

Original Research Article

Clinical profile and laboratory parameters of febrile seizures: a hospital based cross-sectional study in sub-Himalayan region

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ABSTRACT

Background: Febrile seizures occur commonly in the age group of 6 to 60 months, clinical spectrum is variable and range from single, brief episode to status epilepticus which can further progress to long term consequences. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to know the clinical spectrum, pattern of lab parameters and their association as a risk factor for occurrence of seizures.

Methods: A hospital based cross-sectional study was conducted in the department of paediatrics of Indira Gandhi Medical college, Shimla, Himachal Pradesh. All children between 6 to 60 months admitted in our institute during the study period of July 2021 to June 2022 with diagnosis of febrile seizure were considered for the study.

Results: A total of 120 children were included in the present study with a mean age of 26.6 ± 14.2 months. Majority of the study subjects were from rural area (74.2%) and male had slightly higher representation (55.8%). Generalised tonic-clonic seizure (78.3%) was the most common phenotypic presentation, cases with SFS constituted 61.7% and CFS was observed in 38.3% of study subjects. Raised ESR values, elevated CRP values and leucocytosis had significant association in occurrence of CFS.

Conclusions: The study provides valuable insights into the different phenotypic presentations and characteristics of febrile seizures in the study population. The study further identifies a statistically significant association between certain inflammatory markers and CFS.

Key words: Febrile seizures, Complex febrile seizures, GTCS, clinical profile, Laboratory parameters

INTRODUCTION

In acute pediatric care setting seizure accounts for around 1 to 2 % of total emergency department visits.¹ Seizures are one of the most common pediatric neurological disorders presenting to hospital with approximately 4-10% of children experience at least 1 episode of seizure in the first 16 year of life. The incidence of seizure is highest among children <3 years of age, and frequency decreases as the child grows older.² The International League against Epilepsy (ILAE) defines seizure as a transient occurrence of signs and/or symptoms due to abnormal excessive or

synchronous neuronal activity in the brain.³ Febrile seizures occur most commonly in the age group of 6 to 60 months, is associated with body temperature of 38°C (100.4°F) or higher, that is not attributable to central nervous system infection, metabolic imbalance and acute neurological insult and that having occurred in the absence of any prior afebrile seizures.⁴ Clinical spectrum of febrile seizures is variable and can range from single, brief episode to status epilepticus which can further progress to long term consequences and have risk of recurrence or risk of developing epilepsy in future. There is very limited data available from sub-Himalayan belt of northern India,

hence the present study was planned to know the clinical spectrum, pattern of lab parameters and their association as a risk factor for occurrence of seizures.

METHODS

A hospital based cross-sectional study was conducted in the department of paediatrics of Indira Gandhi Medical College Shimla, Himachal Pradesh. Febrile seizures were defined as seizures that occurred in children between the age of 6 to 60 months accompanied by fever with a temperature of 38°C (100.4°F) or higher, that are not the result of central nervous system infection or any metabolic imbalance, acute neurological insult and that occur in the absence of a history of prior afebrile seizures.⁴ All children between 6 to 60 months admitted in our institute during the study period of July 2021 to June 2022 with diagnosis of febrile seizure were considered for the study. Patients with static/progressive neurological disorder, developmental delay, past history of neonatal/afebrile seizure, failure to thrive, or any history of perinatal insult were excluded from the study. In a study conducted by Raju et al the prevalence of febrile seizure was observed to be 3.1%.⁵ At a confidence level of 95% and an absolute error of 5% the minimum sample size was calculated to be 47. All the children admitted with diagnosis of febrile seizure meeting study criteria was included in the study after taking written and informed consent from the parents of the children. Parents were informed, explained about the details and purpose of the study. Children presenting with seizure were given emergency care, managed for control of seizure and stabilized. Following this a detailed history was

obtained from the parents including demographic profile, presenting complaints, detailed description of the seizure, other relevant history i.e., family history of febrile seizure or epilepsy. Further, detailed general and physical examination was carried out, blood sample was collected from peripheral vein for complete haemogram, iron profile, ESR and C-reactive protein.

The data was collected with google form and Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Quantitative data are expressed in terms of mean $\pm$ standard deviation and qualitative data are presented in frequency, percentage and analysed using chi-square and Fisher exact test. A p value of less than 0.05 was considered as statistically significant.

