



Evaluation of Risk Factors in First Episode of Febrile Convulsion

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OPEN ACCESS

Key Words

Febrile seizures, fever, temperature, risk, factor

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Received: 20 July 2024

Accepted: 31 August 2024

Published: 04 September 2024

Citation: G.M. Manoj, Nandini, S. Bheemaraya Shivasharana, B. Manjula and Shashikanth Hugar, 2024. Evaluation of Risk Factors in First Episode of Febrile Convulsion. Res. J. Med. Sci., 18: 40-44, doi: 10.36478/makrjms.2024.10.40.44

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ABSTRACT

The inaugural occurrence of febrile convulsion (FC) typically manifests in individuals ranging from 6 months to 5 years of age, frequently instigated by a sudden escalation in body temperature resulting from infections. The primary objective was to assess the determinants linked to the initial onset of febrile seizure amidst children within our study population. A cross-sectional examination was conducted, encompassing children displaying fever and convulsions aged between 6-60 months, meeting the specified criteria defining febrile convulsion in accordance with AAP guidelines and enrolled in the experimental group. Comprehensive demographic data, exhaustive medical history, thorough physical examination, along with essential investigations to pinpoint the underlying cause of fever, were meticulously carried out and documented. Statistical analysis was executed utilizing SPSS software. The research cohort comprised 47 children aged between 6-60 months. The data indicated a higher prevalence of febrile convulsions among male children compared to females, with the most common age bracket for the initial febrile convulsion episode being between 1-3 years. A substantial portion of cases exhibited simple febrile convulsions, with a few cases revealing notable obstetric history and incomplete immunization. Viral respiratory infections emerged as the primary cause of fever, with 46.8% of cases demonstrating malnourishment and a minor proportion displaying significant familial predisposition. Approximately 70% of cases were diagnosed with anemia and a few cases illustrating hyponatremia and hypocalcemia within the study population. The implementation of preventive measures targeting these risk elements could potentially lead to a reduction in the frequency of febrile seizures.

INTRODUCTION

Febrile seizures manifest between the age range of 6-60 months^[1], peaking at 12-18 months, accompanied by a body temperature of 38 °C (100.4°F) or higher^[2]. These seizures are not associated with central nervous system infections or metabolic disturbances and they occur in the absence of prior afebrile seizure history. Approximately 2%-5% of neurologically sound infants and children encounter at least one such episode of simple febrile seizure.

Although simple febrile seizures cause concern among parents, they do not pose an elevated risk of fatality. Conversely, complex febrile seizures may lead to a twofold increase in long-term mortality rates compared to the general population, likely due to an underlying pathology^[3]. Various risk factors for febrile seizures include developmental delays, discharge from neonatal units after 28 days, attendance in daycare facilities, viral infections, family history of febrile seizures, specific vaccinations and potential deficiencies in iron and zinc^[4].

Risk factors associated with the recurrence of febrile seizures encompass age below 1 year, fever duration less than 24 hours, body temperature ranging from 38-39 °C (100.4-102.2°F), family history of febrile seizures or epilepsy, experience of complex febrile seizures, daycare attendance, male gender and lower serum sodium levels at the time of presentation^[5]. However, extensive research is lacking on risk factors related to the initial episode of febrile convulsions, as well as insufficient studies correlating obstetric history, nutritional status and the occurrence of first and subsequent episodes of febrile convulsions.

It is generally advised against routine neuroimaging following simple febrile seizures, as it does not provide any additional diagnostic or prognostic benefits^[6]. Currently, there is a lack of published data supporting or refuting the necessity of CT or MRI scans in the assessment of children with simple febrile seizures^[7]. Some studies have indicated the development of mesial temporal sclerosis in children with febrile convulsions, particularly in cases of complex seizures and febrile status epilepticus^[8].

In view of all above reasons we would like to conduct an observational case control study on risk factors like age, sex, obstetric factors, developmental factors, nutritional status, family history, vaccination status, aetiology of fever, laboratory values at the time of admission between children with febrile convulsion and children with febrile illness with age, sex matched. And MRI brain studies of complex febrile seizures mainly on temporal lobe oedema for future possibility of temporal lobe epilepsy.

