Original Article

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Paediatrics Section

Evaluation of Risk Factors Associated with First Episode Febrile Seizure

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ABSTRACT

Introduction: Febrile seizure (FS) is the single most common type of seizure seen in children between 6 months to 5 years of age. The purpose of our study was to identify the risk factors associated with the first episode of febrile seizures, which would help in the better management and preventive measures in children at risk for FS episodes.

Aim: To evaluate the risk factors associated with the first episode of febrile seizures in Indian children.

Materials and Methods: This was a hospital based, case control study. The purpose of this study was to identify the risk factors associated with the first FS episode in children. Seventy (70) children between age 6 months to 5 years with their first episode of FS were compared with 70 children with fever but without seizures based on various risk factors.

Results: The mean age was 24.90±16.11 months in cases and 26.34±16.93 months in controls. Male: female ratio was 2:1. A positive family history was found in 31.4% of first degree and 11.4% in second degree relatives. Mean maximum temperature was 102.06±1.1°F and URI (upper respiratory infection) was most common cause of fever. Antenatal complication was significantly higher in the case group. RBC (Red Blood Cells) indices like lower mean haemoglobin, MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Haemoglobin concentration) and higher RDW (Red Cell Distribution Width) values were seen in patients. Serum sodium, Serum calcium and random blood sugar values of the cases were significantly lower than those of controls ($p<0.05$).

Conclusion: Our study shows that male gender, family history of febrile seizures, peak body temperature, underlying cause of fever, antenatal complications, low serum calcium, sodium, blood sugar and microcytic hypochromic anaemia are the risk factors associated with the occurrence of first episode of febrile seizure and, thus, preventive measures in removing these risk factors could lead to a decrease in incidence of FS.

Keywords: Anaemia, Children, Family history, Upper respiratory infection

INTRODUCTION

Febrile seizures (FS) is one of the common convulsive events in children [1]. The 1993 International League against Epilepsy defined a FS as "an epileptic seizure occurring in childhood associated with fever, but without evidence of intracranial infection or defined cause" [2]. Seizures with fever in children who have experienced a previous non-febrile seizure are excluded [3]. They are age-dependent and are uncommon before 6 months and after 5 years of age. It is divided into two types: simple and complex [4].

Between 2 to 5% of neurologically healthy children experience at least 1 FS episode in their lifetime [5]. Although earlier Indian studies [6] suggested that up to 10% of children experience a FS, recent data indicate that the incidence rate in India is similar to western figures [7].

Pathophysiology of FS remains unclear [8]. It is suggested that FS is an age-dependent response of the immature brain to fever, as studies in animal models have suggested that during the brain maturation process, there is an enhanced neuronal excitability [8]. This postulation is supported by the fact that most (65 to 85%) FS occur between 6 months and 3 years of age, with the peak incidence at 18 months [9-11].

Despite its benign nature, the febrile convulsion is one of the most common reasons for admission to pediatric emergency worldwide. In most of the patients, fever is due to upper respiratory system and urinary tract infection (UTI) [11].

Regarding the high prevalence of FS in children and parent's apprehension due to seizure episode, efforts have to be made in identifying the influential risk factors so that parents can be counseled and advised to take necessary precaution at time of seizure episode.

AIM

To evaluate the risk factors associated with the first episode of febrile seizures in Indian Children.

MATERIALS AND METHODS

This was a hospital based, case-control study, conducted at the Department of Pediatric Medicine, Sir Padampat Mother and Child Health Institute (SPMCHI) attached to Sawai Man Singh (SMS) Medical College, Jaipur, from December 2010 to December 2012.

The study group included 70 cases with a 1st episode of FS and 70 controls. Children of 6 months to 60 months who were admitted in various wards with complaints of fever and 1st episode of seizure and having no evidence of central nervous system infection and no previous history of seizure or neurologic deficit in past were included in the study group. They were matched with their control groups (nearly of same age, admitted on date as close as possible) that consisted of patients presenting with fever as complaint but no history of seizure in present or past. However, we did not use sex and anthropometric parameters for matching as majority of our patients enrolled were males, but we did measure the anthropometry (head circumference, weight, length/height) of each of our patients and compared them with the reference values.

After obtaining basic information, detailed history and physical examination was done on each study subject. Informants of each patient were asked about the history of febrile seizure in family, history of epilepsy in family, history of consanguinity in parents and maximum temperature recorded during the illness. The antenatal, natal and perinatal history of the patient was reviewed for any

specific event during that period. Anthropometric measurement of head circumference, weight, and length/height were taken and compared to reference values. Blood sugar values of patients were measured at time of admission using strip method and blood samples sent to lab for complete blood counts, RBC (Red Blood Cell) indices, serum electrolytes and serum calcium to determine the cause of fever. Patients who had evidence of meningitis based on cerebrospinal fluid examination were excluded from the study. A written informed parental consent was obtained for each patient in this study.

