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Clinical profile and predictors of recurrence of first episode of unprovoked seizures in children of the age group 1 month to 12 years

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Abstract: *Background:* Unprovoked seizures in children, occurring without immediate precipitating factors, pose significant challenges due to their potential to recur. *Objectives:* This study aims to identify clinical profile and predictors of recurrence in children aged 1 month to 12 years presenting with their first unprovoked seizure. *Methods:* Conducted over one and a half years in a tertiary care hospital in North Kerala, the study included 61 children. Data on seizure characteristics, past medical history, EEG and neuroimaging findings, and recurrence rates were analysed. *Results:* It was revealed that there is a 52% recurrence rate, with the highest recurrence occurring within the first 3 months (71.9%). Significant predictors of recurrence included seizures occurring during sleep, a history of neurological insults, developmental delay or intellectual disability, and abnormal EEG or neuroimaging findings. Factors such as age, gender, type of seizure, and status epilepticus did not significantly impact recurrence risk. *Conclusions:* The study underscores the importance of identifying these predictors for optimizing treatment and monitoring strategies. Close follow-up is recommended for children with identified risk factors to enhance management and improve long-term outcomes.

Keywords: Unprovoked Seizures, Clinical Profile, Predictors, Recurrence.

Introduction

Unprovoked seizures in children are a significant clinical concern due to their potential to indicate underlying neurological disorders and pose a risk of recurrence. These seizures occur without immediate precipitating factors such as fever, infection, or acute illness, distinguishing them from provoked or symptomatic seizures. Identifying the clinical profile and predictors of recurrence for a first episode of unprovoked seizures is crucial for guiding treatment and management strategies. This study focuses on children aged 1 month to 12 years, a critical developmental period where early intervention can profoundly impact long-term outcomes.

Previous research has highlighted that the recurrence rate of unprovoked seizures in children ranges from 30% to 50% within two years of the first episode [1-2]. Various factors including age at first seizure, seizure type, EEG findings, and family history of epilepsy have been proposed as potential predictors of recurrence [3-4]. This study aims to elucidate the clinical characteristics and identify predictors of seizure recurrence in a cohort of children experiencing their first unprovoked seizure. By delineating these predictors, this study seeks to enhance early diagnosis, optimise treatment protocols, and improve the overall management of paediatric unprovoked seizures.

Material and Methods

A hospital-based prospective cohort study was carried out in children of the age group 1 month to 12 years with a first unprovoked seizure getting admitted or attending the outpatient department of a tertiary care hospital in North Kerala during one and a half years. Children with a first unprovoked seizure defined as a seizure or cluster of seizures all occurring in 24 hours, without association with an acute illness were included in the study [5]. Children with a history of neonatal seizures, past history of febrile convulsions or other provoked seizures were also included. Any acute symptomatic

seizure which is defined as a clinical seizure occurring at the time of a systemic insult or in close temporal association with a documented brain insult was excluded [6]. Non-epileptic events such as syncope was also excluded. Seizures that are known to have a high recurrence rate such as absence, myoclonic seizure and infantile spasms were excluded.

After getting informed consent from parents a detailed history and clinical evaluation were done. The seizure type was classified according to the International League Against Epilepsy criteria [7]. Laboratory investigations done included complete blood count, random blood sugar and serum electrolytes- sodium, potassium, calcium, and magnesium. EEG was done in all patients and the findings were classified as normal, abnormal with nonepileptiform abnormalities and abnormal with epileptiform abnormalities. CSF study was done if indicated. CT or MRI of the brain was done when clinically indicated. The cases were then subdivided based on whether they received continuous antiepileptic drug therapy or not.

The recruited patients were followed up after 1 month, 3 months, 6 months and 1 year after the first episode of seizure to monitor for seizure recurrence. A seizure recurrence is defined as any unprovoked seizure occurring more than 24 hours after the first unprovoked seizure. The study was conducted with the approval of the institutional ethics committee. Age, gender, seizure type, number of seizures in 24 hours, status epilepticus, arousal state, febrile seizures or neonatal seizures in the past, family history of seizures, findings in neuroimaging, EEG findings and the rate of recurrence of seizures were the variables analysed. Statistical analysis was done using chi-square test.

Results

During the study period of one and a half years, there were a total of 61 patients who presented with the first episode of unprovoked seizure. Most children (68%) belonged to the age group of 2 to 10 years. 13 were below 2 years (21%) and 7 (11%) were older than 10 years. 40 patients were boys (66%) and 21 were girls (34%). 34 children (56%) had generalised tonic-clonic seizures with or without focal onset, 24 (39%) had focal seizures with impaired awareness, 2 children (3%) had focal seizures with preserved awareness and 1 had atonic seizure (2 %). Most children, 29 (47%) had the initial event while awake, 23 (38%) had the episode in sleep and 9 (15%) developed seizures on awakening. 13 children (21%) presented as status epileptics. 35 children (57%) had only one seizure and 26 (43%) had 2 or more seizures in the first 24 hours.

