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Original Research Article

Predictors of recurrence of febrile seizures: a prospective cohort study from a tertiary care centre

Aadinadh M. J.*, Arvind Bountra, Preeti Anand

Department of Pediatrics, Max Smart Super Speciality Hospital, Saket, New Delhi, India

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***Correspondence:**
Dr. Aadinadh M. J.,
E-mail: aadinadh.mj@gmail.com

ABSTRACT

Background: This study was done to estimate various risk factors associated with the recurrence of febrile seizures in children aged 6 months to 5 years.
Methods: This prospective cohort study was conducted at Max Smart Super Speciality Hospital, New Delhi, on children aged 6 months to 5 years, admitted from June 2023 to May 2024. A total of 115 children presenting with their first episode of febrile seizures were enrolled and they were followed up for a period of 1 year. Children with CNS infections, afebrile seizures, or other exclusion criteria were omitted. History, clinical examination, and laboratory parameters including haemoglobin and serum sodium were recorded. Follow-up was conducted over one year. Data were analyzed using SPSS v24 with univariate analysis.
Results: Out of 115 children, 35 (30.4%) developed recurrent febrile seizures. Statistically significant associations were observed for age ≤1 year (p=0.008), prolonged seizure >5 minutes (p=0.0001), positive family history of FS (p=0.009), and haemoglobin <11 gm/dl (p=0.028). Gender, fever intensity, duration of fever, seizure type, and serum sodium levels were not significantly associated.
Conclusions: Younger age, prolonged seizures, positive family history, and anaemia were key predictors of FS recurrence. Early recognition of these factors can improve parental counselling and follow-up care strategies.

Keywords: Anemia, Febrile seizure, Fever, Recurrent febrile seizure, Risk factors, Seizure

INTRODUCTION

Febrile seizures (FS) are among the most frequent neurological disorders seen in pediatric practice, affecting 2-5% of children between the ages of 6 months and 5 years. These seizures are defined as convulsions occurring in association with fever in the absence of any central nervous system infection or acute electrolyte imbalance.[1] FS can be classified into two categories- simple and complex- depending on duration, focality, and frequency within a 24-hour period.

Despite their mostly benign nature, febrile seizures are a significant cause of concern for parents and caregivers due to the risk of recurrence and potential future epilepsy.[2] Recurrence is seen in approximately one-third of affected children, and identifying those at higher risk allows for early intervention and parental counselling. Multiple studies have suggested that various factors- including age at first seizure, family history, duration of fever before seizure, anemia, and seizure duration- may influence the recurrence rate.[3]

This study aimed to comprehensively evaluate these potential risk factors in an Indian tertiary care setting, contributing to localized data for better management of FS recurrence.

METHODS

This was a prospective cohort study carried out at the department of pediatrics, Max Smart Super Specialty

Hospital, Saket, New Delhi. The study was conducted from June 2023 to May 2024, after receiving approval from the institutional ethical committee.

Inclusion criteria were children aged between 6 months and 5 years presenting with their first episode of febrile seizure, classified as either simple or complex. Exclusion criteria included history of afebrile seizures, known neurological disorders, metabolic derangements (e.g. hypocalcemia), CNS infections (diagnosed by CSF analysis), trauma, and parental refusal to participate.

Detailed history including age, sex, duration and intensity of fever, seizure type (simple/complex), duration of seizure, family history of FS or epilepsy, developmental status, and previous hospitalizations was obtained. All children underwent baseline investigations including complete blood count, serum electrolytes (sodium, potassium, calcium), random blood sugar, and renal function tests. Neuroimaging and EEG were performed selectively based on clinical indication

Children were categorized based on age (≤1 year versus >1 year), seizure duration (≤5 minutes versus >5 minutes), hemoglobin (<11 gm/dl versus ≥11 gm/dl), and serum sodium (<135 meq/l versus normal). Follow-up was done fortnightly via outpatient visits and telephonic check-ins over a 12-month period to assess for recurrence.

