

A prospective study of single versus recurrent episodes of typical febrile seizure among children attending a tertiary care hospital

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ABSTRACT

Background: Recurrence in the febrile seizures is a significant problem after the seizure episode, and there is up to 30% chance of recurrence after the first episode and 50% chance after 2 or more episodes. **Objective:** The objective of the study is to do a comparative study of sociodemographic and hematologic profile of children aged 6 months–60 months admitted with single and recurrent episodes of typical febrile seizures. **Materials and Methods:** This study was conducted in a tertiary care setting for a period of 2 and a ½ years. History, physical examination and hematologic investigations such as hemoglobin estimation, blood indices, and blood picture were done in all the study participants. Frequency of recurrence after the first episode cases was noted at 1 year after the seizure episode. **Results:** Of 121 total cases, 53.7% were of first, and 46.3% were of recurrent episodes of typical febrile seizure. Statistically, significant difference was noted in the age ($p < 0.001$) and gender distribution ($p < 0.001$). Statistically significant difference was noted between two groups regarding family history of seizure disorder ($p = 0.017$), consanguinity ($p = 0.049$), undernutrition ($p = 0.009$), stunting ($p = 0.002$), and anemia ($p = 0.027$). Follow-up revealed recurrence of seizures in 13.8% after the first episode. **Conclusion:** Recurrence was noted in 13.8% of children with a first typical febrile seizure. We also found a significant association of recurrent episodes with age, gender, family history of seizure disorder, consanguinity, undernutrition, stunting, and anemia.

Key words: Anemia, Recurrence, Typical febrile seizure

Febrile seizures are the most common type of seizures in childhood occurring in about 2–5% of children of age group 6 months–60 months. Febrile seizure is defined as the seizure triggered by fever (body temperature $>100.4^{\circ}\text{F}$ or 38°C) and occurs without any central nervous system (CNS) infections, metabolic abnormality, or due to any other neurologic abnormality to account for the seizures and that occurs in the absence of a history of prior afebrile seizures in children of 6 months–60 months [1]. Most of the febrile seizures occur in the first 24 h of onset of fever and not necessarily when the fever is highest. The peak age of incidence is 18–22 months [2].

Recurrence is a significant problem after the episode of simple febrile seizures. Current evidence reveals that there is 30% chance of recurrence after the first episode simple febrile seizures and 50% chance of recurrence after 2 or more episodes. Risk factors of recurrence of febrile seizures include age of onset <1 year, shorter duration of fever before the occurrence of seizures, lesser degree of fever (38 – 39°C), family history of febrile seizures and epilepsy in first and second degree relatives, complex febrile seizures, daycare attendance, and male gender [3–8]. Approximately 30%–40% of the children with first febrile seizure have a recurrence usually within 12 months [9–12].

Literature evidence reveals that there are several predictors of subsequent epilepsy after febrile seizures. The risk of developing epilepsy varies in different conditions. It is 1% after simple febrile seizures, 4% in recurrent febrile seizures, 6% in complex febrile seizures that are prolonged for >15 min or recurrent within 24 h, 11% in those with short duration fever before the seizure onset (<1 h), 18% in those with family history of epilepsy in first degree relatives, 29% in complex febrile seizures that are focal, and 33% in those with neurodevelopmental abnormalities [13–15].

Simple febrile seizures are of very good prognosis. There is no evidence of risk of mortality or neurocognitive dysfunction compared to the general population after the episode of simple febrile seizures [16–18]. Even though these seizures are of benign nature, complications can occur during each episode. Moreover, it can predispose to very high parental anxiety. Therefore, we planned this comparative study between the first and recurrent episodes of typical febrile seizures mainly focussing on the factors associated with recurrent febrile seizures including sociodemographic and hematologic parameters and to study the frequency of recurrence 1 year after the first episode of typical febrile seizures.