A past history of febrile seizures was present in 25 (41%) and neonatal seizures in 6 (10%) children. 7 children (11%) had developmental delay or intellectual disability. A family history of epilepsy was present in 28 (46%) of patients. Among the 61 patients, 55 children (90%) did not have an identified cause for the seizure. 6 children (10%) were identified to have an aetiology in the remote past. The causes identified were symptomatic hypoglycemia in the neonatal period in 2 children, neonatal meningitis in 2 and birth asphyxia in 2 children. The clinical characteristics of children are summarized in Table 1.

Table-1: Clinical characteristics of children with first episode of unprovoked seizures

Variables	n (%)
Age	
< 2 years	13(21)
2-10 years	41(68)
>10 years	7 (11)
Sex	
Boys	40(66)
Girls	21(34)
Type of Seizure	
Generalized tonic-clonic	34(56)
Focal with preserved awareness	2(3)
Focal with impaired awareness	24(39)
Atonic	1(2)
Arousal State	
Awake	29(47)
Asleep	23(38)
On awakening	9(15)
Status Epilepticus	13(21)
Number Of Seizures In 24 Hours	
1	35(57)
>1	26(43)

Variables	n (%)
Past History of	
Febrile seizures	25(41)
Neonatal seizures	6(10)
Developmental Status	
Normal	54(89)
Delay/ Intellectual disability	7(11)
Family History Of Epilepsy	28(46)
Remote Symptomatic Epilepsy	6(10)
Symptomatic hypoglycemia	2(33.3)
Neonatal meningitis	2 (33.3)
Birth asphyxia	2(33.3)

EEG abnormalities were found in 20 children (33%) of which 90% had epileptiform abnormalities. Abnormal neuroimaging (CT/MRI) findings were detected in 10 (16%) children The EEG and MRI abnormalities are shown in Table 2. Recurrence occurred in 32 children (52%). The time of recurrence is shown in Table 3.

Table-2: Findings in EEG and neuroimaging	
EEG abnormalities	**n (%)**
Epileptiform	18(90)
Generalized spikes and waves	8 (44.4)
Focal spikes and waves	6(33.3)
Asymmetrical slowing of one of the hemispheres	2(11.1)
Generalised slowing	1(5.6)
Rolandic spikes	1(5.6)
Nonepileptiform	2(10)
MRI abnormalities	10(16)
Obstructive hydrocephalus (arrested)	2(20)
Communicating hydrocephalus (arrested)	1(10)
Periventricular hyperintensities	3(30)
Hippocampal volume loss	2(20
Pachygyria	1(10)

Table-3: Time and rate of seizure recurrence		
Recurrence in	**Number of patients**	**%**
< 1 month	13	40.6
1 month to <3 months	10	31.3
3 months to < 6 months	8	25
6 months to < 1 year	1	3.1

33 children (54%) were started on continuous antiepileptic drug therapy after the first episode of unprovoked seizures. In the age group under 2 years, 8 out of 13 children experienced a recurrence (61.5%). Among the children aged 2 to 10 years, 23 out of 41 (56.1%) had a recurrence, and 1 out of 7 (14.3%) older than 10 years had a recurrence.

In terms of gender, 21 out of 40 boys (52.5%) and 11 out of 21 girls (52.3%) experienced a recurrence. Out of the children with focal seizures, 15 out of 26 (57.7%) had a recurrence, and out of those with generalized seizures, 17 out of 34 (50%) had a recurrence.

Regarding the circumstances of the initial episodes, 16 out of 23 children (69.5%) who experienced their first seizure while asleep had a recurrence, 14 out of 29 (48.3%) with initial events while awake, and 2 out of 9 (22.2%) with initial seizures upon awakening had a recurrence. Recurrence occurred in 26 out of 49 children (53%) without status epilepticus and in 6 out of 12 children (50%) with status epilepticus.

Furthermore, 16 out of 35 children (45.7%) with one seizure in the first 24 hours and 16 out of 26 (61.5%) with more than one seizure in 24 hours had a recurrence. Additionally, 13 out of 27 children (48.1%) with a family history of epilepsy had a recurrence. All 6 children with a history of neonatal seizures had a recurrence, as did all 6 children with a history of neurological insult in the past, while only 47.3% of those with idiopathic seizures had a recurrence.

Out of the 7 children with developmental delay/intellectual disability, all of them had a recurrence. 95% of those with EEG abnormalities experienced a recurrence, and 100% with abnormal neuroimaging studies had a recurrence. Of the children who received continuous antiepileptic drug therapy after the initial episode, 26 (78.6%) experienced a recurrence, while 6 (27.3%) who were not on continuous medications had a recurrence. The relation of clinical characteristics and seizure recurrence is shown in Table 4.

