Original Article

To Study The Risk Factors For Recurrence of Febrile Seizures in Children in Southern India.

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Abstract

Background: Febrile seizures (FS) are the most common neurological emergency which usually present in casualty and is of parental concern.

Objectives: To estimate the various risk factors associated with recurrence of febrile seizures in children between 6monthsto 5 years.

Methods: This is a descriptive retrospective study conducted in a tertiary care hospital setting on children with aged6monthsto5 years presenting with recurrence of both simple and complex febrile seizures admitted in Paediatric department done over a period from April-September 2022.

Result: Recurrence was more common in children <12 months (66%) as compared to children ⩾12 months (34%).Out of 50 children ,64% were male with recurrent febrile seizure. About 35 patients (70%) developed seizures within 24 hours of onset of fever. Among children with recurrent FS (50), 39(78%) children did not have family history of febrile seizure either in 1° or 2° relatives. Recurrence of febrile seizure was significantly more common in children with a family history of epilepsy (68%) as compared to those without a family history of epilepsy (32%). Out of 50 children with FS, 30 children (60%) had Hb < 11g/dl.

Conclusion: Onset of first febrile seizure less than 1 year, male gender, recurrence of seizures within 24 hours of onset of fever, family history of epilepsy and presence of anemia are the important risk factors for recurrence of febrile seizures. Our study emphasizes the importance of counseling the parents about the possibility of recurrence of febrile seizure with the presence of these factors.

Keywords: Anemia; Epilepsy; Febrile seizures; Recurrence.

INTRODUCTION

Febrile seizures are the most common neurologic disorder among infants and young children. They are an age-dependent condition, occurring in 2 to 5 percent of children younger than five years of age. Simple febrile seizures, defined as generalized seizures lasting less than 5 minutes and not recurring for 24-hour period.

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Usually they are benign condition but they can recur in one-third of children during their early childhood. Febrile seizures which are focal and lasting for more than 5 minutes and recurs within the first 24 hours or associated with post-ictal neurologic abnormalities, more frequently a post-ictal palsy (Todd's palsy), or with previous neurologic deficits are defined as complex febrile seizures1. Complex febrile seizures are a more heterogeneous cluster of phenomena, associated with a greater risk of recurrence during early childhood and an increased probability of a febrile seizures in the future.2

Incidence of febrile seizure is between 2 % and 5% amongst Caucasian children, 5 to10% in India and 8.8% in Japan 3, 4. About 3 to 4% of all children had at least one febrile seizure. The Peak of occurrence of febrile seizure is between 12-18 months of age. Recurrence rate ranges from 21 to 29.3% in the third world. In the west the recurrence rate was 30 to 50%. There were so many risk factors present for febrile seizure recurrence. There are environmental and genetic factors which influences the recurrence of febrile seizures. Age was also considered as the risk factor responsible for recurrence in earlier time but other factors are also been identified5.

History of febrile seizures in the family, history of epilepsy in the family, CFS during the first episode, and neurodevelopmental problems are considered as high risk for recurrence of febrile sizure6. After vaccination with diphtheria, measles, mumps, rubella vaccine (MMR) and tetanus toxoids and whole-cell pertussis vaccine there are report of increased risk for febrile seizures in the children7. Iron deficiency has also been associated with increased risk of febrile seizures. In the present study we try to investigate and identify the risk factors, associated with recurrence of febrile seizures including the effect of age, gender, temperature, past history of seizure, developmental and family history, duration, type and number of seizure on recurrence of febrile seizures which can be useful for counsel and better understanding by the care takers during future episodes.

Very few studies have been reported from India. Therefore, this study was conducted to assess the associated risk factors for recurrence of febrile seizures in Indian children.

MATERIAL & METHODS:

Study design and procedure: Descriptive retrospective study was done after obtaining approval from ethical committee where patients were recruited by consecutive, enumerative and non-probability convenient sampling period of 4 months (1st April 2022-31st July 2022). Seizure semiology details obtained were onset, duration, frequency, loss of consciousness, automatisms and treatment whether on monotherapy or polytherapy anti-epileptic drugs. Children underwent electroencephalogram and neuroimaging, lumbar puncture.

Study period: The study period extended from April 2022 to September 2022.

Study area: Department of Pediatrics, Saveetha medical college & hospital, Chennai.

Aims & Objectives: To estimate the various risk factors for recurrence of febrile seizures in children aged 6 months to 5 years admitted in a tertiary care hospital. To investigate and describe the distribution of the effect of age, gender, temperature, past history of seizure, developmental and family history, duration, type and number of seizure on recurrence of febrile seizures.