Follow-up was done fortnightly in the outpatient department or via telephonic consultation. Each child was followed for one year to monitor recurrence of febrile seizures.

Statistical analysis

The collected data was entered into Microsoft Excel after preparing a Master-chart. Data analysis was done using licensed SPSS software version 24.0 (Chicago, Illinois). Univariate analyses were done initially and the results were presented with the help of tables, text, bar-diagrams and pie-charts.

Descriptive statistics were used to calculate frequencies of categorical variables, and measures of central tendencies and dispersion were used to describe continuous variables. For quantitative variable we used unpaired t-test. P value <0.05 was considered as statistically significant.

RESULTS

Distribution of study participants according to age group

Among the 115 study participants, 33 individuals (28.7 percent) were aged 1 year or younger, while 82 individuals (71.3 percent) were older than 1 year.

Distribution of study participants according to gender

The study included 40 female participants (34.8 percent) and 75 male participants (65.2 percent), indicating a higher proportion of male children in the study.

Distribution of study participants according to intensity of fever

Among the participants, 83 individuals (72.2 percent) had a fever of less than 102.2°F, while 32 individuals (27.8 percent) had a fever exceeding 102.2°F.

Distribution of study participants according to duration of fever

A total of 95 participants (82.6 percent) had a fever lasting less than 24 hours before the onset of seizures, while 20 participants (17.4 percent) had a fever persisting for more than 24 hours.

Distribution of study participants according to type of seizure

Simple febrile seizures were observed in 90 participants (78.3 percent), while complex febrile seizures were recorded in 25 participants (21.7 percent).

Distribution of study participants according to duration of seizure

A total of 96 participants (83.5 percent) experienced seizures lasting 5 minutes or less, while 19 participants (16.5 percent) had seizures lasting longer than 5 minutes.

Distribution of study participants according to family history of febrile seizure

Among the participants, 103 individuals (89.6 percent) did not have a family history of febrile seizures, while 12 individuals (10.4 percent) had a positive family history.

Distribution of study participants according to family history of epilepsy

A total of 112 participants (97.4 percent) had no family history of epilepsy, while only 3 participants (2.6 percent) had a positive family history.

Distribution of study participants according to hemoglobin

Among the participants, 61 individuals (53.0 percent) had hemoglobin levels below 11 gm/dl, while 54 individuals (47.0 percent) had hemoglobin levels of 11 gm/dl or higher.

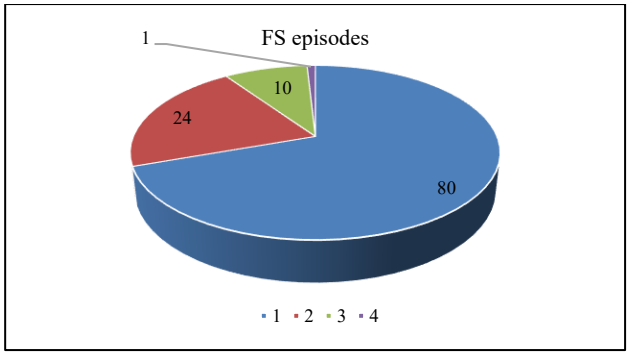

Figure 1: Distribution according to total FS episodes in one year follow-up.

Distribution of study participants according to serum sodium level

A total of 49 participants (42.6 percent) had serum sodium levels below 135 meq/l, while 66 participants (57.4 percent) had normal sodium levels between 135-145 meq/l.

Distribution of study participants according to total FS episodes in one year follow-up

During the one-year follow-up, 80 participants (69.6 percent) had only one episode of febrile seizure, while 24 participants (20.9 percent) had two episodes. Additionally, 10 participants (8.7 percent) experienced three episodes, and 1 participant (0.9 percent) had four episodes.

