

Original research article

## Etiology, Clinical Profile and Outcome of First Episode of Seizure in Children

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### **Abstract**

**Background:** Seizure is a commonly encountered problem in pediatric practice. Convulsive disorder constitutes a heterogeneous group with a varied etiology. Arriving at the cause of seizure is important as it plays a vital role in managing the child. Chances of recurrence to be analyzed, after the first episode of seizure for management. The aim was to study the etiology and the causes of recurrence after a first episode seizure.

**Methods:** A prospective observational study was done on 135 children for a period of six months admitted in tertiary care center. Proper history, complete neurological and other systemic examinations was done. Blood investigations and imaging with EEG was done when indicated. All children were classified according to International League against epilepsy and followed up for recurrence rate and history leading to recurrence. Co- relation between recurrence and risk factors was analyzed.

**Results:** Electroencephalogram tracing was abnormal in 62 out of 105 children. 19 out of 62 had recurrence while only 2 among 43 normal EEG had recurrence. This was statistically significant (P value 0.001). Children with remote symptomatic etiology constitutes the majority in those with abnormal EEG tracings. In children with remote symptomatic etiology, only one child had normal EEG. Remote symptomatic had higher number of abnormal EEG when compared to others and was found to have more recurrence.

**Conclusions:** Children with EEG abnormalities after the first episode of afebrile seizure have more chance of recurrence. Children with seizure secondary to remote symptomatic etiology had more recurrences.

**Keywords:** Pediatric first seizures, Recurrent seizures, Unprovoked seizures

### **Introduction**

Seizure is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, needing at least one epileptic seizure. A seizure is defined as abnormal paroxysmal neuronal discharge, which is clinically manifested by motor, sensory, autonomic or behavioral disturbances.<sup>1</sup> Encountering seizure in children has been a common scenario in Pediatric practice and according to study, it is estimated that 10% of the population will experience it.<sup>2</sup> Half of these will occur during childhood and adolescence, and the highest risk before 1 year of age.<sup>3</sup>

First episode of any seizure can leave behind tremendous mental and physical consequence to the child and the family. It requires the physician for a prompt proper evaluation and management.

Different characteristics in seizure manifestation are noticed in infants in comparison with the older children.<sup>4</sup> The causative factors are also varied in early seizures ranging from infection, toxin, metabolic, structural anomaly of the brain. Hence, the right assessment and scrutiny of a first seizure is crucial, for the decision to label the index event is epilepsy and to further evaluate the recurrence risk. These will further guide up for initiating anti epileptic drugs for the child.

The recurrence rate after first unprovoked seizure in adults and children is high (21 to 71%). Several factors predicting the recurrence have been pointed out, e.g. the etiology of seizures, abnormal EEG, family history of epilepsy, age of the onset and the occurrence of seizure during sleep.<sup>4</sup>

Seizure characteristics in older children and adults are well described and classified. Evidence base studies and literature for profile of seizures in younger children are scarce. Hence, this study is on etiology, clinical profile and immediate outcome of first episode of seizure in children between 2 month and 2 years of age in a tertiary care hospital. Recurrence of seizure in those children and the risk factors were analyzed in this study.

A prospective observational study was done in a tertiary care center for a period of six months after ethical committee approval.

Study population included children in the age group of 2 months to 2 years with onset of first seizures were included who were admitted in the hospital. 135 children were included in the study. Children with seizure onset between 2 months to 2 years of age who were being treated as outpatients and febrile seizure cases were excluded from the study.

Informed consent was obtained from the subject's parents or guardians. A detailed history was obtained including age, sex, socioeconomic, consanguinity, seizure characteristics, duration and number of seizures, history of prior provoked seizure, prior neurological insult, developmental history, birth history and family history of seizure were included.

Complete physical examination and neurological examination of the child was performed. An electroencephalogram (EEG) scheduled for most patients as soon as feasible.

Biochemical studies including fasting blood sugar and electrolytes checked wherever necessary. USG cranium, computer tomography scan and/or magnetic resonance imaging of the brain were performed when clinically indicated and as per protocol.

Children was classified based on latest guidelines of international league against epilepsy as symptomatic (acute and remote), idiopathic and cryptogenic. Children were started on AED appropriately. After enrollment, the patients were followed up in a clinic or by telephone interview. Recurrence rate and positive history leading to recurrence was noted. The correlation between recurrence and risk factors was analysed. The data analysis was computed using the SPSS software and p value <0.05 was considered statistically significant.

## **RESULTS**

The following results were obtained from the study.

