Original Article

Clinico Etiological Profile of "First Seizure" in Children. Experience from an Armed Forces Tertiary Care Hospital in Eastern India

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Abstract

Introduction: Seizure in the pediatric group is one of the most common emergencies encountered. The aim of this study was the evaluation of the etiology of a first episode of seizure in children so as to assess the short term as well as long-term prognosis. **Materials and Methods:** We evaluated 86 children 2 months − 12 years presenting to the emergency/outpatient department with the first episode of seizure. Children were further sub-grouped into two age groups of 2 months − 5 years (n = 60) and 5–12 years (n = 26) and acute symptomatic versus unprovoked seizures. Variables assessed were demographics, seizure semiology, laboratory tests, neuroimaging, and outcome at discharge. **Results:** 69.7% and 30.2% of children were in the age group 2 months to 5 years and 5–12 years, respectively. The mean age of the children was 4.11 ± 3.44 years. 45.3% of cases of acute symptomatic seizures and 54.6% of cases of unprovoked seizures were observed. Acute symptomatic seizures predominated in 2 months − 5 years (60%) while unprovoked seizures predominated in 5–12 years (88.4%). Focal seizures were predominant in the older age group (46.1%) as compared to the younger age group. About 10.4% of cases of seizures first presented as status epilepticus. The most common etiology identified was febrile seizures (27.9%) followed by central nervous system (CNS) structural lesions (19.7%) and CNS infections (10.4%). CSF was done in 18.6% of patients out of which 56.25% samples were positive for CNS infections. 68.6% of children underwent neuroimaging and abnormalities were reported in 67.7% of cases. About 18.6% of children had focal neurological deficits at discharge. Mortality in the entire cohort was 2.3% with 1 child in each vascular and CNS infections group. **Conclusions:** Children with a first episode of seizure should be evaluated for co-existence of fever, preexisting developmental delays, other associated symptomatology, head trauma, and seizure semiology. Investigations should be done based on a detailed history and clinical examination. Despite a meticulous approach allowing identification of etiology of the first episode of seizure in children, it is possible that no etiology be identified in a substantial number of children, especially in the older age group.

Keywords: Acute symptomatic, etiology, first seizure, semiology

Introduction

Seizure is the most common pediatric neurologic disorder with 4% to 10% of children suffering at least one seizure in the first 16 years of life.[1] 1% of these children present to the emergency department with their first episode. The incidence of seizures is highest in children younger than 3 years of age with a decreasing frequency in older children. Febrile seizures account for 2%–5% of the first episode of seizures in children 6 months −5 years.[2] However, the etiological profile of a first seizure is known to be diverse and differs amidst the developed and the developing countries.[3,4] A comprehensive etiological assessment allows planning of relevant investigations and deciding the management protocols as well as offering a prognostic outcome. There is the scarcity of appropriate literature depicting the etiological profile of the first episode of seizure from developing countries especially India. Furthermore, India being a land of varying populations, etiologies may differ from region to region and sparse availability of literature from the eastern region of the country

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necessitated this study. This study, therefore, was planned with the objective of studying and obtaining an adequate and clear understanding of the clinical spectrum and etiological factors determining the first episode of seizure in children attending our emergency department to offer an acute short term as well as a long-term prognostic management plan. Etiological determination of a first seizure may determine the risk of recurrence as well as a diagnosis of epilepsy.

Materials and Methods

Study Design

This was a prospective observational study.

Study setting

This study was conducted between June 2018 and December 2019 at the Paediatric Department of Armed forces tertiary care hospital in Eastern India. All consecutive children presenting with the first episode of seizure were eligible.

Sample size

Since the study period was predefined 86 children presenting with the first episode of seizure during the study period were eligible for inclusion.

Study period

This study was conducted between June 2018 and December 2019.

The study was approved by the institutional ethics committee of the center vide letter number IEC SC/05/01/2018.

Procedure

The study participants were included after written informed consent was obtained from caregivers of participating children. All consecutive children between 2 months and 12 years of age, presenting with the first episode of seizure were considered for inclusion. The exclusion criteria included (i) children who had semiology suggestive of nonepileptic events (like breath-holding spells, severe gastroesophageal reflux, syncope, tics, and night terrors) (ii) children with the previous history of epilepsy or having received treatment for seizures and (iii) those who presented with recurrence of seizures or breakthrough seizures.

