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Study of Etiology of First Episode of Seizure in Children below 5 Years

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ABSTRACT
Seizure has various etiology among the children below 5 years of age which has paucity of data. To find out the etiology of first episode of seizure in children less than 5 years of age and to co-relate laboratory and other investigations. A prospective study was conducted with a total of 120 patients less than 5 years of age who presented to the Pediatric department, Tertiary care hospital in Northern India with first episode of seizure. All subjects were subjected to a detailed clinical history, laboratory investigation, CSF studies and EEG. Seizure was more prevalent in children less than 1 year of age and affected males more than females. The most common etiology was febrile seizures. As regard to duration, majority of seizures were short lasting. Metabolic abnormalities found were hypocalcemia and hypoglycemia. Asymmetrical slowing was found in EEG. Pediatric seizures are emergencies that require early and effective treatment. This is possible only after understanding the correlation between etiology and clinical findings. Children diagnosed with seizure require long term follow up.

INTRODUCTION

Seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Seizure is not a specific disease, but rather a condition arising from a variety of pathological insults involving the cortex, such as tumours or genetic channelopathies. If you have two or more seizures or a tendency to have recurrent seizures, you have epilepsy[1]. In 2014 the International League Against Epilepsy (ILAE) Task Force proposed the operational (practical) clinical definition of epilepsy, intended as a disease of the brain defined by any of the following conditions: 1. At least two unprovoked (or reflex) seizures occurring >24 h apart, 2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years and 3. Diagnosis of an epilepsy syndrome

At least 1 percent of children and adolescents in the United States will experience at least one a febrile seizure by age 14. The incidence is greatest in the first year of life, approximately 120 cases per 100,000 population. Fever with seizure is the most common type of seizure in infants and young children. Between 2 and 5% of children experience one or more febrile seizures by 5 years of age. The overall prevalence of epilepsy in India is 5.59-10 per 1000 and the prevalence in males (5.1 per 1000) is significantly higher than that in females (2.2 per 100)[2,3]. Different types of seizures may occur in different parts of the brain and may be classified as localized or widespread. Seizures in newborn are very different from seizures in toddlers and school going children. Most common type of seizure is febrile seizure which occurs when a child contracts an illness like ear infection, cold or chicken pox accompanied by fever. About 2-5% of children have febrile seizure at some point during childhood. Neonatal seizures occur within 28 days of birth. Most occur soon after the child is born. They do not have convulsions but eyes appear to look in different directions, may have lip smacking or periods of no breathing[4].

The common causes of neonatal seizures are hypoxia-ischemia, cerebral infarction, stroke, intracranial haemorrhage, cerebral malaria and tuberculous meningitis. Biochemical disturbances occur frequently in neonatal seizures. Metabolic disturbances like hypoglycaemia, hypocalcaemia, hypophosphatemia and hyponatremia may be present. The principal risk factors for seizures in children are positive family history, high temperature, mental disability, delayed discharge from NICU or premature birth, mother's alcohol abuse and smoking in pregnancy[5-7]. The recognition and treatment of seizure is important during acute illness. Investigations in the form of work-up for infection and metabolic disorders, CSF studies, CT scan and EEG may be needed. Hence the study was done to find out the various types of etiologies that lead to first episode of seizure in children less than 5 years of age and to study the clinical biochemical, metabolic profile of the patients.

MATERIALS AND METHODS

It was a prospective study done for a period of 2 years from September 2020 to September2022. All patients less than 5 years old admitted in Pediatric Ward of tertiary care hospital in the northern India with first episode of seizure were considered eligible for this study. Patients with age >5 years, patient with previous history of seizures and patients with inborn errors of metabolism were excluded from the study. All the above patients were evaluated using detailed history, clinical examination and laboratory investigations and recorded on a predetermined proforma.

Statistical Analysis: Data was tabulated and analyzed using appropriate statistical tool to meet the objectives of the study using SPSS 28.0. Chi square test and p-value was applied to test the significant difference.