Study participants and sampling: Study participants were children aged 6 months to 5 years, with recurrence of both simple and complex febrile seizures admitted in Paediatric department were included. Total 50 children were enrolled.

Inclusion &exclusion criteria: Childrenaged6monthsto5 years presenting with recurrence of both simple and complex febrile seizures admitted in Paediatric department having core body temperature of 100.4°F or 38°C, were included in the study. Childrenwithseizuresuspectedtohavecentralnervoussystemin fection(meningitis,encephalitis)onfirstdayitselfandalsodiagn osedfollowinglumbar puncture(LP), children with seizure due to hyponatremia, hypernatremia, hypocalcaemia and hypomagnesaemia, children with atleast one episode of afebrile seizure, seizure following trauma, drug or toxin intake, seizure in children with CSOM, cerebral palsy, epilepsy, and those unwilling to participate in the study were excluded from the study.

Study instruments and measures:

Ethical aspects: The study design was approved by Institutional Review Board (IRB) and after obtaining approval from ethical committee where patients were recruited for the study.

Data analysis: The data collected from the selected subjects were recorded in master chart. The values analyzed with the help of SPSS version 23 to describe the effect of various risk factors for the recurrence of febrile seizure. To describe about the data, descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & S.D. were used for continuous variables, the probability value >0.05 is considered as significant level. Microsoft word & excel sheet were used to create tables, charts and graphs.

METHODOLOGY:

After getting informed written consent from the parents or care givers, childrenfrom6monthsto5 years of age having recurrence of simple or complex febrile seizure were admitted and investigated regarding various risk factors for recurrence of febrile seizure. Other etiologies causing fever with seizure were excluded by history, clinical examination and relevant investigations. Children with recurrent febrile seizures were reviewed with their old records. All children with recurrence of febrile seizure were followed up

fortnightly in specialty OPD during the study period. Missed children were followed up whenever they had come to OPD.

They were asked about general information like name, age, sex, address and about presenting complaints. Screening questions to verify that the child was having complaints of fever with seizure, then they were investigated regarding duration of fever prior to seizure, intensity of fever, type of seizure, duration of seizure, number of seizure, associated other symptoms, past history of febrile seizure, family history of febrile seizure and epilepsy and regarding developmental milestones. Children with past history of febrile seizure were asked about the age of onset of febrile seizure, total number of seizures episode. According to history, children who had seizure associated with

Fever following trauma or drug /toxin intake were excluded.

Clinical examination: Children were examined for other causes of fever associated with seizure mainly for features of increased intra cranial pressure and chronic serous otitis media. If any child had the above mentioned features, he/she was excluded from the study. The remaining children were subjected to the following investigations.

Children with elevated urea >40 mg / dl and Creatinine >1mg/dl, Random blood sugar less than54mg/dl, Serum calcium: < 9mg/dl, anemia if haemoglobin <11g/dl, serum sodium(Na+) level less than 135meq/L, with potassium (K+) either < 3.5meq/L or >5meq / L.. Brain imaging and EEG were done in selected children when there was suspicion of CNS infection or other seizure disorders or epilepsy syndromes. CSF analysis was done in the following situations and the report was abnormal, then the child was excluded from this study.

Patients presenting with meningeal signs or symptoms or other clinical features suggestive of a possible meningitis or intracranial infection LP was performed when there are and also LP was considered in infants between 6 and 12 months if the immunization status forH.InfluenzaetypeborStreptococcuspneumoniaisdeficientorcan‘tbedetermined and when the patient is on antibiotics since antibiotic therapy can mask the signs and symptoms of meningitis. After exclusion, the data was entered in the proforma. Then the children were categorized as following.

Categorization of Risk factors:

1. Age (< 12 months, ≥ 12 months)
2. Gender (male, female)
3. Duration of fever (< 24hrs, ≥ 24hrs)
4. Intensity of temperature (< 12.2° F, ≥ 102.2° F)
5. Type of febrile seizure (simple, complex)
6. Duration of seizure (< 5min, > 5 min)
7. Past history of febrile seizure (recurrence) (yes, no)
8. Number of recurrence (single, multiple)
9. Family history of febrile seizure (positive, negative)
10. Family history of epilepsy (positive, negative)
11. Developmental history (normal, delayed)
12. Hemoglobin (< 11g/dl, ≥ 11g/dl)
13. Serum Sodium (< 135meq, 135-145meq)

RESULTS:

A total of 50 children, between the aged of 6 months to 5 years with recurrence of febrile seizures (FS), were included in the study. Among 50 children with recurrent FS, 37 children (74%) had febrile seizure when they were <1 year old. But, other 13 (26%) developed their first febrile seizure after their first birth day. Most of the children with recurrent FS had experienced their initial febrile seizure prior to their first birth day. Hence age of onset of first febrile seizure is one of the most important risk factor for recurrent FS. Recurrence was more common in children <12 months (66%) as compared to children ≥12 months (34%).

