconsciousness, postictal confusion, presence of status or recurrent seizures, history of febrile seizure, delayed milestones. Data of birth history, past history of seizure

or family history of seizures were also collected. Laboratory test results like complete blood count, serum electrolytes, blood sugar level, Cerebrospinal fluid (CSF) analysis; neuroimaging (CT and MRI) and electroencephalogram (EEG) findings were also obtained.

Management was given according to standard protocol [13]. Classification of seizures was done according to International League against Epilepsy (ILAE) classification 2017[14]. These include generalised tonic clonic seizures (GTCS), tonic clonic, clonic, tonic, absence, myoclonic, atonic, focal (without impaired consciousness, with impaired consciousness, focal to bilateral tonic clonic seizure), unknown onset seizure (if there was not enough clinical information available) and unclassified seizure (if the clinical characteristics of a seizure are unusual and a determination of onset cannot be made despite adequate workup). According to ILAE, status epilepticus is defined as a single seizure which lasts more than 30 minutes or a series of epileptic seizures in which function is not retrieved between ictal events for 30 minutes[15]. Febrile seizure is defined as a seizure occurring in childhood after one month of age, associated with a febrile illness not caused by an infection of the central nervous system, without previous neonatal seizure or unprovoked seizure and not meeting criteria for other acute symptomatic seizure [15]. Febrile seizure is further classified into simple and complex variety.

Etiological distribution of seizures was made by clinical history, laboratory investigations, neuroimaging and EEG findings. Final outcome was classified as discharged without sequelae, discharged with sequelae and death. Simple febrile seizures were treated conservatively whereas status epilepticus, recurrent seizures and those with abnormal EEG or neuroimaging required single or multiple antiepileptic drugs.

Preceding the study, approval for the study was obtained from ethics committee for institutional research of Calcutta National Medical College.

Descriptive statistics and testing of hypothesis were used for analysis. The data was analysed using Statistical Package for the Social Sciences (SPSS) for Windows version 16.0 (SPSS Inc ; Chicago, IL, USA). Chi Square test was applied at 5 % significance level.

RESULT**Table-1: Characteristics of study population (n=491)**

CHARACTER	NUMBER(n)	PERCENTAGE (%)
GENDER		
MALE	289	59
FEMALE	202	41
AGE AT ONSET		
1m-5Y	255	52
6Y-9Y	142	29
10Y-12Y	94	19
PAST H/O FEBRILE SEIZURE		
YES	86	18
NO	405	82
FAMILY H/O SEIZURE		
YES	113	23
NO	378	77
MILESTONE DELAY		
YES	118	24
NO	373	76
BIRTH HISTORY		
NORMAL	370	75
ASPHYXIA	59	12
PREMATURITY	39	8
SEPSIS/MENINGITIS	23	5
PAST H/O SEIZURE		
YES	109	22
NO	382	78

Table -2: Clinical examination (n=491)

PARAMETER	NUMBER	PERCENTAGE
FEVER	280	57.0
HEADACHE	89	18
VOMITING	157	32
MENINGEAL IRRITATION	59	12
UNCONSCIOUSNESS	265	54
POST ICTAL CONFUSION	199	41
STATUS EPILEPTICUS	54	11
RECURRENT SEIZURE	365	74

Table-3: Classification of seizure type according to age (n=491)

TYPE OF SEIZURE	1m-5Y(255)	6Y-9Y(142)	10Y-12Y(94)	p value=0.013 X ² (6)=16.065
GENERALISED ONSET SEIZURE	178(70%)	99(70%)	51(54%)	
TONIC CLONIC	116(65%)	64(65%)	28(55%)	
CLONIC	20(11%)	12(12%)	8(15.7%)	
TONIC	16(9%)	8(8%)	6(11.8%)	
MYOCLONIC	14(8%)	6(6%)	3(6%)	
ATONIC	10(6%)	5(5%)	5(10%)	
ABSENCE	2(1%)	4(4%)	1(2%)	
	26(10%)	23(16%)	24(25.5%)	
	9(35%)	9(39%)	13(54%)	
	17(65%)	12(52%)	10(42%)	
	0	2(9%)	1(4%)	
UNKNOWN ONSET	30(12%)	13(9%)	12(13%)	
UNCLASSIFIED	21(8%)	7(5%)	7(7.5%)	