MATERIALS AND METHODS

This descriptive study was conducted in the department of pediatrics of a tertiary care hospital in South India (Kerala) from April 2014 to September 2016. The study population was children of age group 6 months–60 months presenting with first and recurrent episodes (more than one episode) of typical febrile seizures during the study period. Case definition of typical febrile seizure was based on AAP guidelines [2], and it was defined as primary generalized seizures associated with fever (temperature >100.4°F or 38°C) occurring within the first 24 h of onset of fever, of short duration, i.e., lasting for <15 min and do not recur within the first 24 h of onset of fever, age group 6 months–5 years, no prior history of afebrile seizures and occurs without CNS infections, metabolic abnormality, or due to any other neurologic abnormality to account for the seizures. Child is otherwise neurologically healthy and without any neurological abnormality before and after the episodes of seizures.

Children with atypical febrile seizures, afebrile seizures, chronic neurodevelopmental problems and those having clinical features of meningitis were excluded from the study. All consecutive cases satisfying the inclusion and exclusion criteria were recruited for the study. Informed consent was taken for each study participant. Ethics clearance was obtained from the Institutional Ethics Committee.

A structured pro forma was used for recording the information. A detailed history was taken, and physical examination including the anthropometric measurements was done in each case. Relevant investigations did include hemoglobin estimation, blood indices, and blood picture. Hemoglobin and blood indices were done with the help of an automated hematology analyzer. WHO cutoffs were used for diagnosing anemia [23]. Blood picture examination was done by the expert pathologist in a tertiary care teaching hospital. For assessing growth parameters (underweight and stunting), WHO growth charts were used. For diagnosing anemia, WHO cutoffs of hemoglobin values were used. Socioeconomic status was assessed using modified Kuppuswamy's socioeconomic status scale [25]. Sociodemographic and hematologic parameters of first and recurrent episodes were compared. Variables

associated with the recurrent episodes were noted, and the frequency of recurrence after the first episode was noted at 1 year after the seizure episode.

The data were entered into Microsoft Excel and analysis was done using statistical Software SPSS Version 22. Chi-square test was used for categorical variables. Frequency was expressed in percentage. *p* value was set at <5% (0.05).

RESULTS

A total number of cases studied was 121, and their demographic characteristics have been presented in Table 1. As shown in Table 1, the statistically significant difference was noted in the age ($p<0.001$) and gender distribution ($p<0.001$) of children with first and recurrent episodes. Male dominance was noted in the first episode, and more frequency of recurrence was noted in female children. No significant difference was noted in the socioeconomic status of both groups.

As shown in Table 2, no significant difference was noted among two groups according to family history of febrile seizure ($p=0.673$) and premature birth ($p=0.263$). Statistically, significant difference was noted regarding the frequency of family history of seizure disorder ($p=0.017$), consanguinity ($p=0.049$), and anemia ($p=0.027$) among two groups. Regarding the nutritional status of children, 52.3% of children with first episode had undernutrition (underweight) and 76.8% of children with recurrent episodes had undernutrition ($p=0.009$). Stunting was noted in 21.5% of the children with the first episode and 34.7% of children with recurrent episodes ($p=0.002$).

DISCUSSION

This comparative study describes the clinical and hematologic profile of children aged 6 months–60 months with first episodes of typical febrile seizure versus the recurrent episodes and the frequency of recurrence within 1 year after the first episode febrile seizure group. Case definition of typical febrile seizure was based on AAP guidelines [1]. These criteria were strictly adhered for the selection of study participants.

Table 1: Sociodemographic characteristics of first and recurrent episodes

Variable	First episode n (%)	Recurrent episode n (%)	Chi-square	Significance
Age (years)				
<1	20 (30.8)	0 (0)	27.85	<0.001
1–2	10 (15.4)	27 (48.2)		
2–5	35 (53.8)	29 (51.8)		
Total	65	56		
Gender				
Male	44 (68.8)	14 (25)	22.892	<0.001
Female	21 (31.2)	42 (75)		
Socioeconomic status				
Upper middle	1 (1.5)	1 (1.8)	3.65	0.168
Lower middle	39 (60)	24 (42.9)		
Upper lower	25 (38.5)	31 (55.4)		