Table-4: Clinical characteristics and seizure recurrence

Clinical variable	Total no of patients (n)	Patients with recurrence (n, %)	P value
Age group (years)			
<2	13	8(61.5)	0.094
2-10	41	23(56.1)	
>10	7	1(14.3)	
Sex			
Male	40	21(52.5)	0.993
Female	21	11(52.3)	
Type of seizure			
Generalized	34	17(50)	0.452
Partial	26	15 (57.7)	
Others	1	1(100)	
Arousal state			
Awake	29	14(48.3)	0.045
Asleep	23	16(69.5)	
On awakening	9	2(22.2)	
Status epilepticus	12	6 (50)	0.849
No of seizures in 24 hours			
1	35	16(45.7)	0.221
>1	26	16(61.5)	
Past history of			
Febrile seizure	25	14(56)	0.644
Neonatal seizure	6	6(100)	0.014
Aetiology			
Idiopathic seizures	55	26(47.3)	0.014
Remote symptomatic epilepsy	6	6(100)	
Family history of epilepsy	27	13(48.1)	0.548
Developmental status			
Normal	54	25(46.3)	0.007
Developmental delay / intellectual disability	7	7(100)	
EEG			
Normal	41	14(34.1)	0.000
abnormal	20	19(95)	
Neuroimaging			
Normal	51	22(43.1)	0.001
Abnormal	10	10(100)	

Discussion

In this study conducted among 61 children with a first episode of unprovoked seizure, most of them were 2 to 10 years old and predominantly males. The study conducted by Hans et al. was similar, with the key distinction of female participants predominating [8]. Dedeoglu O. et al. reported most children below 2 years, while Sartori et al. reported ages ranging from 6 months to 6 years with mostly males in their studies [9-10]. In our cohort, generalised seizures were the major seizure type agreeing with other similar studies [9-10].

The occurrence of the initial seizure in the awake state in most children is reported by other studies also [8, 11]. Status epilepticus as the initial presentation was 21% in our study; in another study, it was 6 % [11]. Single episode in 24 hours than multiple episodes were described in other studies also [10-11]. In our study, there was a higher incidence of past history of febrile seizures and a family history of epilepsy compared to other studies (8, 11-12). The presence of developmental delay and a history of neurological insult in the study group was almost comparable to other studies [8, 12].

The proportion of children with EEG abnormalities and abnormal MRI (33% & 16%) in our study was almost similar to the study by Dedeoglu O. et al (33.8 % & 19%) [9]. A narrative review based on literature research revealed the following: An early EEG showed that 19% of patients with new-onset seizures had epileptiform discharges. According to an analysis of 18 studies, 50% of imaging studies in children with new-onset epilepsy and seizures showed abnormalities [13].

The overall seizure recurrence rate was 52% at 1 year, with 61.5% below 2 years of age. Other studies on unprovoked seizures have shown recurrence rates between 35% and 65%, depending on the follow-up duration (2–5 years) and the study designs [10]. In a study by Lawn et al. and Dedeoglu O. et al., most patients (75%) had recurrent episodes within three months of the first event [9, 14]. Our study also showed maximum recurrence

within the first 3 months (71.9%). Age, gender, type of seizure, status epilepticus, number of seizures in the first 24 hours, history of febrile seizures and family history of epilepsy did not have any significant role in predicting recurrence as per our study. Children with focal seizures had a higher recurrence rate, but the association was not significant, consistent with other studies [2]. Most studies did not show any increased risk of recurrence in patients with status epilepticus during the initial episode, which aligns with our study. [2, 15-16].

Seizures that occur during sleep are a major risk factor for seizure recurrence because previous events may have gone unnoticed. [11, 17-18]. Our study also found a significant association between seizures during sleep and recurrence. The rate of recurrence was found to be higher with a significant association in children with a history of neurological insult in the past (remote symptomatic seizures), developmental delay, and intellectual disability, as in other studies [3, 8, 11].

A systematic review and meta-analysis found a 66% probability of seizure recurrence after a first unprovoked seizure in children and 77% in adults with epileptiform discharges in EEG [19]. Our study found a 95% risk of recurrence for children with an abnormal EEG. Similarly, abnormal neuroimaging is considered a risk factor for recurrence, as per the literature [8, 20]. This was proven true in our study as well.

Limitations: The main limitations of the present study include the fact that it is based on experiences from a single centre, a restricted number of cases, and a limited duration of follow-up. Additionally, the type of seizure and its duration were mostly determined based on information provided by the parents. Prospective multi-centre studies, incorporating multidisciplinary evaluations, are imperative for definitively identifying risk factors for seizure recurrence and developing an effective evaluation and management algorithm for these patients.

Conclusions

A comprehensive clinical assessment of a first episode of unprovoked seizure and the identification of risk factors for seizure recurrence is necessary to guide diagnostic workup and treatment decisions. In our study, we found that the main indicators of potential seizure recurrence include seizures during sleep, remote symptomatic seizures, developmental delay or intellectual disability, abnormal EEG and abnormal neuroimaging. It is advisable to maintain close monitoring when one or more of these risk factors are present. This information is valuable for providing appropriate counselling and deciding whether to initiate antiepileptic therapy.

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