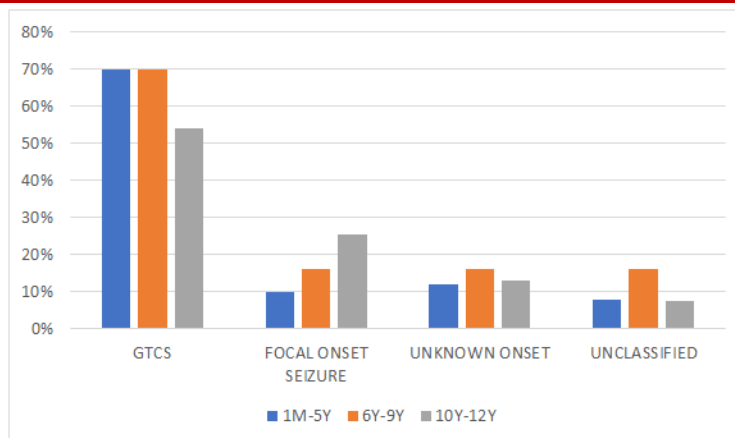


Fig-1: Age Wise Variation of Types of Seizure

Table-4: Etiological distribution of seizure

DIAGNOSIS	1m-5Y(n=255)	6Y-9Y(n=142)	10Y-12Y(n=94)	p value=0.0001 x ² (10)=43.652
FEBRILE	71 (27.8%)			
SIMPLE	60 (84.5%)	-----	-----	
COMPLEX	11(15.5%)			
CNS INFECTION	96 (37.7%)	51 (36%)	34 (36.2%)	
PYOGENIC	46 (48%)	10(19.6%)	6 (17.6%)	
VIRAL	26 (27%)	30 (58.8%)	25(73.6%)	
TB	24 (25%)	11 (21.6%)	3 (8.8%)	
SOL	13 (5.0%)	27 (19%)	20 (21.3%)	
NCC	6 (46.2%)	13 (48%)	15 (68.2%)	
TB	5 (38.5%)	10 (37%)	5 (22.8%)	
BRAIN TUMOR	2 (15.3%)	4 (15%)	2 (9%)	
SEIZURE DISORDER	36 (14.1%)	34 (24%)	18 (19.2%)	
CEREBRAL PALSY	23 (9.0%)	10 (7.0)	2 (2.1%)	
METABOLIC	9 (3.7%)	3 (2%)	3 (3.2%)	
HYPOCALCEMIA	3 (33.3%)	0	0	
HYPOGLYCEMIA	5 (55.6%)	1 (33.3%)	0	
HYPONATREMIA	1 (11.1%)	2 (66.7%)	3 (100%)	
MISCELLANEOUS	7 (2.7%)	17 (12.0%)	17 (18%)	

Table-5: Outcome in relation to clinical and investigation parameters

	Discharged without sequelae	sequelae	Death	p value<0.0001 x ² (10) =69.61
Status (n=55)	41(74.6%)	9(16.3%)	5(9.1%)	
Recurrent Seizure(n=365)	307(84.1%)	31(8.5%)	27(7.4%)	
CNS Infections(n=181)	96(53.1%)	57(31.5%)	28(15.4%)	
Abnormal neuroimaging(n=183)	119(65%)	40(22%)	24(13%)	
Metabolic(n=16)	14(86.6%)	1(6.7%)	1(6.7%)	