Children in age group 2-12 months formed the majority with idiopathic seizure being the most common type. Males had a higher incidence (65%) with acute symptomatic seizure forming the major group whereas in females' idiopathic seizure continued to be predominant. Male to female ratio was 1.5:1. In the study period, febrile seizure remained the most common etiology in children up to 2 years presenting with first episode seizure. Of the remaining 135 children, an acute symptomatic etiology was seen in 54 (40%) cases, idiopathic or cryptogenic etiology was seen in 42 (31.1%) cases and remote symptomatic etiology in 39 (28.8%) cases. In 135 cases with first episodes of seizures between 2 months to 2 years of age strong positive family history of seizures in first or second degree relative was seen in 45% of cases. Strong family history of developmental delay was seen in 23% of cases and history of birth asphyxia was seen in 17.7% of cases. 19 out of 39 children with remote symptomatic etiology had positive family history and 29 children out of 42 children with idiopathic or cryptogenic etiology had positive family history (Table-1).

**Table 1: Positive family history and types of seizures.**

Positive family history of seizures	
Acute symptomatic seizure	22%
Remote symptomatic seizure	48%
Idiopathic	62%

Electroencephalogram was done in 105 (77.7%) out of 135 children of whom 62 children had abnormal recordings and the remaining 43 children had normal recordings. Children with remote symptomatic etiology constitute the majority in those with abnormal EEG tracings. In children with remote symptomatic etiology, only one child had normal EEG. Remote symptomatic group had higher number of abnormal EEG when compared to others ( $p=0.00$ ). No statistical significance was observed in children having seizures and abnormal neuroimaging.

In our study when etiology was analyzed, 54 children out of 135 had seizure secondary to acute symptomatic etiology. The etiological factor in the acute symptomatic group includes CNS infection, electrolyte abnormalities, head injury, metabolic and toxin exposure. Out of these factors CNS infection and toxin exposure was the most common etiology  $n=13$  (24%) children, followed by traumatic head injury (13%), and hypocalcemia (11.1%). In toxin exposure main cause was, seizure secondary to neem oil poisoning and accidental camphor ingestion (Table 2)

**Table 2: Etiology of acute symptomatic seizures**

Acute symptomatic seizure etiology	N(Percentage)
Toxic	13 (24%)
Meningitis	13(24%)
Head injury	79(12%)
Hypocalcaemia	6(11%)
Hyponatremia	5(9%)
Hypoxia	3(5%)
Cerebrovascular accident	3(5%)
Hypoglycemia	3(5%)
CNS tumor	1(1.8%)

In remote symptomatic etiology group, mental retardation, prematurity or hypoxic ischemic encephalopathy together were responsible major cause (61%), followed by CNS

malformation (39%), cerebrovascular disease (7%) and 2 weeks after head injury (5%) were other causes

In our study out of 22 children who had recurrence, 50% had positive family history of seizure in first or second degree relative. History of birth asphyxia and developmental delay were seen more often in children without seizure recurrence. Of the children with recurrence, 63.6% had no developmental delay and 36.3% had developmental delay. 77.5% had history of birth asphyxia while 22.7% had no history of birth asphyxia. Children with positive family history of seizures were noted to have very less recurrence (only 18%). Birth asphyxia and developmental delay was also noted to be having less recurrence 20 % and 25% respectively. EEG abnormality was found to be having significant association with recurrence. 19 out of 62 with abnormal EEG had recurrence while only 2 among 43 normal EEG had recurrence.

In children with recurrence, 19 out of 22 children had abnormal EEG. The recurrence rate was more in children with abnormal EEG when compared to those with normal EEG and was statistically significant (P value 0.001). Seizure recurrent risk in children with abnormal EEG is higher than children with normal EEG after first episode of seizure.

## DISCUSSION

In our study, 64.4% of children were between 2 months to 12 months of age and 35.5% were between 1 year and 2 years. According to Inaloo et al, among the children with first unprovoked seizure, 54.5% were between 2 months to 3 years of age.<sup>6</sup> Shinnar S et al, had reported in his prospective cohort study of 407 children with a first unprovoked afebrile seizure, 27% of them were less than 3 years age.<sup>7</sup>

In our study, acute symptomatic etiology constitutes the majority of the total sample. 40% (54 children) with first seizure had acute symptomatic etiology as the cause. This is followed by idiopathic (31.1%) and remote symptomatic etiology (28.8%). The frequency of acute symptomatic seizures is poorly known, in part because of the difficulties involved in their identification. Hauser and Anneger et al, suggest that acute symptomatic etiology account for more than half of all newly occurring seizures.<sup>8</sup> In a hospital-based study from South India, acute symptomatic seizures account for 22.5% of the total patient population studied of newly occurring seizures. Most acute symptomatic or provoked seizures occur before the age of 3 years because many of the responsible disorders such as meningitis, trauma, or acute dehydration, take place predominantly in infancy and early childhood and because the brain may be more sensitive to certain stimuli.