All children with first episode of seizure were admitted, in accordance with the existing unit protocol. Children were stabilised before being evaluated for inclusion. Detailed history of perinatal events, developmental history, immunization status, family history, and provoking factors were taken. Seizure classification was done as per the International League against Epilepsy classification 2017. Seizure semiology was determined based on the care giver description as well as observation by the pediatrician. Children having seizure with a history of fever, meningeal signs, altered sensorium, trauma, and electrolyte disturbances were considered to have acute symptomatic causes while others were considered to have unprovoked seizures. All children meeting inclusion criteria were managed as per the standard unit treatment protocol. This involved following investigations as indicated based on treating physicians discretion and patients history/examination: (a) Complete blood count, sugar and electrolytes; (b) evaluation of cerebrospinal fluid (CSF) was performed in all infants with febrile seizures at <12 months of age, children with signs of meningeal irritation, febrile status epilepticus and in children with suspected metabolic causes such as mitochondrial cytopathy, hyperglycinaemia and glucose transporter defects; and (c) brain magnetic resonance imaging (MRI) was performed if there was history of adverse perinatal events, focal onset of seizures, children presenting in status epilepticus as their first episode of seizure, persistent high-grade fever, altered sensorium, signs of meningeal irritation, abnormal CSF findings, presence of neurocutaneous markers, focal neurological deficit, developmental abnormalities, unarousable even after the precipitating event is over or if there was a recurrence of seizure during the hospital stay.

Statistical analysis

All data were entered in a Microsoft Excel sheet. Using principles of descriptive and inferential statistics, descriptive statistics were represented as number and percentage, mean and median as applicable. The strength of association of etiological conditions with the outcome was analyzed using Chi-square test and expressed as odds ratio. $P < 0.05$ were considered statistically significant. The data were analyzed using IBM SPSS 16 (2007) software (IBM ,New York USA).

Results

Patients

Eighty-six (4.4% of total admissions during the study period) children with the first episode of seizure were analyzed. The flow of the study is illustrated in Figure 1. The study included 56 males. The mean age of the study population was 4.11 ± 3.44 years (range 0.2–12 years). Table 1 illustrates the demographic profile of the study population.

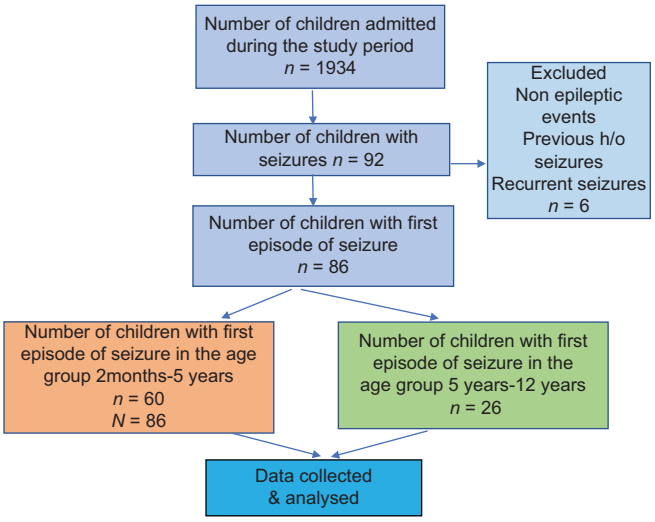

Figure 1: Flow of the study

Outcomes

The proportion of children with different types of seizures is shown in Table 2. For the purpose of analysis, children were subdivided into two age groups of 2 months − 5 years and 5–12 years. Children in the 5–12 years age group predominantly had focal and absence seizures as compared to the younger group (n = 16). Fifteen children (17.4%), 7 in 2 months to 5 years age group, and 8 in the 5–12 years age group had recurrences of seizures during admission**.** The etiology could be ascertained in 70 (81.3%) children [Figure 2]. No underlying etiology could be identified in 4 (6.6%) children in the younger group and in 12 (46.2%) children in the older age group [$P < 0.001$, Table 3].

CSF analysis was performed in sixteen (18.6%) children, of which 9 (56.3%) analyses were suggestive of central nervous system (CNS) infections. In addition, three CSF samples demonstrated CSF pleocytosis (>5 white blood cells [WBC]/mm^3 but <10 WBC/mm^3) without any other signs suggestive of CNS infections. Neuroimaging was done in 59 (68.6%) children, of which 40 (67.7%) showed abnormalities. Amongst children with focal seizures abnormalities on neuroimaging were found in 16 (72.7%) children. Amongst the other types of seizures, abnormalities on neuroimaging were found in 24 (37.5%) children. There was no statistically significant difference in the abnormalities of CSF and neuroimaging between the two groups [Table 3].

The outcome was assessed in terms of any residual neurological deficit and mortality. Focal neurological deficits at discharge had a strong positive association with CNS structural and vascular lesions and a strong negative association with febrile seizures as shown in Table 4. The mortality rate in our cohort was 2.3% with one child each in the vascular and CNS infections group.