RESULTS

A total of 120 children were included in the present study with a mean age of 26.6 $\pm$ 14.2 months. Around one-fourth of study participants were in the age group of 25 to 36 months (32 cases, 26.7%), followed by 13 to 24 months (30 cases, 25%). A little above one-fifth of subjects were in the age group of 6 to 12 months (26 cases, 21.7%). 19 cases (15.8%) were in the age group of 37 to 48 months and 13 cases (10.8%) in the age group of 49 to 60 months. Majority of the study subjects were from rural area (89 cases, 74.2%) and male had slightly higher representation (67 cases, 55.8%) compared to female children (53 cases, 44.2%).

Table 1: Comparison of seizures phenotype with clinical presentation (n=120).

Symptoms	Type of seizure N (%)				Total
	Atonic	Tonic	Focal	Status Epilepticus	
Clenching of teeth	-	45 (37.5)	-	-	45 (37.5)
Aura	2 (1.7)	10 (8.3)	05 (4.2)	-	17 (14.2)
Up rolling of eyeball	08 (6.7)	45 (37.5)	05 (4.2)	-	58 (48.3)
Bluish discoloration of lips	08 (6.7)	30 (25.0)	04 (3.3)	01 (0.8)	43 (35.8)
Deviation of the angle of the mouth	-	-	12 (10.0)	-	12 (10.0)
Frothing from mouth	07 (5.8)	30 (25.0)	07 (5.8)	01 (0.8)	45 (37.5)
Urinary incontinence	04 (3.3)	16 (13.3)	01 (0.8)	-	21 (17.5)
Bowel Incontinence	-	14 (11.7)	02 (1.7)	01 (0.8)	17 (14.2)
Vacant stare	05 (4.2)	05 (4.2)	02 (1.7)	-	12 (10.0)
Total	13 (10.8)	94 (78.3)	12 (10.0)	01 (0.8)	120 (100)

Generalised tonic-clonic seizure (94 cases, 78.3%) was the most common phenotypic presentation of febrile seizures followed by atonic seizures (13 cases, 10.8%) and focal seizures (12 cases, 10%). One patient (0.8%) of febrile seizure had presented with status epilepticus and the presenting symptoms included bluish discoloration of lips, frothing from mouth and bowel incontinence. Up-rolling of eyeball was the most common presenting symptom (58 cases, 48.3%), followed by clenching of teeth (45 cases,

37.5%) and frothing from mouth (45 cases, 37.5%). Clenching of teeth was only observed in tonic-clonic seizures (45 out of 94 cases) whereas deviation of angle of mouth was only observed in focal seizures (all 12 cases). Up-rolling of eyeball (45/94 cases), bluish discoloration of lips (30/94 cases) and frothing from mouth (30/94 cases) were other common presenting symptoms in tonic-clonic seizure cases (Table 1). Majority of study subjects had single episode of seizure (79 cases 65.8%) and most of the

study participants didn't have prior history of febrile seizure (91 cases, 75.8%).

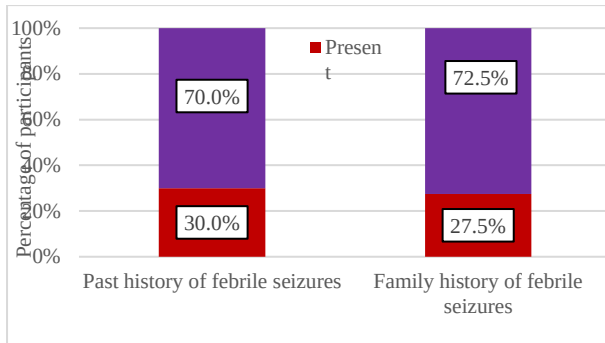


Figure 1: Comparison of history of study participants.

Nearly a third of study participants (36 cases, 30%) had family history of febrile seizures (Figure 1). Around three-fifth (73 cases, 60.8%) of the study subjects had seizure within six hours of onset of fever, nearly one-fifth (23 cases, 19.2%) had seizure between 6 to 12 hours after the onset of fever. Ten patients (8.3%) in the present study had after seizure episodes. The cases were further classified as simple and complex febrile seizures, it was observed that 74 cases (61.7%) fit into the criteria of simple febrile seizures (SFS) and remaining 46 cases (38.3%) were classified as complex febrile seizures (CFS). On gender-wise comparison, there was no significant difference in the occurrence of simple or complex febrile seizures.