STATISTICAL ANALYSIS

Data were analysed by using SPSS software and chi-square test. A p-value <0.05 was considered as significant. Ethical clearance was taken from the Review and Research Board, SMS Medical College, Jaipur, Rajasthan and the study was performed according to the Declaration of Helsinki for medical research involving human subjects. Data were analysed using SPSS software.

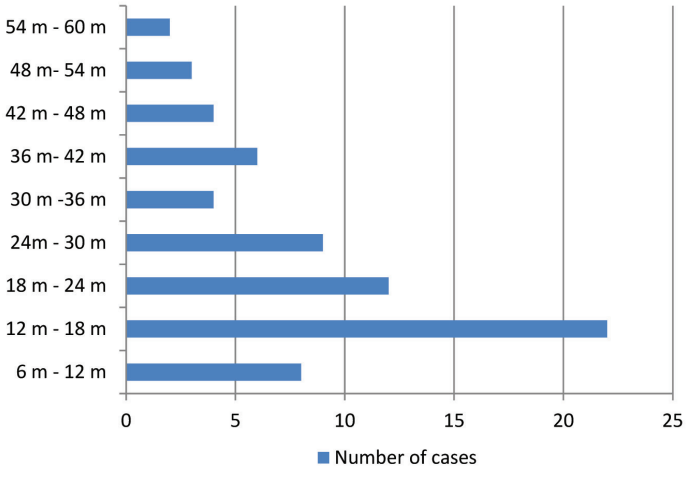
RESULTS

During the study period, a total of 140 patients between the age of 6 months and 60 months were enrolled. The study group included 70 cases and 70 controls. The mean age of the cases were 24.9±16.1 months and 26.3 ± 16.9 months in controls. Ninety-eight patients (70%) were boys and 42 patients (30%) were girls. We had subdivided our patient's age group at six month interval i.e. from age group 6 months to 12 months, 12 months to 18 months and so forth. The majority of FS were noted in the 6 to 24 months age group, which included 42 children (60%) [Table/Fig-1].

Whereas, the lowest incidence of FS belonged to the age group of 36-60 months, which comprised of only 14 children (20%). The male: female ratio was 2:1. Among the cases, 13 (18.57%) children had complex FS and 57 (81.43%) had simple FS.

A positive family history of FS in first degree relatives was found in 22 cases (31.4%; p-value<0.05) and in 8 cases (11.4%; p-value<0.003) in second degree relatives which was statistically significant as compared to controls. In contrast, there was no significant statistical difference noted when considering the positive family history of epilepsy in first (p-value 0.11) and second (p-value 0.30) degree relatives.

Upper Respiratory Infection (URI) was the most common cause of febrile illness in our study [Table/Fig-2]. The mean temperature (measured from axilla) in the case group during the FS attack was 102.06±1.1 ºF which was significantly higher compared to the control group which was 101.1±1.04 ºF (p-value <0.005). The majority of patients (64.2%) had an episode of FS early in the course of illness [Table/Fig-3].



[Table/Fig-1]: Distribution of febrile seizures incidence versus age groups.

Variables	Cases	Controls	p-value
Mean age	24.9 ± 16.1	26.3 ± 16.9	0.60
Sex Male Female	 48 22	 50 20	 0.71
Febrile seizure in 1st degree relatives Present Absent	 22 48	 2 68	 <0.05
Febrile seizure in 2nd degree relatives Present Absent	 8 62	 0 70	 0.003
Epilepsy in 1st degree relatives Present Absent	 8 62	 3 67	 0.11
Epilepsy in 2nd degree relatives Present Absent	 6 64	 3 67	 0.30
Etiology of fever URI UTI Others	 57 8 5	 1 1 68	 <0.001 <0.016
Mean maximum temperature	102.06 ± 1.1 ºF	101.13 ± 1.0 ºF	<0.005
Antenatal period complication Bleeding	 9	 2	 0.027
History of difficult labour	15	3	0.002

[Table/Fig-2]: Risk factors associated with first episode febrile seizures.

Duration	Number of cases
< 24 hours	45
24 – 72 hours	20
>72 hours	5

[Table/Fig-3]: Time interval between fever and seizure episode.

Parameters	Unit	Cases	controls	p-value
Red blood cell indices Mean haemoglobin Mean MCV Mean MCH Mean RDW	 g/dl fL pg/cell %	 7.3 ± 1.1 63.8 ± 10.2 25.0 ± 2.2 18.5 ± 1.5	 8.4 ± 1.5 75.2 ± 10.8 28.0 ± 2.3 16.7 ± 1.8	 <0.001
Serum Sodium Mean value	 meq/L	 138.2 ± 3.1	 142.7 ± 3.8	 <0.001
Serum total calcium Mean value	 mg/dl	 8.2 ± 0.6	 9.0 ± 0.6	 <0.001
Blood sugar Mean value	 mg/dl	 82.3 ± 30.0	 119.8 ± 30.8	 <0.001

[Table/Fig-4]: Baseline laboratory findings.