Table 1: Demographic profile of the study population

	2 months-5 years (n=60), n (%)	5-12 years (n=26), n (%)	P
Male: female	42:18	14:12	0.15
Family history of epilepsy	9 (15)	4 (15.3)	0.96
Abnormal perinatal history	10 (16.6)	2 (7.6)	0.27
Abnormal developmental history	15 (25)	2 (7.6)	0.06
Acute symptomatic seizures	36 (60)	3 (11.5)	0.005
Unprovoked seizures	24 (40)	23 (88.5)	0.03

Table 2: Semiology of seizures

	2 months-5 years (n=60), n (%)	5 years-12 years (n=26), n (%)	P
Focal	10 (16.6)	12 (46.1)	0.004
Generalised tonic clonic seizures	28 (46.6)	4 (15.3)	0.006
Myoclonic	4 (6.6)	3 (11.5)	0.44
Status epilepticus	7 (11.6)	2 (7.6)	0.58
Absence	1 (1.6)	4 (15.3)	0.01
Epileptic spasms	7 (11.6)	0	0.07
Others	3 (5)	1 (3.8)	0.82

Discussion

Seizures affect children more than any other age group and the incidence of status epilepticus is also reported to be higher in children than in adults.[1,5] In our study the incidence of the first episode of seizure in children was 4.4% which is similar to the incidence reported in other studies.[6] In the younger age group, the commonest etiology of a first seizure was febrile seizures which is similar to that reported by Chen *et al*.[1] Contrary to this, other studies have reported CNS infections as the most common cause of the first episode of acute symptomatic seizure in the younger age group.[7] Seizures predominantly occur in young children possibly because of the vulnerability of the immature developing brain to acute insults and this fact was substantiated in our study with the first episode of acute symptomatic seizure predominantly reported in the age group 2 months − 5 years. Possible explanations for the enhanced susceptibility of the young children to develop seizures due to acute insults include immaturity of the Gamma-aminobutyric acid-aminergic responses, enhanced synaptic transmission, incomplete clearance of the excitatory neurotransmitters, and propensity for the nonsynaptic spread.[8] CNS structural lesions were another major factor contributing to seizures in the younger age group. Possible reasons include early life insults in the critical period of development inducing a state of neuronal hyperexcitability and the creation of abnormal neuronal circuitry. In the absence of an acute symptomatic etiology as a possible etiological factor for seizures, in this age group, an early neuroradiology consultation for MRI/computed tomography should be asked for to look for structural changes. Metabolic etiology in the form of hyponatremia and hypocalcemia was identified in the younger age group in only two children with no cases being identified in the older age

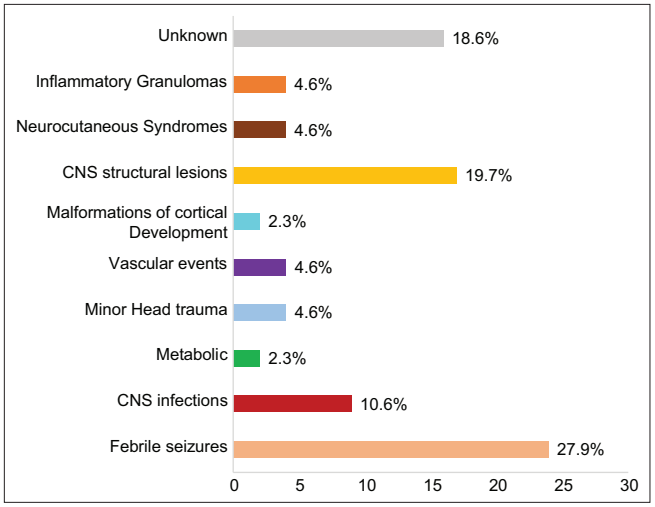

Figure 2: Distribution of the etiological profile of first episode of seizure amongst children

Table 3: Comparison of cerebrospinal fluid, neuroimaging, etiology and outcome at discharge amongst the two groups

	2 months-5 years, *n* (%)	5-12 years, *n* (%)	*P*
CSF study (*n*=16)			
Normal study	4 (40)	3 (50)	0.69
Abnormal CSF	6 (60)	3 (50)	
Neuroimaging (*n*=59)			
Normal imaging	12 (28.6)	7 (41.2)	0.35
Abnormal neuroimaging	30 (71.4)	10 (58.8)	
Etiology (*n*=86)			
Known etiology	56 (93.3)	14 (53.8)	0.00015
Unknown etiology	4 (6.6)	12 (46.1)	
Outcome at discharge (*n*=86)			
Discharge without focal neurological deficit	44 (73.3)	24 (92.3)	0.07
Discharge with focal neurological deficit	14 (23.3)	2 (7.6)	