Table 2: Comparison of factors associated with type of febrile seizure.

Parameters N (%)		SFS	CFS	P value
Gender	Male	40 (54.1)	27 (58.7)	0.619
	Female	34 (45.9)	19 (41.3)	
Number of seizures in 24 hours	One	48 (64.9)	31 (67.4)	0.930
	Two	20 (27.0)	11 (23.9)	
	Three or more	06 (8.1)	04 (8.7)	
Time of seizure onset from fever	Up to 6 hours	44 (59.5)	29 (63.0)	0.963
	7-12 hours	14 (18.9)	09 (19.6)	
	13-24 hours	08 (10.8)	04 (8.7)	
	> 24 hours	01 (1.4)	01 (2.2)	
	After seizures	07 (9.5)	03 (6.5)	
Hemoglobin	<11 g/dl	20 (27.0)	20 (43.5)	0.063
	≥11 g/dl	54 (73.0)	26 (56.5)	
ESR	0-10	59 (79.7)	25 (54.3)	0.003
	≥11	15 (20.3)	21 (45.7)	
C-reactive protein	<5	33 (44.6)	10 (21.7)	0.011
	≥6	41 (55.4)	36 (78.3)	
Total leucocyte count	Normal	47 (63.5)	15 (32.6)	<0.001
	Leucopenia	07 (9.5)	01 (2.2)	
	Leukocytosis	20 (27)	30 (65.2)	

The number of seizures in 24 hours and the time of seizure onset from fever also didn't have significant difference between the types of seizures. More than two-fifth (43.5%) of the study subjects who had CFS had haemoglobin of less than 11 g/dl whereas only 27% of patients having SFS had haemoglobin of less than 11 g/dl, however the difference was statistically not significant (p value=0.063). Nearly half of the participants having CFS had raised ESR, but only one-fifth (20.3%) of patients with SFS had raised ESR. Similarly, patients with raised C-reactive protein were relatively more in patients with CFS than SFS cases. Nearly two-third of cases (63.5%) with SFS had normal leucocyte count whereas only 32.6% of cases with CFS had normal leucocyte count and majority of the patients in this group had leukocytosis (65.2%). All the above differences were found to be statistically significant with a p value of less than 0.05 (Table 2).

DISCUSSION

Febrile seizures are the most common neurologic disorder in the pediatric age group. Although primarily benign, childhood febrile seizures can be frightening and anxiety-provoking events for parents and caregivers.⁴ This study highlights the common age of presentation, clinical manifestation and risk factors associated with febrile seizures in sub-Himalayan region of India. The mean age of study participants in this study was observed to be 26.6±14.2 months. 26.7% cases were in the age group of 25 to 36 months, followed by 25% cases in 13 to 24 months, 21.7% cases between 6 to 12 months, 15.8% between 37 to 48 months and 10.8% cases in the age group of 49 to 60 months. Similar were the findings in the studies conducted by Raju et al, Aliabad et al, Shrestha et al, Takasu et al and Hussain et al wherein the mean age of patients presenting with febrile seizures varied from 22 to

26 months.⁵⁻⁹ Male preponderance was observed in our study wherein 55.8% study participants were male and 44.2% were female with a ratio of 1.2:1. Similar were the findings in a study by Aliabad et al where the authors observed a male:female ratio of 1.19:1, studies by Shrestha et al and Raju et al though had similar findings but the ratio was slightly higher (Male: female ratio of 2:1 and 1.7:1 respectively).⁵⁻⁷ However, in another study by Carman et al there was equal number of boys and girls (1:1 ratio).¹⁰

Majority of the study participants in the present study belonged to rural area (74.2%). This can be explained by the fact that, majority of the population of Himachal Pradesh (89.97%) reside in rural area with only 10.03% in urban area (Census of India report 2011).¹¹ Thirty percent of study participants in the present study had positive family history of febrile seizures which is similar to study conducted by Raju et al wherein the authors observed 33% of cases with positive family history and another study by Han et al noted positive family history in 24.8% of patients.^{5,12}