Table 1: Association with age while developing recurrent febrile seizure

Age	Total number (n)	Percentage (%)
< 12 months	33	66%
>12 months	17	34%
Total	50	100%

Most of the children (64%) are male among 50 children with recurrent febrile seizure. Other 36% are female children. So, male children are more prone for developing recurrent febrile seizure. As seen in figure 1.

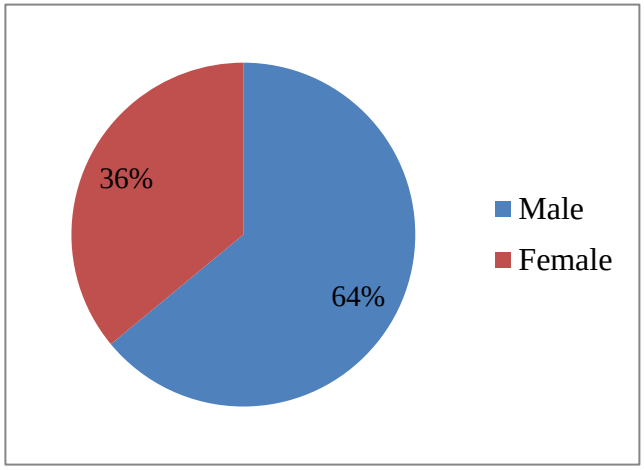

Fig 1: Sex distribution of recurrent febrile seizure.

Out of 50 patients with recurrent febrile seizures, 35 patients (70%) developed seizures within 24 hours of onset of fever. Rest of the 15 patients (30%) developed after 24 hours of onset of fever as seen in table no. 2. Hence, duration of fever less than 24 hours from the onset of fever has a strong association with the development of recurrent febrile seizure.

Table no 2: Association of fever duration with recurrent febrile seizures.

Duration of the fever	Total number (n)	Percentage (%)
<24 hours	35	70%
>24 hours	15	30%
Total	50	100%

Among children with recurrent FS (50), 39 children (78%) did not have family history of febrile seizure either in 1° or 2° relatives. 11 children (22%) had significant family history of FS in table no. 3. This shoed that family history of FS either in 1° or2° relatives does not affect the recurrence of febrile seizure.

Table no. 3: Association with family history of FS:

Family history of febrile seizures	Total number (n)	Percentage (%)
No	39	78%
Yes	11	22%
Total	50	100%

Among 50, 44 (88%) had experienced simple febrile seizure and others, 6(12%) had complex febrile seizure in table no. 4. Hence, simple febrile seizure is the most common type of febrile seizure in our study group.

Table no. 4: According to type of seizure:

Type of Febrile seizure	Frequency (n)	Percent (%)
Simple	30	60%
Complex	20	40%
Total	50	100%

Around 60% of the children with duration of seizure ≥5 min developed recurrence as compared to only 40% of the children with duration of seizure <5 min and this difference was not statistically significant (P = 0.072). Among children with temperature 101° F during the seizure, recurrence was seen in 52.5%, there was a significant declining trend with increase in temperature and recurrence was seen in only 17.2% in children with temperature ≥105° F (P = 0.001).

In recurrence of febrile seizure were significantly more common children with a family history of febrile seizures (48%) as compared to those without a family history of febrile seizures (22%) and also in children with a family history of epilepsy (68%) as compared to those without a family history of epilepsy (32%). Recurrence of febrile seizures was not associated with type of seizure, history of vaccination, and presence of iron deficiency.

According to WHO guidelines anemia is defined as hemoglobin level <11g/dl. Out of 50 children with FS, 30 children (60%) had Hb < 11g/dl. Other 20 children (40%) had Hb > 11g/dl. hence; anemia may be a risk factor for development of febrile seizure as seen in table no 5. But, this is not statistically significant (p=0.6).

Table no.5: Association with anemia:

Hb (g/dl)	Frequency (n)	Percent (%)
<11	30	60%
>11	20	40%
Total	50	100%

DISCUSSION:

The study conducted by Ausi Indirani et.al showed that 43% experienced a first FS at the age of <12 months, of which 72% were male, 46% had experienced fever within 24 hours before the onset of FS8. Another study by Yusra Fayyadh Alwan et.al concluded that 67% cases with recurrent FS were aged between 4 and 12 months9. This was consistent with our study where nearly 74% had experienced there first seizure in age less than 1 year.