Table-6: Outcome in relation to mode of therapy

	CONSERVATIVE MANAGEMENT	REQUIRED SINGLE ANTIEPILEPTIC	REQUIRED MULTIPLE ANTIEPILEPTIC
FEVER		124(44.3%)	
PRESENT (n=280)	60(21.4%)	109(51.7%)	96(34.3%)
ABSENT(n=211)	42(19.9%)		60(28.4%)
STATUS		19(34.6%)	36(65.4%)
PRESENT (n=55)		279(64%)	157(36%)
ABSENT(n=436)			
EEG(n=307)		93(75.6%)	30(24.4%)
NORMAL(n=123)		77(41.8%)	107(58.2%)
ABNORMAL(n=184)			
SINGLE SEIZURE(n=126)	77(61.1%)	49(38.9%)	-
RECURRENT SEIZURE(n=365)	-	140(38.4%)	225(61.6%)

Total 491 children aged 1 month to 12 years were admitted with acute seizure during this one year study period. Most of the children 255(52%) were below 5years, 142 (29%) were between 6years to 9years and 94(19%) were 10-12years of age. In our study 289(58.8%) were male and 202 (41%) were female. Male and female ratio was 1.4:1. Among 491 children 86 (17.5%) had past history of febrile seizure, whereas family history of febrile seizure was present in only 56 (11.5%) children. A total 113(27.5%) children had family history of seizure disorder. History of delayed developmental milestone was present in 118 (24%) children. Birth history were normal in 370 (75.3%) cases whereas 59 (12%) children had history of birth asphyxia and 39 (7.9%) were prematurely delivered. History of neonatal sepsis was present in 23(4.6%) cases only. Among 491 children 109 (22%) had past attack seizure and 74(15%) had epileptic disorder [T-1].

Fever was present on admission in 280 (57%) of children. It was more common in less than 5years 175 (68.6%). Afebrile seizure 54 (57.5%) was most common in age group of 10 years to 12 years, whereas it was 54% in 6 – 9 years age group and only 31.4% in less than 5years of age (p value <0.0001). Vomiting, meningeal irritation, unconsciousness, postictal confusion were other clinical findings. 55 children (10.9%) presented with status in emergency department. At time of presentation 167 children (34%) presented with first episode of seizure [T-2].

Generalized onset seizure was most common seizure type in all age group in this study. Among 491 children, 328 (66.8%) presented with generalized onset seizure. Generalized onset tonic clonic was most common subtype. It was present in 116 children (65%) in 1m- to 5yr age group, 64 (65%) in 6- 9 years age group and 28 (55%) in 10 to 12yr age group. Other subtypes were tonic, clonic, myoclonic, atonic and absence seizure. These were followed by focal onset seizure which were seen in 26(10%) in less than 5years age, 23(16%) in 6 - 9years age and 24(25.5%) in 10-12 yr age. Incidence of focal onset seizure increases with advances of age. Focal seizure was further subclassified in focal seizure without impaired consciousness, focal seizure with impaired consciousness, focal to bilateral tonic clonic seizure.

30 (12%) children in 1st group, 13 (9%) in 2nd group and 12 (13%) in last group were classified as unknown onset seizure as there were not enough clinical information available. Seizures were grouped as 'unclassified' where clinical characteristics were unusual. It was seen in 21(8%) of children in less than 5years age, followed by 7(5%) and 7(7.5%) of children in 6 – 9 yr and 10-12 yr of age respectively. Type of seizure varied significantly with age (p value = 0.013). [Table- 3][Fig 1].

CNS infection was the most common cause of seizure in all three age groups. It accounts 96 (37.7%) in 1m – 5yrs age group. Febrile seizure 71 (27.8 %) was the second common cause followed by seizure disorder 36 (14.1%) cases. Other etiologies in these age group were, cerebral palsy 23 (9%), intracranial SOL 13 (5 %), metabolic 9 (3.7 %) and miscellaneous 7 (2.7%). Apart from CNS infection, seizure disorder 34 (24%) was the second common cause in 6 – 9yrs of age group followed by intracranial SOL 27(19%). Other etiologies were cerebral palsy 10(7%), metabolic causes 3(2%), and miscellaneous 17(12%).