Antenatal period complications such as bleeding (12.8%, p-value 0.02), and history of difficult labour (21.4%, p-value 0.002) were seen in both groups but it was found to be statistically significant more often in the case group.

[Table/Fig-4] shows the abnormal laboratory findings in patients with febrile seizures in comparison to the control groups.

DISCUSSION

In the present study, age less than two years, male sex, positive family history of FS in first and second degree relatives, maximum mean temperature, upper respiratory and urinary tract infection as cause of fever, antenatal complications like bleeding, difficult labour, low mean haemoglobin and RBC indices (low MCV, MCH & high RDW) were found to be the risk factors for first episode of FS.

Most of the children with FS were male below 2 years of age in our study. Fetveit et al., showed that the peak incidence of FS was at 18 months of age, with male predominance [12]. As far as positive family history is concerned, 31.4% patients had a history of FS in 1st degree relatives and 11.4% in 2nd degree relatives. Abolfazl and colleagues showed that 55% of patients with FS had a positive

family history [13]. In another study, it was 10-45% [14]. A family history of epilepsy was found in 11.4% of the relatives and it is not considered as a risk factor in the present study. Hesdorffer et al., found younger age, lower temperature, longer duration (1-24 hours) of recognized temperature before FS, female sex, structural temporal lobe abnormalities, and first-degree family history of FS as risk factor for FS epilepticus [15]. Many studies include developmental delay, discharge from a neonatal unit after 28 days, day care attendance, viral infections, a family history of FS, certain vaccinations, and possibly iron and zinc deficiencies [16-18].

In our study, the mean maximum temperature was 102.06ºF in cases and 101.13ºF in controls, 64.28% of the patients had the seizure within 24 hours of fever onset. Millar JS and Anne T Berg also had similar findings that the height of temperature plays a role in eliciting a FS and that most of the episodes occurred in the initial part of illness [1,19]. In the study group URI was the most common cause of fever (81.4% cases), followed by UTI in 11.4% and other infections like otitis media, gastroenteritis (7% of a cases). Various studies reported similar findings with URI, gastroenteritis and UTI as most common cause of fever [20,21].

We found some antenatal complications like antepartum and intrapartum haemorrhage, and difficult labour as significant risk factors for the 1st episode of febrile seizure. These factors by contributing to lower iron store in mother and subsequently in child may contribute to FS. Iron deficiency is considered to be a risk factor for FS by some [22]. Ellatif reported that prematurity and difficult labour is the major risk factors [23]. In another series it was revealed that preterm and difficult labour and prenatal asphyxia to be considered the risk factors for 1st episode FS [23,24].

Our results indicate that S. sodium, S. calcium and random blood sugar values of the cases were significantly lower than controls. Thoman and colleagues found that lower mean serum sodium values were associated with first and subsequent episodes of FS [25]. In another study, Nickawar A et al., found that serum sodium values were significantly lower in cases but not significantly differ from the controls [26].

RBC indices in the present study showed statistically significant lower mean haemoglobin, MCV, MCH and higher RDW values in patients compared to controls. Similar results were observed by Yousefichaijan et al., who observed significant differences between the febrile convulsion group and the control group regarding blood indices such as Hb, Haematocrit, MCV, MCH, and MCHC as well [27]. In another study, Vaswani et al., observed that low serum ferritin level is a risk factor for first febrile seizure [28].

FS are the most common type of convulsive event in children. Although FS is usually a benign and self limited condition, it can cause a high level of anxiety and fear in parents. The exact cause of febrile seizure is unknown, however, there are several factors considered as risk factors as outlined in this study associated with incidence of the first FS.

LIMITATION

The main limitation of our study was lack off follow-up of our patients to assess for risk factors associated with recurrence of FS and long term outcome like incidence of development of epilepsy.

CONCLUSION

Based on our study, there is strong evidence that parameters such as gender, family history of febrile seizures, peak body temperature, underlying cause of fever, antenatal & natal complications, low serum calcium, sodium, blood sugar & microcytic hypochromic anaemia are the risk factors in occurrence of the first febrile seizure episode.

ABBREVIATIONS

FS	Febrile seizure
MCV	Mean corpuscular volume
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
RDW	Red cell distribution width
RBC	Red blood cell
SMS	Sawai man singh
URI	Upper respiratory infection
UTI	Urinary tract infection

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