In the present study, 32(64%) children with recurrence FS were males and 17(36%) were females, with male to female ratio (M:F) of 1.77:1. Similarly results were seen in study done Z.Habib et.al, where children presenting with recurrent FS, 57% were males and 43% were females showing that males are 1.3 time more prone for recurrent FS than females10. Another study by Yusra Fayyadh Alwan et.al concluded that 70.6% of male children had recurrent FS9. Similar results were seen in study done by Jyoti Agrawal et.al where 83% were males compared to 17% were females with recurrent FS have M:F ratio of 4.88:111. In the study of Ausi Indriani et,al, among children with recurrent FS, 72% were males and 28% were male to female ratio of 2.5:18. In contrast, the study done by Anil Raj Ojha et.al found that 54% of female children had experienced recurrent FS which was not statistical significance12. Hence, male gender is one of the most significant risk factor for recurrence of FS.

In our study, 70% of children with recurrence FS had seizure within 24 hours of fever and rest of them 30% after 24 hours. Similar results were obtained in the following study of Berg AT et.al where 67% of children had recurrent FS within 24 hours of fever and 13%, after 24 hours13. Similar results were seen in study done by Anil Raj Ojha et.al where 60% children had developed recurrent FS within 12 hours of fever12. Another study by Ausi Indriani et.al found that 46% of children with recurrence had seizure within 24 hours of fever and 31%, within 24 to 48 hours of fever in their study8. Another study done by Nadirah Rasyid Ridha et.al revealed that the children having FS within 12 hours of fever were 4.96 times more prone for developing recurrent FS14. Hence, duration of fever less than 24 hours is a significant risk factor for FS recurrence.

In our study, children presenting with recurrent FS, only 22% had positive family history (1° relative or 2° relative).

This finding was similar to the study done by Ausi Indriani et.al where they found that family history was positive in only 28% of patients with recurrent FS and negative in 57% of patients8. In meta-analysis conducted by Offringa et.al 43% children with recurrent FS had positive family history (1˚ relative) and 32%, without family history15. Berg et.al, found that 36% of children with positive family history had recurrence at one year and 20% in children without family history of febrile seizures16. In contrast study by Berg et.al showed that patients with positive family history (1˚ relative) were 1.62 times more prone for having recurrent FS. Hence, family history of febrile seizure does not affect the risk of recurrence of febrile seizure.

In our study 60% of the children with duration of seizure >5 min developed recurrence as compared to only 40% of the children with duration of seizure <5 min and this difference was not statistically significant (P = 0.072). Among children with temperature 101° F during the seizure, recurrence was seen in 52.5%, there was a significant declining trend with increase in temperature and recurrence was seen in only 17.2% in children with temperature ≥105° F (P = 0.001). A descriptive study depending upon the parameters like age, temperature, and recurrence of febrile seizure conducted by Margriet Van Stuijvenberg et.al, reported that 52% of recurrent FS occurred within two hours of onset of fever and they had low median temperature (102.7°F) while rest of them (48%) experienced recurrence of FS after 2 hours of onset of fever and temperature of 104°F. Finally, they concluded that younger age, high temperature at onset of fever and high temperature during the fever episode were the important risk factors for recurrence of FS18.

In the present study, shown that 60 % of children with FS had anemia (Hb < 11g/dl). Similar findings were seen in study done by Mashaer Abidlqader et.al found that 62.7 % children with febrile seizure had anemia19. But, it may not be a significant risk factor for recurrent febrile seizure as it was not statistically significant.

LIMITATIONS OF THE STUDY:

Major limitations of the present study are the small sample size and single hospital based study. We did not include the treatment history regarding the prophylaxis or any anti epileptic drugs the child is receiving. Large multi-centric and community based studies are needed to generalize the results in general population.

CONCLUSION:

Onset of first febrile seizure less than 1 year, male gender, recurrence of seizures within 24 hours of onset of fever, family history of epilepsy and presence of anemia are the important risk factors for recurrence of febrile seizures. So, we must follow up the children with these risk factors for recurrent febrile seizure and to educate the parents regarding the management of the febrile seizures at their home in an emergency situation. Awareness should be created about the chance of recurrent FS in the future in children having the above mentioned risk factors. Long term prophylaxis should prescribe cautiously because of benign nature of febrile seizure and adverse effects of antiepileptic drugs should be kept in mind if at all prescribing.

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