RESULT

Demographic Profile: A total of 120 children less than 5 years of age were included in the study. They were divided into three groups based on their age (<1 month, 1 month-1 year, 1-5 years). There were 66 children below 1 year and 54 children between 1-5 years with a definite male predominance. The difference between the groups was not statistically significant (Table 1).

Characteristics of Seizure: According to etiology of seizures 26% of cases were due to febrile convulsions and 21% of cases due to metabolic convulsions (Fig. 1). In neonate, hypoxic ischemic encephalopathy was the most common etiological factor, whereas in older children (1 month-1 year, 1-5 year group) metabolic convulsions accounted for 11 cases each.

Sixty Five patients had generalized convulsions. Neonatal seizures accounted for 26% of cases (Table 2). Majority of patients (58) had convulsions for less than 5 minutes and 34 of them had convulsions for 5-10 minutes Fig. 2. There were 24 cases of hypoxic ischemic encephalopathy and 7 cases of idiopathic origin. Meningitis accounted for 7% of the cases (Table 3).

Most of the patients had hypocalcemia and 27% in the age group of 1 month-1 year had serum calcium levels <4 mg (%). Difference was not significant statistically among the groups. Hypoglycemia was seen in 71% of patients in the age group of 1-5 years (Table 4)

According to CSF analysis, 7 cases had pyomeningitis, 3 had viral meningoencephalitis and 2 had tubercular meningitis (Table 5).

EEG was done in 50% of the cases. Major abnormality seen was asymmetrical slowing in 12% of the cases (Fig. 3). In our study of neonatal seizures, clonic was the most common type of convulsion (39%). Subtle type accounted for 32% and subtle with clonic for 10% of cases among 31 neonates (Fig. 4).

Around 19 (61%) male and 12 (39%) female patients suffered from simple and complex febrile seizures. Since p-value was 0.5, the difference was not statistically significant Table 6.

Table 1: Distribution of Cases According to Age and Sex:

	Sex				
	Male		Female		
Age	Number	Percentage	Number	Percentage	Total
< 1 month	18	58%	13	42%	31
1 month-1 year	25	71%	10	29%	35
1-5 years	31	57%	23	43%	54
Total	69		51		120

Chi square: 1.9, p-value = 0.3 (p>0.05, not significant)

Table 2: Distribution of Cases According to Type of Convulsion

Type of seizure	Frequency	Percentage
Generalized	65	54
Simple Partial	18	15
Complex Partial	6	5
Neonatal	31	26
Total	120	100

Table 3: Distribution of Etiology According to Age of Presentation of First Seizure

	Etiology							
Age	Febrile	Metabolic	HIE	Meningitis	Idiopathic	Sepsis	Others	Total
<1 month	2	4	13	4	0	7	1	31
1 month-1 year	13	11	4	4	2	0	1	35
1-5 years	16	11	7	10	5	1	4	54

Table 4: Distribution of Cases of Metabolic Convulsion

	Serum calcium levels				Random blood sugar levels			
	4-7.5 mg (%)		<4 mg (%)		<4 mg (%)		<50 mg (%)	
Age	No of cases	Percentage	No of cases	Percentage	No of cases	Percentage	No of cases	Percentage
<1 month	2	8%	2	8%	0	0%	0	0%
1 month-1 year	4	15%	7	27%	2	29%	0	0%
1-5 years	6	23%	5	19%	2	29%	3	42%

Chi Square: 0.7, p-value = 0.68, (p>0.05, not significant)