Association of recurrent febrile seizure with various factors

Among children aged 1 year or younger, 16 individuals (48.5 percent) experienced recurrent febrile seizures, while 17 individuals (51.5 percent) did not. In children older than 1 year, 19 individuals (23.2 percent) had recurrent seizures, whereas 63 individuals (76.8 percent) remained seizure-free. The association was statistically significant (p=0.008), indicating that younger children were at a higher risk for seizure recurrence.

Table 1: Association of recurrent febrile seizure with age.

Age	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
≤1 year	16	48.5	17	51.5	0.008
> 1 year	19	23.2	63	76.8	
Total	35	30.4	80	69.6	

Table 2: Association of recurrent febrile seizure with gender.

Gender	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
Female	12	30.0	28	70.0	0.941
Male	23	30.7	52	69.3	
Total	35	30.4	80	69.6	

Table 3: Association of recurrent febrile seizure with fever intensity.

Fever	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
<102.2°F	29	34.9	54	65.1	0.191
> 102.2°F	6	18.8	26	81.3	
Total	35	30.4	80	69.6	

Table 4: Association of recurrent febrile seizure with duration of fever.

Duration of fever	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
<24 hours	28	29.5	67	70.5	0.625
>24 hours	7	35.0	13	65.0	
Total	35	30.4	80	69.6	

Among female participants, 12 individuals (30.0 percent) had recurrent febrile seizures, while 28 individuals (70.0 percent) did not. Among male participants, 23 individuals (30.7 percent) experienced recurrence, while 52 individuals (69.3 percent) remained seizure-free. The association was not statistically significant (p=0.941), suggesting that gender does not influence febrile seizure recurrence.

A total of 29 individuals (34.9 percent) with fever below 102.2°F had recurrent febrile seizures, while 54 individuals (65.1 percent) did not. Among those with fever exceeding 102.2°F, 6 individuals (18.8 percent) experienced recurrent seizures, whereas 26 individuals (81.3 percent) remained seizure-free. The association was not statistically significant (p=0.191), indicating that fever severity does not have a strong correlation with seizure recurrence.

Among participants with fever lasting less than 24 hours, 28 individuals (29.5 percent) had recurrent seizures, while 67 individuals (70.5 percent) did not. In those with fever lasting longer than 24 hours, 7 individuals (35.0 percent) had recurrent seizures, whereas 13 individuals (65.0 percent) remained seizure-free. The association was not statistically significant (p=0.625), indicating that the duration of fever does not strongly predict seizure recurrence.

Table 5: Association of recurrent febrile seizure with type of seizure.

Type of seizure	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
Complex	10	40.0	15	60.0	
Simple	25	27.8	65	72.2	0.241
Total	35	30.4	80	69.6	

Table 6: Association of recurrent febrile seizure with duration of seizure.

Duration of seizure	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
≤5 minutes	22	22.9	74	77.1	
>5 minutes	13	68.4	6	31.6	0.0001
Total	35	30.4	80	69.6	

Table 7: Association of recurrent febrile seizure with family history of FS.

Family history of FS	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
No	30	29.1	73	70.9	
Yes	5	41.7	7	58.3	0.009
Total	35	30.4	80	69.6	

Table 8: Association of recurrent febrile seizure with hemoglobin.

Hb	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
<11 gm/dl	24	39.3	37	61.7	
>11 gm/dl	11	20.4	43	79.6	0.028
Total	35	30.4	80	69.6	

Table 9: Association of recurrent febrile seizure with serum sodium level.

Sodium level	Recurrent FS		No recurrent FS		P value
	Count	%	Count	%	
<135 meq/l	17	34.7	32	65.3	
135-145 meq/l	18	27.3	48	72.7	0.392
Total	35	30.4	80	69.6	

Among participants with complex febrile seizures, 10 individuals (40.0 percent) had recurrent episodes, while 15 individuals (60.0 percent) did not. In contrast, among those with simple febrile seizures, 25 individuals (27.8 percent) had recurrence, whereas 65 individuals (72.2 percent) remained seizure-free. The association was not statistically significant (p=0.241), suggesting that seizure type alone does not predict recurrence risk.