MATERIALS AND METHODS

This study, conducted in the Department of Pediatrics at our tertiary health care centre, was based on a

hospital setting and followed a cross-sectional design for duration of 6 months. Following the acquisition of ethical approval from the institutional ethics committee, cases were recruited for participation in the study upon provision of informed consent. Over the 6-month period, a total of 47 cases presenting with a first episode of seizure linked to fever and meeting the criteria for simple febrile seizures were included in the investigation. The selection criteria encompassed children falling within the age range of 6-60 months, as defined by the American Academy of Pediatrics (AAP), who were diagnosed with febrile convulsions and whose parents had consented to their inclusion^[1]. Conversely, children experiencing fever-induced convulsions that did not align with the AAP's definition of febrile convulsions and those whose parents did not grant consent were excluded from the study.

A comprehensive medical history and thorough physical examination were conducted on the pediatric patients with febrile seizures to ascertain the fever's etiology and rule out conditions such as meningitis or underlying neurological issues. The axillary temperature of the cases was recorded using an electronic digital thermometer and adjusted by 0.5 °C to establish the "corrected body temperature". Diagnostic tests including hemogram, CRP, serum sodium, serum calcium and random blood sugar levels were carried out to determine the cause of the fever. Risk factors associated with the initial occurrence of simple febrile seizures were evaluated through a questionnaire administered to the parents of the cases during individual interviews. Appropriate outpatient and inpatient treatments were administered and in relevant cases, an MRI brain scan was scheduled post-stabilization of the patient with due precautions prior to discharge, following AAP guidelines. The data collected was meticulously recorded in an Excel spreadsheet and subsequently analyzed using SPSS software.

RESULTS AND DISCUSSIONS

Our study investigation encompassed a cohort of 47 children ranging from 6-60 months old. Among the 47 cases, 27 (57.4%) were male and 20 (42.6%) were female. When categorized by age groups, there were 9 (19.1%) cases from 6 months to 1 year, 13 (27.7%) cases from 1-2 years, 10 (21.3%) cases from 2 years to 3 years, 7 (14.9%) cases from 3-4 years and 8 (17%) cases from 4-5 years (Table 1).

Table 1: Demographic Data of Febrile Convulsion Cases

Demographic data	N	%
Age group		
6 months to 1 year	9	19.1
1 year to 2 years	13	27.7
2 years to 3 years	10	21.3
3 years to 4 years	7	14.9
4 years to 5 years	8	17
Gender		
Male	27	57.4
Female	20	42.6

The nutritional background revealed severe acute malnutrition in 3 out of 47 cases, moderate acute malnutrition in 19 out of 47 cases and normal weight in the remaining 25 cases. Family history analysis indicated that 1 out of 47 cases had a family history of epilepsy, 1 case had a family history of febrile convulsions among siblings and the rest had a normal family history. Additionally, two cases had significant obstetric histories and one had an incomplete vaccination status (Table 2).

Table 2: Clinical and Family History of Febrile Convulsion Cases

Clinical status	N	%
Nutritional status		
Normal	25	53.2
Moderate Acute Malnutrition (MAM)	19	40.4
Severe Acute Malnutrition (SAM)	3	6.4
Family history		
No Family History	45	95.7
Epilepsy	1	2.1
Febrile seizures	1	2.1
Vaccination status		
Up to date	46	97.9
incomplete	1	2.1

In the current investigation, febrile symptoms were present in 31.9% of cases, while 68.1% exhibited afebrile characteristics. The average temperature recorded in the study was 101.03°F. Among the 47 cases of febrile convulsions, 29 were classified as simple febrile convulsions and 18 as complex febrile convulsions. Respiratory tract infections were identified as the primary cause of fever in the study group (61.7% of cases), followed by viral fevers (25.5%), urinary tract infections (8.5%) and gastrointestinal infections (4.3%) as depicted in (Table 3).