Generalised tonic-clonic seizure (78.3%) was the most common phenotypic presentation in the present study followed by atonic seizures (10.8%), focal seizures (10%) and one patient (0.8%) had presented with status epilepticus. Uprolling of eyeball was the most common initial event as seizure accounting for 48.3% of cases followed by clenching of teeth (37.5%), frothing from mouth (37.5%), bluish discoloration of lips (25%), urinary incontinence (17.5%), with aura (14.2%), bowel incontinence (14.2%), deviation of angle of mouth (10%) and vacant stare (10%). Takasu et al also observed similar events in their study among 106 participants, 84.9% had oral symptoms, 76.4% had focal features, nearly three-fourth (73.6%) had ocular symptoms, 50% participants had change in facial expression and 41.5% had limbic features.⁸

Cases with SFS constituted 61.7% and CFS was observed in 38.3% of study subjects. Studies carried out by Aliabad et al, Delpisheh et al and Han et al also observed SFS to be the predominant type of febrile seizure (61.9%, 69.3% and 82.5% cases of SFS respectively).^{6,12,13} Storz et al also observed that 42% of children in their study had atleast one CFS features which is similar to the findings in our study.¹⁴ Contrary to the above findings, Winkler et al in their hospital based cross-sectional study in rural Tanzania observed majority of the study subjects were classified as having CFS.^{14,15}

The higher incidence of CFS in Winkler et al compared to the present study may be because of the limited facility available in their hospital leading to relatively higher chances of admitting complex cases and simple cases being treated and discharged on out-patient basis. Majority of study subjects had single episode of seizure (65.8%) and most of the study participants didn't have prior history of febrile seizure (75.8%). Study done by Han et al showed similar finding with more number cases presenting with

one episode of febrile seizure within 24 hours.¹² Storz et al observed relatively higher incidence of recurrence (38%) compared to the present study, this difference may be because Storz study was a community based cross-sectional study and our's was a hospital based cross-sectional study.¹⁴ In our study around three-fifth (60.8%) of the study subjects had seizure within six hours of onset of fever, 19.2% had seizure between 6 to 12 hours and ten patients (8.3%) had after seizure episodes. There was wide variation in onset of seizure between the studies, Ateşoğlu et al found that 62% seizure occur within 1 hour of onset of fever and only 6.6% cases had seizures after 24 hours whereas Han et al observed only 24.8% cases had seizures within first six hours, 16.1% cases had seizure between 24 to 72 hours and 1.2% had seizure after 72 hours from onset of fever.^{12,16}

It was noticed in the present study that gender, frequency of seizures in 24 hours, time of seizure onset from fever didn't reveal any significant difference in the occurrence of simple or complex febrile seizures. Though prevalence of anaemia was relatively higher among patients with CFS, the difference was statistically not significant. Similar, results were demonstrated by Farhad Heydarian et al in their cross-sectional study wherein no significant relationship was seen between anaemia and type of febrile seizures (SFS vs. CFS).¹⁷ Association between raised ESR values, elevated CRP values and leucocytosis with CFS was found to be statistically significant in our study. Similar finding was noted by Biyani et al when comparing febrile seizure (FS) patients and non-FS children, they encountered a significant increase of WBC ($p=0.0005$) in children with FS.¹⁸ However, there was no significant difference regarding CRP levels ($p=0.66$) between the two groups. Sohn et al also observed a positive association between leucocytosis and elevated C-reactive protein levels in patients with any type of seizure.¹⁹ Contrary to our finding, Eskandarifar et al observed relatively higher level of WBC count among SFS patients, however in their study the proportion of CFS patients was only 19% (93 cases out of 271).²⁰

Limitations

Limitations of current study were Study design and small sample size.

CONCLUSION

In conclusion, the study provides valuable insights into the different phenotypic presentations and characteristics of febrile seizures in the population under investigation. It highlights the predominance of generalized tonic-clonic seizures and the varied initial events preceding seizures. The study further identifies a statistically significant association between certain inflammatory markers (raised ESR, elevated CRP, and leucocytosis) and CFS. However, further research and larger-scale studies are necessary to validate and generalize these findings across different populations.

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