Among participants with seizures lasting 5 minutes or less, 22 individuals (22.9 percent) experienced recurrence, while 74 individuals (77.1 percent) did not. In contrast, among those with seizures lasting longer than 5 minutes, 13 individuals (68.4 percent) had recurrence, whereas only 6 individuals (31.6 percent) remained seizure-free. The association was statistically significant (p=0.0001), indicating that prolonged seizure duration is a strong predictor of recurrence.

Among participants without a family history of febrile seizures, 30 individuals (29.1 percent) experienced recurrence, while 73 individuals (70.9 percent) did not. Among those with a positive family history, 5 individuals (41.7 percent) had recurrent seizures, whereas 7 individuals (58.3 percent) remained seizure-free. The association was statistically significant (p=0.009), suggesting that a family history of febrile seizures increases the risk of recurrence.

Among participants with hemoglobin levels below 11 gm/dl, 24 individuals (39.3 percent) experienced recurrent seizures, while 37 individuals (61.7 percent) did not. Among those with hemoglobin levels of 11 gm/dl or higher, 11 individuals (20.4 percent) had recurrence, whereas 43 individuals (79.6 percent) remained seizure-free. The association was statistically significant (p=0.028), suggesting that anemia may contribute to seizure recurrence.

Among participants with serum sodium levels below 135 meq/l, 17 individuals (34.7 percent) had recurrent seizures, while 32 individuals (65.3 percent) did not. Among those with normal sodium levels (135-145 meq/l), 18 individuals (27.3 percent) experienced recurrence, whereas 48 individuals (72.7 percent) remained seizure-free. The association was not statistically significant (p=0.392), indicating that hyponatremia does not strongly predict seizure recurrence.

DISCUSSION

This study aimed to investigate the effect of various factors, including age, gender, temperature, past history of seizure, developmental and family history, duration, type, and number of seizures, on the recurrence of febrile seizures in children admitted to a tertiary care hospital. Additionally, the study sought to describe the distribution of age, gender, duration of fever, type, and duration of seizure in the occurrence of febrile seizures.

Age

The current study found that the majority of participants (71.3%) were older than 1 year, while 28.7% were aged 1 year or younger. However recurrent seizure was associated with the younger age group in the current study.

Several of the compared studies have reported a higher risk of febrile seizure recurrence in younger children. Gulab Chaudhary et al found that recurrence was more common in children <12 months (66%) compared to children ≥12 months (34%).[4] Kumar et al also reported a higher recurrence rate in children <18 months (41.3%) compared to children ≥18 months (24.1%).[5] Agrawal et al identified age <1 year as a significant risk factor for febrile seizure recurrence.[6] It is important to note that the current study's age distribution refers to the occurrence of febrile seizures, while the compared studies focus on the risk of recurrence.

Gender

The current study found a higher proportion of male participants (65.2%) compared to female participants (34.8%), suggesting a possible gender-related variation in the occurrence of febrile seizures.

This finding is consistent with several of the compared studies. Chaudhary et al reported that 64% of children with recurrent febrile seizures were male.[4] Agrawal et al identified male gender as a significant risk factor for febrile seizure recurrence.[6] Karimi et al found no difference in febrile seizure prevalence between genders, but their study focused on the overall prevalence rather than recurrence risk.[7]

The higher proportion of male children in the current study and the consistent reports of male gender as a risk factor for febrile seizure recurrence in the compared studies suggest that gender may play a role in the susceptibility to febrile seizures and their recurrence.

Fever distribution and duration

The current study found that the majority of participants (72.2%) had a fever of less than 102.2°F, indicating that high fever may not be the sole determinant of seizure occurrence. Additionally, 82.6% of participants had a fever lasting less than 24 hours before the onset of seizures, suggesting that febrile seizures tend to occur relatively early in the febrile episode.