Table 3: Type and Etiology for Fever in Febrile Convulsion Cases

Type and Etiology	N	%
Temperature		
Afebrile	32	68.1
Febrile	15	31.9
Type of febrile seizure		
Simple febrile seizure	29	61.7
Complex febrile seizure	18	38.3
Etiology for fever		
Upper respiratory tract infection	28	59.6
Lower respiratory tract infections	1	2.1
Gastrointestinal tract	2	4.3
Urinary tract infections	4	8.5
Viral fever	12	25.5

In our study, the mean haemoglobin, total leukocyte count and platelets in the study group were measured at 10.8 ± 1.6g/dL, 12817±6367/μl and 3.076±1.2 lakh /μl, respectively. A significant portion of cases (70.2%) were diagnosed with microcytic hypochromic anemia, while 10.6% exhibited leukopenia and 40.4% showed leukocytosis. Thrombocytopenia was observed in only 6.4% of cases. The ratio of neutrophils to lymphocytes was calculated, indicating that 42.6% of cases had a ratio higher than 3, suggesting severe infection and inflammatory conditions. This finding was supported by elevated serum CRP levels in 34% of cases (Table-4). The mean serum levels of calcium, sodium, potassium,

chloride and glucose were determined to be 9.2±1.1mg/dl, 137.3±3.03 mEq/L, 7.12±19.6 meq/L, 103.03±15.3 meq/L, and 103 ± 15.3 mg/dL, respectively. Approximately 14.9% of cases presented with hyponatremia (<135 mg/dL) and hypocalcemia upon admission, accounting for 29.8% of cases (Table-4).

Table 4: Data on Laboratory Investigations

Lab parameters	N	%
C-reactive protein (CRP)		
Normal	31	66
High	16	34
Hemoglobin (Hb)		
Normal	14	29.8
Anemia	33	70.2
Leukocytes		
Normal	23	48.9
Leukopenia	5	10.6
Leukocytosis	19	40.4
Neutrophil		
Normal	11	23.4
Neutropenia	9	19.1
Neutrophilia	27	57.4
Lymphocyte		
Normal	9	19.1
Lymphopenia	22	46.8
Lymphocytosis	16	34
Neutrophil/lymphocyte ratio		
Normal	24	51.1
Less than 0.7	2	4.3
More than 3	20	42.6
Platelet		
Normal	44	93.6
Thrombocytopenia	3	6.4
Calcium		
Normal	33	70.2
Hypocalcemia	14	29.8
Sodium		
Normal	40	85.1
Hyponatremia	7	14.9

This cross sectional study done in the department of pediatrics identified few risk factors for 1st episode of febrile convulsion. As per study male children affected more than female, common age of incidence of 1st episode of febrile convulsion was 1-3 years age group, most cases were simple febrile convulsion. Significant obstetric history and incomplete immunization were identified in few cases of febrile convulsion. The most common cause of fever was viral respiratory infections, 46.8% cases were malnourished, few cases had significant family history. The reports similar to the Berg *et al.*, Al-Obeidi *et al.*, study, Leela Kumari *et al.*, Sharawat *et al* and Saleem *et al.*, whereas in the Pathan *et al* study they reported that the female cases were more in their study^[5-9-13].

The prevalence of nutritional status in the initial onset of febrile convulsion (FC) has been investigated in various studies, unveiling a significant correlation between malnutrition and the manifestation of FC. Saleem and Siddique noted that malnutrition, particularly deficiencies in micronutrients, could heighten the susceptibility to convulsions during febrile episodes^[14]. Singh *et al.* emphasized that the frequency of FC was notably higher in undernourished children, implying that interventions related to nutrition could potentially alleviate this risk^[15]. Nevertheless, Kumawat

et al. pointed out that despite the existence of an association, the precise mechanisms linking nutritional status and FC remain ambiguous, underscoring the necessity for further investigation to establish causality^[16]. Neyazuddin and Nistane stressed the significance of addressing nutritional inadequacies in pediatric healthcare to diminish the occurrence of FC^[17]. In general, these results underscore the pivotal role of nutritional status in the prevalence of febrile convulsions.