Second common cause of acute seizure in 10-12 yr age group was intracranial SOL 20(21.3%). Among these neurocysticercosis (NCC) 15(68.2%) was most common followed by tuberculoma 5(22.8%) and brain tumour 2(9%). Other etiologies in this age groups were seizure disorder 18(19.2%), cerebral palsy 2(2.1%), metabolic 3(3.2%) and miscellaneous 17(18%). Hypertensive encephalopathy, poisoning, vascular causes, demyelination, congenital CNS malformations were included in the miscellaneous groups. Etiologies were varied significantly with age groups (p value < 0.001) [Table – 4].

We conducted CSF analysis in total 235 children as per indication. CSF was abnormal in 105 (45%) cases and normal in 129 (55%) cases. We also found that patients with generalized onset seizure, EEG were abnormal in 53% cases whereas 47% had normal EEG and in patient with focal seizure 52% had normal EEG and 48% had abnormal EEG. There was no significant difference in EEG in both the groups (p value = 0.3504).

Final outcome was made at the time of discharge as discharged without sequelae, discharge with sequelae and death. Outcome was analysed on the basis of presence of status epilepticus, presence of recurrent seizure, with abnormal EEG, abnormal neuroimaging and presence of CNS infection and metabolic abnormality. Maximum recovery were seen in metabolic abnormality 13(86.7%) followed by recurrent seizure 307(84%). CNS infection 96(53.1%) had minimum recovery without sequelae. Highest mortality was seen in patients with CNS infection 28(15.4%) followed by patients with abnormal imaging 24(13.1%). Sequelae were maximum in patients with CNS infection 57(31.5%) followed by abnormal neuroimaging 40 (22%), patient with abnormal EEG 30 (16.3%) and presence of status 9(16.3%). Outcome was statistically significant (Pvalue <0.0001) [Table-5].

126 children presented with single seizure of whom 77 (61.1 %) required no anti-epileptic drugs (AED) and rest 49 (38.9 %) responded with single AED. 365 children presented with recurrent seizure of

whom 140 (38.4%) required monotherapy and rest 225 (61.6%) required multiple therapy. 55 children presented with status of whom 19 (34.6%) responded with monotherapy and rest 36 (65.4%) required multiple therapy. In comparison 436 children had no status of which 64% required only monotherapy and rest 36% required polytherapy. 123 children had normal EEG of whom 75.6% required monotherapy and rest 24.4% required polytherapy. In comparison children with abnormal EEG required more polytherapy (58.2%) than monotherapy (41.8%) which was statistically significant (P value < 0.001) [Table-6].

DISCUSSION

This study had shown prevalence of seizure amongst admitted children in the age group 1m to 12 yrs was 9% which is similar to the other studies [16, 17]. Most studies show high incidence of seizure in younger children with a decreasing frequency in older age group and more common in males [6, 9].

In our study most children were younger than 5 yrs of age as compared to other age groups which is also similar to other study [18]. Male- female ratio of our study was also quite similar to the other study [19]. In this study, 17.5% children had past history of febrile seizure and family history of seizure disorder was present in 27.5% cases. Another study conducted by Dragoumi *et al.* [20] had shown similar findings. In our study family history of epilepsy was present in 11.5% cases which is also similar to other study [21]. History of delayed developmental milestones, history of birth asphyxia or premature delivery were also almost similar to other study [22].

Seizure presented with fever in 57% of cases. Another study by Tauhid Iqbali *et al.* [17] had also shown similar findings. In the current study 79% of children were presented with first episode of seizure whereas 21% of children already had one or more episodes before. Similar findings were also seen in other study [19].

Generalised onset seizure was found to be the most common clinical type and had higher incidence among children presented with febrile seizure which also corroborated with previous studies [9, 18]. Focal onset seizure was the second most common type of seizure in the current study.