1 child each in vascular insults and CNS infections died during hospital admission. CSF: Cerebrospinal fluid, CNS: Central nervous system

Table 4: Outcome of first seizure at discharge as per etiology

Etiology	Discharged with focal neurological deficits (*n*=16)	Discharged without focal neurological deficits (*n*=68)	Odd's ratio (95% CI)	*P*
Febrile seizures (*n*=24)	0	24	0.06 (0.003-0.96)	0.046
CNS infections (*n*=9)	1	7	0.58 (0.07-5.09)	0.623
CNS structural lesions (*n*=11)	11	0	286.45 (14.82-5537.53)	<0.001
Metabolic causes (*n*=2)	-	2	0.81 (0.04-17.61)	0.89
Minor head trauma (*n*=4)	-	4	0.43 (0.02-8.48)	0.58
Vascular events (*n*=4)	3	-	35.5 (1.73-727.95)	0.02
Inflammatory granulomas (*n*=4)	-	4	0.43 (0.02-8.48)	0.58
Neurocutaneous syndrome (*n*=4)	-	4	0.43 (0.02-8.48)	0.58
Others (*n*=24)	1	23	0.13 (0.02-1.05)	0.06

1 child each in vascular insults and CNS infections died during hospital admission. CNS: Central nervous system, CI: Confidence interval

group. There are studies suggesting that the greatest yield of these laboratory tests is in the age Group <6 months, and these should be routinely tested in any patient with the first episode of seizure whereas there is also conflicting data recommending metabolic testing based only on clinical findings such as acute illness and failure to return to baseline rather than as routine.[9] We did test glucose and electrolytes in all our cases as a protocol, however, we did not find statistically significant results to recommend its routine use in children presenting with the first episode of seizure. These differences in observations may be attributable to the better nutritional status of the children in our cohort. Although statistically not justified by our study, this is a sub-group that is readily amenable to definitive therapy and hence transient metabolic disturbances should be investigated based on the age (<6 months) and the sickness status of the child with the first seizure. Vascular infarcts, CNS structural abnormalities, and inflammatory granulomas were the most common identifiable etiology for the focal seizures in our cohort. Other studies on the first episode of seizure in the age group 3–12 years have documented inflammatory granulomas as the most important etiology of focal seizures.[10] No etiology for the seizures could be ascertained in a sizeable number in the 5–12 years age group similar to that reported by Sartori *et al*.[11] This probably suggests that the first seizure in this age group is either an isolated solitary unprovoked event or probably heralds the onset of epilepsy syndrome. The incidence of status epilepticus in our study was 10.4% which is in consonance with other studies that have an incidence between 7.3% and 10.9%.[12,13] In our study, febrile status epilepticus and CNS infections accounted for the commonest etiology for progression to status in the younger age group and vascular insults were the major cause of status epilepticus in the older age group. Febrile seizures followed by cryptogenic causes have been found to be the commonest etiological factors for a first episode of status epilepticus in other studies.[14,15] Quick progression to status may be due to a delay in the identification of the seizure, access to emergency care, and institution of rescue medications.

The other essential aim of this study was to describe the semiology of the first episode of seizure on admission to the emergency department. Correct assessment of semiology is the mainstay of accurate categorization of seizures especially when relevant investigations are being planned. Rational antiseizure therapies are also prescribed based on the exact semiological assessment. The predominant semiology of seizure in our study was generalized tonic-clonic seizures in the age group 2 months − 5 years and focal and absence seizures in 5–12 years group. Published reports have shown that epileptic spasms, clonic seizures, tonic seizures, and hypo motor

seizures are the commonest semiology in younger children.[16] It is possible that the children in our setting were brought to the pediatric emergency with a secondary generalization of the seizure and the initial semiological event was not witnessed by the parents.

CSF examination was done in sixteen children in our study aided by the following findings: clinical signs of meningeal irritation, children <1 year of age with fever and seizures, children with febrile status epilepticus and in a child with early onset absences where suspicion of a possible diagnosis of GLUT-1 deficiency was kept. Positive results on CSF aided in establishing a definitive etiology and management of seizures. Based on the results of this study we feel that CSF examination should be done in all children with signs of CNS infection, infants with fever and seizures, children presenting with febrile status epilepticus and in children wherein metabolic causes like mitochondriopathies, hyperglycinemia, vitamin responsive states, and GLUT-1 deficiency are suspected. In our cohort abnormalities on neuroimaging were found in almost two-thirds of children. Abnormal neuroimaging findings after a first seizure have been found in up to one-third of children in other studies.[17] However abnormal neuroimaging findings requiring urgent intervention may not be a significant proportion as was observed in our study. Focal seizures, focal neurological deficits, and developmental abnormalities were the strongest predictors of abnormal neuroimaging while CNS infections, vascular events, and inflammatory granulomas were the strongest predictors of abnormal neuroimaging requiring urgent intervention.