It can be inferred that the initial occurrence of febrile convulsion (FC) is impacted by various factors, such as age, gender, nutritional status, family medical history and vaccination status, all of which collectively contribute to the probability of experiencing a first episode of febrile convulsion, underscoring the importance of monitoring these variables in populations at risk.

The incidence and etiology of fever in the primary instance of febrile convulsion (FC) have been investigated in numerous studies. A common discovery is that viral infections, particularly respiratory infections, are the primary cause of fever leading to FC, constituting a substantial portion of cases. Furthermore, urinary tract infections were also identified but were less prevalent compared to respiratory infections, which aligns with our research^[18-20].

In our study, approximately 70% of cases exhibited anemia characterized by microcytic hypochromic features. We propose that anemia primarily resulted from iron deficiency. Similar findings were reported by Vaswani *et al* and Papageorgiou *et al.*, who identified iron deficiency as a risk factor for the initial febrile seizure^[11-21-22].

Nearly 10.6% of the individuals exhibited leukopenia, while 40.4% displayed leukocytosis. Thrombocytopenia was noted in a mere 6.4% of the cases. The ratio between neutrophils and lymphocytes was computed, revealing that 42.6% of the cases exhibited a ratio exceeding 3, indicating severe infection and inflammatory conditions in our investigation. Studies have indicated that children who experience febrile convulsions often manifest elevated white blood cell counts, particularly in terms of neutrophils, suggesting an inflammatory reaction. A study demonstrated that the Neutrophil-to-Lymphocyte Ratio (NLR) was significantly higher in patients with febrile convulsions in comparison to the control group, suggesting a possible involvement of neutrophils in the pathophysiology of these occurrences. Conversely, lymphocyte levels could be reduced in these patients, contributing to the altered NLR^[11-23-25]. Nevertheless, the discrepancies in results among various studies imply that although there is a tendency towards increased neutrophil levels and altered ratios, further investigation is necessary to elucidate these associations and their clinical significance. In general,

the data indicates a potential inflammatory aspect in the initial episodes of febrile convulsions, necessitating additional exploration.

A significant finding was that few cases had hyponatremia and hypocalcemia in our study. Studies indicate that hyponatremia, characterized by low sodium levels, can arise due to various factors, including excessive fluid intake or underlying infections, which are prevalent in febrile conditions. Additionally, hypocalcemia, or reduced calcium levels, may result from metabolic disruptions during febrile illnesses, potentially exacerbating seizure activity. Research has highlighted that both conditions could impact the severity and frequency of convulsions, underscoring the necessity for meticulous monitoring of electrolyte levels in pediatric patients presenting with febrile seizures^[11-26-27]. However, the precise mechanisms linking these electrolyte imbalances to febrile convulsions remain unclear, necessitating further research to establish causal relationships and clinical implications. Overall, comprehending these connections is vital for effective management and prevention strategies in affected children.

CONCLUSION

From our study we conclude that vigilance for febrile convulsions is warranted in children aged 6 months to 3 year presenting with fever, particularly those with a history of significant obstetric and antenatal factors, incomplete or lack of immunization, as well as malnutrition, clinical anemia and electrolyte imbalance.

Take Home Message:

- Needs larger prospective case control studies to prove above hypothesis.
- Need to define major and minor risk factor for 1st episode of febrile convulsion in similar way as there is defined major and minor risk factors for recurrence.
- Need to define meaning of low serum sodium and calcium cut off in febrile convulsion as risk factor, need studies on causes of hyponatremia and hypocalcemia in cases of febrile convulsion.

Acknowledgment: Authors acknowledge the doctors of the Department of Pediatrics and Multidisciplinary Research Unit (DHR New Delhi) and Administrators of Shimoga Institute of Medical Sciences, Shivamoga.

Conflicts of Interest: The authors declare no conflict of interest.

Funding: Nil.

Ethical Approval: Obtained from Institutional Ethics Committee, Shimoga Institute of Medical Sciences, Shivamoga. Ref. No: SIMS/IEC/622/2021-22.

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