Table 2: Distribution of risk factors among first episode and recurrent episodes

Risk factor	First episode n (%)	Recurrent episode n (%)	Chi-square	p value
Family history of febrile seizure				
Yes	37 (56.9)	34 (60.7)	0.178	0.673
No	28 (43.1)	22 (39.3)		
Family history of seizure disorder				
Yes	6 (9.2)	16 (28.6)	5.744	0.017
No	59 (90.8)	40 (71.4)		
Consanguinity				
Yes	2 (3.1)	7 (12.5)	3.880	0.049
No	63 (96.9)	49 (87.5)		
Maturity at birth				
Term	58 (89.2)	46 (82.1)	1.252	0.263
Preterm	7 (10.8)	10 (17.9)		
Anemia				
Yes	24 (37.9)	31 (56.4)	4.7	0.027
No	41 (62.1)	25 (43.6)		
NICU admission in Newborn period				
Yes	6 (9.2)	8 (14.3)	0.751	0.386
No	59 (90.8)	48 (85.7)		

NICU: Neonatal intensive care unit

We found a significant difference in the age distribution of children with the first episode and recurrent episode of typical febrile seizures. Among the children with first episode, 30.8% were <1 year, 15.4% were of age 1–2 years, and 53.8% were in the age group 2–5 years. Among the children with recurrent episodes, 48.2% were in the age group 1–2 years and 51.8% were in the age group 2–5 years. None of the children in this group were <1 year. Age distribution in this study was similar to the observations in the study by Berg *et al.* Male dominance was noted in the first episode group, but female dominance was noted in the recurrence group. In a study by Kantamalee *et al.* also [3], male dominance was noted in the first episode seizures (male:female ratio was 1.8:1). Ojha *et al.* also noted male dominance in the first episode of seizures but recurrence was more commonly noted in female children [19]. In our study, recurrence was noted in 13.8% children whereas the recurrence was 51% in a study by Ojha *et al.* [19] and 19.92% in the study by Kantamalee *et al.* [3]. This shows the ethnic variation in the incidence and recurrence of febrile seizures.

No significant association was found between the family history of febrile seizure and febrile seizure recurrence in our study. However, in the study by Pavlidou *et al.* [6], family history of febrile seizure was found as a risk factor for febrile seizure recurrence so also in the study by Berg *et al.* [14]. In our study, a significant association was found between febrile seizure recurrence and family history of seizure disorder. We also found a significant association between consanguinity and recurrence of febrile seizures. This was comparable to the results of study done by Shinnar *et al.* [16]. In the study by Singhi *et al.* [17] family history of seizure disorder and febrile seizure in first degree relatives were noted as risk factors for seizure recurrence [16].

No significant association was found between prematurity and febrile seizure recurrence in our study. Prematurity is reported as a risk factor for febrile seizures in many studies [18–20]. A significant association was found between febrile seizure recurrence and anemia and undernutrition in the present study. Iron deficiency was noted as a risk factor for febrile seizures in many previous studies also [18–22]. In a meta-analysis done by Habibian *et al.* [26] anemia was found to be a significant risk factor for febrile seizures (pooled odds ratio - 2.84; confidence interval - 1.46–2.85) [24].

Anemia and undernutrition are found to be the modifiable risk factors for recurrence of typical febrile seizures. Therefore, prevention and treatment of anemia and undernutrition are essential to prevent recurrence of febrile seizures. More chance of recurrence after the first episode may be anticipated in children of age 2–5 years, female gender, born by consanguineous marriage, having family history of seizure disorder, and preventive measures should be more stressed in these children. Therefore, anticipatory guidance for febrile seizures should be given to the parents and caretakers of these children. They should be made aware of simple febrile seizures, nature and prognosis, preventive measures, first aid, and types of management of seizures.

Merits of this study is that criteria for case definition were strictly adhered throughout the study and thus controlling the selection bias. Limitation of this study is that it is a hospital-based study and observations may be different from a community setting.

CONCLUSION

Recurrence was noted in 13.8% of children with a first typical febrile seizure at 1 year after the seizure episode. Male dominance is noted in the first episode of typical febrile seizures. Recurrence rate is more in female children. The maximum frequency of

recurrence was noted in the age group 2–5 years. Variables found to have a statistically significant association with recurrence were age, gender, consanguinity, family history of seizure disorder, undernutrition, stunting, and anemia.

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