In our study, positive family history was observed in 45% of cases and in remote symptomatic group, 48.7% had positive family history. Inaloo et al, had reported positive family history in 28.8% of children in first unprovoked seizure.<sup>6</sup> In our study, considering only unprovoked seizure i.e. excluding provoked or acute symptomatic seizure 48 (59.2 %) out of 81 children had positive family history which is much higher to study by Inaloo et al. In our study, in considering children with cryptogenic seizure, 69% had positive family history which is higher when compared to study by Shinnar S et al where in 14% positive family history had in children (1 month to 19 years) with cryptogenic first seizures.<sup>7</sup>

Among all the children with abnormal EEG, majority of them (53.2%) had seizures secondary to remote symptomatic cause. Out of 34 children from remote symptomatic group, 97% had abnormal EEG recordings. This was similar to another study by Shinnar S et al where abnormal EEGs were more common in children with remote symptomatic first seizures.<sup>12</sup>

Neuroimaging abnormalities were seen in 51.5% of children in our study. Wael et al had reported that 70% of children aged less than 2 years with seizure disorder had CT lesion

which is comparable to other studies from subcontinent.<sup>9</sup> In our study, considering only unprovoked seizures i.e. excluding provoked seizure (acute symptomatic seizure), 54% (24 children out of 44) had abnormal imaging. In study by Inaloo S et al, abnormal findings were detected on imaging in children with first unprovoked seizure in 9%.<sup>6</sup> An Indian study was done by Mathur S et al, on CT findings in children with first unprovoked seizures.<sup>10</sup> In their study, they observed that neuroimaging after a first unprovoked seizure showed significant abnormalities. In their study, 32% of all children with a first apparent unprovoked seizure had an abnormal CT scan result. In our study, 24% of seizure in acute symptomatic group was due to intracranial infection. In one series, Ellenberg et al, intracranial infection was the common cause of symptomatic seizure with fever.<sup>11</sup> In another study of clinical profile of Epilepsy during the first two years of life CNS, infection was an etiological factor in 15% of cases.<sup>12</sup> Infections of the CNS accounted for 15% of all acute symptomatic seizures in the Rochester, Minnesota study whereas these etiologies accounted for 77% in the Indian study.<sup>13, 14</sup> The risk of developing epilepsy is four fold following bacterial meningitis especially in patients with acute symptomatic seizures.

In the series by Ellenberg et al, 34% of cases resulted from head injury and 20% from toxic encephalopathy.<sup>11</sup> In our study head, injury was the cause in 12.9%. In our study in children presenting as acute symptomatic seizure after head injury, of the total 7 cases CT scan was abnormal in 6 children (85.7%) and was normal in one child (14%). Few other studies have shown that normal brain CT scan was seen in posttraumatic seizures in 5.6% cases.<sup>15, 16</sup>

Accidental intoxications are common; with drug intoxication accounting for a significant proportion of cases. 24% of children in acute symptomatic group had toxin exposure dominated by neem oil and camphor ingestion.

In our study, hypocalcaemia was the etiology in 6 children (11.1%); hypocalcaemia though unusual beyond the neonatal period should be systematically investigated.

Perinatal asphyxia is an important determinant of infant's neurological outcome.<sup>17</sup> In our study definitive history of asphyxia was seen in 20 out of 39(52.6%) children in remote symptomatic etiology and prematurity was observed in 25.6%. It was reported in literature that seizures are common sequelae to severe perinatal asphyxia. In another study of clinical profile of Epilepsy during the first two years of life, prematurity was relevant finding in history of 5% of studied cases and perinatal asphyxia was the most frequently observed cause accounting for 55%.<sup>12</sup> In developing countries perinatal brain damage would account for 13-14% of the causes of seizure disorder in children.<sup>18</sup>

## CONCLUSION

Febrile seizures remain the most common cause for seizures in children between 2 months to 2 years followed by seizures secondary to acute symptomatic cause. Children with EEG abnormalities after the first episode of afebrile seizure have more chance of recurrence. In our study, neuroimaging abnormality in children did not correlate with recurrence risk. Children with remote symptomatic etiology have increased risk of seizure recurrence as compared to other groups. We observed no statistical significance between seizure recurrence and non recurrence group with regard to age, gender, birth asphyxia, developmental delay or family history of seizure.

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