The compared studies have reported mixed findings regarding the relationship between fever characteristics and febrile seizure recurrence. Kumar et al found a significant declining trend of recurrence with increasing temperature, with a recurrence rate of 52.5% in children with a temperature of 101°F during the seizure and only 17.2% in children with a temperature ≥105°F.[5] Kazemi et

al identified seizures with low levels of fever as a significant risk factor for recurrence.[8] Canpolat et al reported a 17.8-fold increase in recurrence risk for children with a fever interval <1 hour before convulsion.[9]

The current study's findings suggest that lower fever grades and shorter fever durations are more common in children with febrile seizures, but these factors may not necessarily predict recurrence risk.

Type and duration of seizure

The current study found that simple febrile seizures were more common (78.3%) than complex febrile seizures (21.7%), and the majority of seizures (83.5%) lasted 5 minutes or less. These findings align with the typical characteristics of febrile seizures reported in the literature.

The compared studies have reported variable associations between seizure type, duration, and recurrence risk. Indirani et al identified complex febrile seizures as a significant risk factor for recurrence.[10] Habib et al emphasized that seizure duration was the most crucial prognostic factor for recurrence, but early treatment did not appear to reduce recurrence risk.[11]

The compared studies suggest that seizure type and duration may influence recurrence risk, but the specific relationships may vary across different populations and study designs.

Family history of febrile seizure and epilepsy

The current study found that 10.4% of participants had a positive family history of febrile seizures, while only 2.6% had a positive family history of epilepsy. This suggests that while a family history of febrile seizures may be a risk factor for occurrence, febrile seizures can still occur in the absence of a genetic predisposition.

Several of the compared studies have reported a significant association between family history of febrile seizures and recurrence risk. Chaudhary et al found that recurrence was significantly more common in children with a family history of epilepsy (68%) compared to those without a family history of epilepsy (32%).[4] Kumar et al reported a significantly higher recurrence rate in children with a family history of febrile seizures (45.5%) compared to those without a family history (27.8%).[5] Tosun et al identified a family history of febrile seizures as a significant risk factor for recurrence (OR=1.933, 95% CI=1.121-3.333).[12]

The compared studies consistently report a significant association between family history of febrile seizures and recurrence risk, highlighting the importance of considering genetic factors when assessing the risk of febrile seizure recurrence.

Hemoglobin and serum sodium levels

The current study found that 53.0% of participants had hemoglobin levels below 11 gm/dl, suggesting a possible association between lower hemoglobin levels and febrile seizures. Additionally, 42.6% of participants had serum sodium levels below 135 meq/l, indicating that electrolyte imbalances might contribute to febrile seizure susceptibility.

Several of the compared studies have investigated the relationship between iron deficiency anemia and febrile seizures. Jang et al found that children with febrile seizures had significantly lower levels of serum iron, plasma ferritin, and transferrin saturation compared to controls, and iron deficiency was more common in the febrile seizure group (49.2%) than in the control group (16.9%).[13]

Karimi et al found no statistically significant difference in iron deficiency anemia prevalence between children with febrile seizures, afebrile seizures, and fever without seizures.[14]

The current study's findings on hemoglobin levels suggest a possible association between anemia and febrile seizures, which is consistent with some of the compared studies reporting a higher prevalence of iron deficiency anemia in children with febrile seizures. The findings on serum sodium levels provide insight into the prevalence of hyponatremia in this population, but the compared studies did not specifically investigate the association between serum sodium levels and febrile seizure recurrence.

Total febrile seizure episodes in one year follow-up

The current study found that during the one-year follow-up, 69.6% of participants had only one episode of febrile seizure, while 20.9% had two episodes, 8.7% had three episodes, and 0.9% had four episodes. This suggests that the majority of children experienced a single febrile seizure episode, with recurrence observed in a smaller subset.