First attack of seizure can have many possible etiologies like CNS infection, metabolic disturbances, toxins, poisoning, demyelinating diseases, febrile seizures, etc. [10]. Seizures which developed during hospital admission were mainly due to hypoxia, infection or metabolic causes [23]. In our study, CNS infection was the most common etiology in fewer than 5 children followed by febrile seizure. This also corroborated with the study done by Singh *et al.* [24] but according to Chen *et al.* [9], febrile seizure was the

most common cause followed by infection, trauma, and epilepsy. The reason behind this discrepancy might be due to more referral of patients with CNS infection from periphery. CNS infections were also the most common etiology in more than 5 years of age group. Amongst these patients with viral encephalitis were the most common followed by, tuberculous meningitis and pyogenic meningitis. Other important causes were seizure disorder, and intracranial SOL. In our study, NCC was the most common SOL followed by tuberculoma and brain tumour amongst all age groups.

Worldwide literature reveals that abnormal neuroimaging seems to be more associated with focal seizure than generalised seizure [25]. We too performed neuroimaging in as many cases as possible (335/491) observing the same. We found abnormal imaging in 37.3% cases which is similar to Poudel *et al.* [26]. Gibbs *et al.* [27] found abnormality in 21% of cases. We performed EEG in 62.5% of the cases (307/491) and found it abnormal in cases which were similar to Poundel *et al.* [26]. In our study EEG was abnormal in 63% of cases with generalised onset seizure and 58% in focal onset seizure. Chen *et al.* [9] showed 26% of cases with abnormal neuroimaging and 22% with abnormal EEG. In our study 32% children with febrile seizure showed EEG abnormality. Similar findings were also seen in other study [19].

In our study, the mortality rate during hospital stay among children admitted with acute episode of seizure was 8.9%, which was similar to other study.

Fever was found to be independently associated with increased mortality during acute illness. Mortality among febrile patients with seizure was 11.2% compared to non-febrile patients which were 7.2%. Similar findings were also shown by Tauhid Iqbali *et al.* [17]. In our study the maximum mortality was found in patients with CNS infection followed by patients presented with status epilepticus, with abnormal neuroimaging and abnormal EEG finding. Viral encephalitis was the leading cause of death in our study. Similar findings were also seen by Idro *et al.* [8]. In our study maximum sequelae were seen in patients with CNS infection. Maximum number of complete recovery was found in patients with metabolic abnormality followed by with recurrent seizure. No mortality was seen in febrile seizure. All cases of death had refractory status epilepticus, presented late to the hospital and succumbed within few hours of admission

Patient with recurrent seizures required more polytherapy than with single seizure. Patient with status epilepticus required more polytherapy than without status. Children with abnormal EEG required more multiple therapies than with normal EEG which was statistically significant.

Limitation of the study- In this study outcome was defined as mortality during stay in hospital and morbidities at the time of discharge. Long term sequelae like residual neurodeficit, cognitive dysfunction or seizure disorder were not studied in follow up. We included neither newborn nor children having seizure from the outpatient department. This might alter the findings of the present study significantly. Future multicentric studies with larger sample may be required to solve this problem.

CONCLUSION

Acute episode of seizure is one of the commonest causes of hospitalization with high mortality. It can be inferred from our study that most of acute symptomatic seizures are caused by CNS infections like meningitis and encephalitis, febrile seizure or epileptic disorder. Group of children presenting with unprovoked seizure require long term follow up studies including neurophysiologic studies and neuroimaging for better understanding of childhood seizure disorder in developing countries.

Competing interests

The authors do not have any conflict of interest arising from the study.

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Abbreviation

CT- Computed Tomography
MRI- Magnetic Resonance Imaging
CNS- Central Nervous System
SOL- Space Occupying Lesion
NCC- Neurocysticercosis
AED- Antiepileptic Drugs
CSF- Cerebrospinal Fluid

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