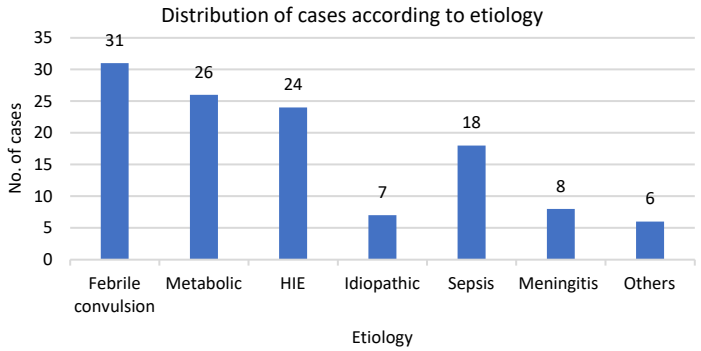

Fig. 1: Distribution of cases according to etiology

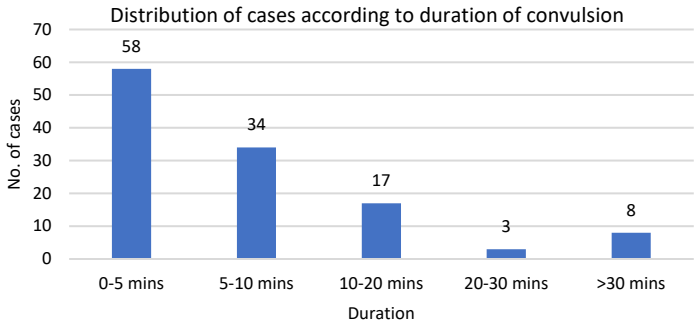

Fig. 2: Distribution of cases according to duration of convulsion

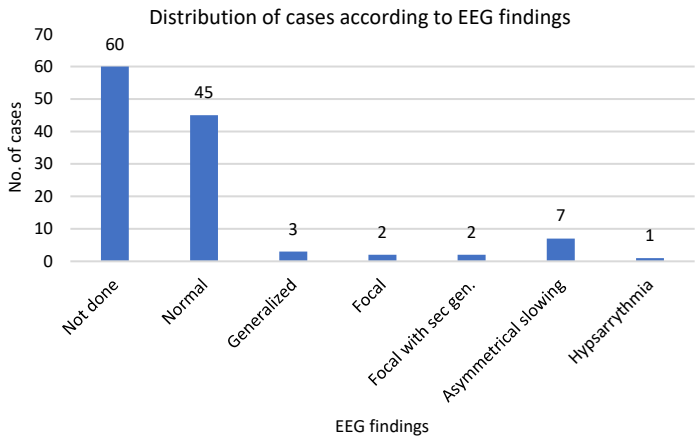

Fig. 3: Distribution of cases according to EEG findings

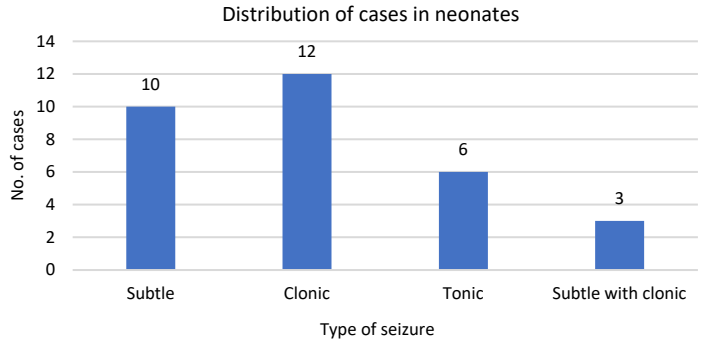

Fig. 4: Distribution of cases in neonates

Table 6: Distribution of Cases According to CSF Analysis Suggestive of Meningitis in Different Age Groups

Age	Total No. of cases	CSF done	Normal	Bacterial	Viral	TB
<1 month	31	25 (81%)	20 (80%)	4 (16%)	1 (4%)	0 (0%)
1 month-1 year	35	17 (49%)	13 (76%)	2 (12%)	1 (6%)	1 (6%)
Total	120	62 (52%)	50 (81%)	7 (11%)	3 (5%)	2 (3%)