A major limitation of this study was a restricted sample size of convenience, single center study, lack of video graphic evidence of the semiology of seizures, and video electroencephalogram (EEG) data thereby contributing to the absence of clinical and electrographic correlation. A small sample size was inherently linked to the size of the population being served by our hospital and therefore was an inflexible factor. We also acknowledge the fact that in our cohort children with unknown etiology would have probably been diagnosed with an epilepsy syndrome if we had analyzed the EEG for the purpose of this study.

Conclusions

This study provides data about the possible etiological factors underlying the occurrence of a first episode of seizure across the various age groups and accordingly assists pediatricians to plan investigations and counseling the family about the possibilities. Though febrile seizures form a substantial proportion of first seizures in children, CNS structural lesions and CNS infections are other possible key etiologies warranting further investigations. Febrile seizures are more likely to recover without any focal neurological deficits whereas CNS structural lesions and vascular insults are likely to be discharged with focal neurological deficits.

Declaration of patient consent

The authors hereby certify that they have obtained all appropriate patient consent forms. In the form, the patients have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Chen CY, Chang YJ, Wu HP. New-onset seizures in pediatric emergency. Pediatr Neonatol 2010;51:103-11.
2. Shinnar S, Glauser TA. Febrile seizures. J Child Neurol 2002;17 Suppl 1:S44-52.
3. Auvin S, Vallée L. Febrile seizures: Current understanding of pathophysiological mechanisms. Arch Pediatr 2009;16:450-6.
4. Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, Camfield P, *et al.* Practice parameter: Evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Neurology 2000;55:616-23.
5. Benn EK, Hauser WA, Shih T, Leary L, Bagiella E, Dayan P, *et al.* Estimating the incidence of first unprovoked seizure and newly diagnosed epilepsy in the low-income urban community of Northern Manhattan, New York City. Epilepsia 2008;49:1431-9.
6. Martindale JL, Goldstein JN, Pallin DJ. Emergency department seizure epidemiology. Emerg Med Clin North Am 2011;29:15-27.
7. Millichap JG, Millichap JJ. Role of viral infections in the etiology of febrile seizures. Pediatr Neurol 2006;35:165-72.
8. Holmes GL, Ben-Ari Y. The neurobiology and consequences of epilepsy in the developing brain. Pediatr Res 2001;49:320-5.
9. Nikunj NK, Mishra D, Juneja M, Talukdar B. Etiology and short-term outcome of first seizure in hospitalized infants. Indian Pediatr 2016;53:924-6.
10. Rinu D, Priya P, Padmavathi P. A clinical study of new onset seizures in children aged 3-12 years. Int J Contemp Pediatr 2019;6:774-80.
11. Sartori S, Nosadini M, Tessarin G, Boniver C, Frigo AC, Toldo I, *et al.* First-ever convulsive seizures in children presenting to the emergency department: Risk factors for seizure recurrence and diagnosis of epilepsy. Dev Med Child Neurol 2019;61:82-90.
12. Singh RK, Gaillard WD. Status epilepticus in children. Curr Neurol Neurosci Rep 2009;9:137-44.
13. Berg AT, Shinnar S, Levy SR, Testa FM. Status epilepticus in children with newly diagnosed epilepsy. Ann Neurol 1999;45:618-23.
14. Adhikari S, Sathian B, Koirala DP, Rao KS. Profile of children admitted with seizures in a tertiary care hospital of Western Nepal. BMC Pediatr 2013;13:43.
15. Idro R, Gwer S, Kahindi M, Gatakaa H, Kazungu T, Ndiritu M, *et al.* The incidence, aetiology and outcome of acute seizures in children admitted to a rural Kenyan district hospital. BMC Pediatr 2008;8:5.
16. Hamer HM, Wyllie E, Lüders HO, Kotagal P, Acharya J. Symptomatology of epileptic seizures in the first three years of life. Epilepsia 1999;40:837-44.
17. Sadeq H, Karim J, Marwan Y, AlSaleem T. Neuroimaging evaluation for first attack of unprovoked nonfebrile seizure in pediatrics: When to order? Med Princ Pract 2016;25:56-60.