The compared studies have reported variable recurrence rates and follow-up periods. Kumar et al found that 32.9% of children experienced recurrence over a one-year follow-up period.[5] Agrawal et al reported that one-third of patients had experienced recurrence, with most recurrences occurring within one year of the first febrile seizure.[6] Kazemi et al observed a recurrence rate of 25.7% during a one-year follow-up.[15]

The recurrence rates reported in the compared studies are generally higher than the proportion of children with recurrent episodes in the current study, but the specific follow-up periods and study designs may contribute to these differences

Association of recurrent febrile seizure with various factors

The current study investigated the association of recurrent febrile seizures with several factors, including age, gender, fever, duration of fever, type of seizure, duration of seizure, family history of febrile seizure, hemoglobin levels, and serum sodium levels.

Age

The study found a statistically significant association between age and recurrent febrile seizures (p=0.008), with children aged ≤1 year having a higher risk of recurrence (48.5%) compared to children >1 year (23.2%). This finding is consistent with several of the compared studies, as discussed in the "age distribution" section.

Gender

The study found no statistically significant association between gender and recurrent febrile seizures (p=0.941), suggesting that gender does not influence febrile seizure recurrence in this population. This finding differs from some of the compared studies that identified male gender as a risk factor for recurrence, as discussed in the "gender distribution" section.

Fever and duration of fever

The study found no statistically significant associations between fever (p=0.191) or duration of fever (p=0.625) and recurrent febrile seizures. This finding differs from some of the compared studies that reported associations between fever characteristics and recurrence risk, as discussed in the "fever distribution and duration" section.

Type and duration of seizure

The study found no statistically significant association between seizure type and recurrent febrile seizures (p=0.241) but identified a statistically significant association between seizure duration and recurrence (p=0.0001), with prolonged seizures (>5 minutes) having a higher risk of recurrence (68.4%) compared to shorter seizures (22.9%). This finding is consistent with Habib et al, which emphasized seizure duration as the most crucial prognostic factor for recurrence.[16]

Family history of febrile seizure

The study found a statistically significant association between a positive family history of febrile seizures and recurrent febrile seizures (p=0.009), with a higher risk of recurrence in children with a positive family history (41.7%) compared to those without a family history (29.1%). This finding is consistent with several of the compared studies, as discussed in the "family history of febrile seizure and epilepsy" section.

Hemoglobin levels

The study found a statistically significant association between lower hemoglobin levels (<11 gm/dl) and recurrent febrile seizures (p=0.028), with a higher risk of recurrence in children with lower hemoglobin levels (39.3%) compared to those with normal hemoglobin levels (20.4%). This finding is consistent with some of the compared studies that reported associations between iron deficiency anemia and febrile seizures, as discussed in the "hemoglobin and serum sodium levels" section.

Serum sodium levels

The study found no statistically significant association between serum sodium levels and recurrent febrile seizures (p=0.392), suggesting that hyponatremia does not strongly predict recurrence risk in this population. The compared studies did not specifically investigate the association between serum sodium levels and febrile seizure recurrence.

The current study's findings on the associations between various factors and recurrent febrile seizures provide valuable insights into the potential risk factors for recurrence in this specific population. The significant associations identified for age, seizure duration, family history of febrile seizures, and hemoglobin levels are generally consistent with the findings of the compared studies, although some discrepancies were noted for gender, fever characteristics, and seizure type. These discrepancies may be due to differences in study populations, sample sizes, and methodologies, highlighting the need for further research to clarify the relationships between these factors and febrile seizure recurrence in different settings.

Limitations of our study include its single-center design, relatively small sample size, and reliance on parental reporting for follow-up. Nonetheless, the study adds valuable prospective data to the Indian context, where FS recurrence remains underexplored.

CONCLUSION

In this prospective cohort study, we identified younger age (≤1 year), prolonged seizure duration (>5 minutes), a positive family history of febrile seizures, and low hemoglobin (<11 gm/dl) as significant risk factors for recurrence within one year. These easily identifiable clinical features should prompt closer follow-up, anticipatory guidance to parents, and appropriate investigation. While most febrile seizures are benign, recognizing high-risk children can help prevent parental anxiety and ensure timely intervention.

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