Table 7: Analysis of Febrile Seizures

Etiology	Male	Female	Total
Simple febrile seizure	14	10	24 (77%)
Complex febrile seizure	5	2	7 (23%)
Total	19 (61%)	12 (39%)	31

Chi Square: 0.3, p -value = 0.5 (p>0.05, not significant)

DISCUSSION

A seizure is a sudden, uncontrolled electrical disturbance in the brain. It can cause changes in your behavior, movements or feelings and in the levels of consciousness. Despite advances in treatment, it is still associated with significant morbidity and mortality. A total of 120 children were enrolled in this study who experienced first episode of seizure. The prevalence rate was age dependent and 68 out of 120 children were less than 1 year old. According to a study by Babu *et al*.[8]. Seizures were predominantly observed in neonates (49 %) followed by infants and children (37%) and adolescents (14%). Overall the incidence of seizures decreased with increase in age. There was a slight male predominance in all the three age groups. Among neonates 18% were males and 13% were females. A study by Jan *et al*.[8] also noticed more seizures in males as compared to females.

Hypoxic ischemic encephalopathy was the most common cause of seizure in neonates followed by septicemia and hypocalcemia. A study by Rabindran *et al*.[10] gave the same statistics. A study by Bui *et al*.[11] showed that most cases of seizures to be idiopathic (32%). Neonatal infection 28/43 (65.1%) and falciparum malaria 476/821 (58%) were the main diseases associated with neonates and in children greater than 1 year respectively[12].

Among infants and children, febrile seizures were most common. Out of the 31 neonates 77% and 23% suffered from simple febrile seizures and complex febrile seizures respectively. A study by Ghasem et al found that 61.9% children had simple seizures and 38.1% had complex seizures out of 160 children having febrile seizures. Gastroenteritis was the most common cause of fever in their patients[13]. The two most common causes of status epilepticus in the study by Selvan *et al*.[14] were an atypical febrile seizure in 33.3% (22/66) and meningitis in 22.7% (15/66). Duration of

seizures varies with etiology. Simple febrile seizures last for few minutes. Seizures of longer duration may be due to underlying lesion. In our study 48% of cases had seizures for 5 minutes, 28% of cases for 10 minutes and 14% of cases upto 20 minutes. A study by Berg *et al*.[15] showed about 50% of cases having seizure of more than 5 minutes.

According to type of seizure, 54% were generalized while20% were partial. The commonest seizure was generalized seizure of which the most common subtype was GTCS followed by generalized tonic and then myoclonic seizures in a study by Singh *et al*.[16].

The metabolic abnormalities that cause seizure are hypocalcemia and hypoglycemia. In our study, 12 cases had serum calcium of 4-7.5 mg (%) and 14 cases had less than 4 mg (%). Hypoglycemia (<50 mg (%)) was seen in 3 cases. Chen *et al*.[17] reported that there is very little correlation between seizures and metabolic etiology.

CSF studies were done in 62 patients out of which 50 were normal. Cases of pyomeningitis was more in the age group of less than 1 year. In a study by Edraki *et al*.[18], meningitis (bacterial or aseptic) was identified in 19 cases and bacterial meningitis in 7. None of the patients with bacterial meningitis had meningeal irritation signs. Complex febrile seizures, first attack of febrile seizures and impaired consciousness were more common in patients with meningitis when compared to non-meningitis patients[18].

EEG epileptiform abnormalities might be detected in up to 59% of children with first non-febrile seizure. Estimation of recurrence risk depending on EEG record is been studied as well with variable outcomes[19]. In our study, the major abnormality detected in EEG was asymmetrical slowing followed by generalized and focal epileptiform.

CONCLUSION

We found that seizures are one of the commonest causes of hospitalization in children less than 1 year old and males are affected more than females. The most common etiology of seizure is febrile seizures followed by metabolic convulsions, hypoxic ischemic encephalopathy and meningitis. Generalized seizure type is more common than partial seizures. The understanding of Etiopathogenesis of seizures will help in initiation of early and effective treatment.

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