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ORIGINAL ARTICLE

To investigate the relationship between febrile seizures and iron deficiency anaemia

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ABSTRACT:
Aim: To investigate the relationship between febrile seizures and iron deficiency anaemia. **Material and methods:** The study population consisted of 80 patients aged 6 to 60 months admitted in the Department of Pediatrics. 40 children with febrile seizures and 40 controls with febrile illness only were included in the study. The febrile seizure group (n = 40) included patients with seizure accompanied by fever ≥38 °C without central nervous system infection or metabolic disorders. The control group (n = 40) was selected randomly from among children admitted for febrile illnesses, such as gastroenteritis, otitis media, or respiratory tract infections, without seizure around the same time with the cases. The laboratory results regarding blood indices and iron status were analyzed using complete blood count (CBC), serum iron, plasma ferritin, total iron binding capacity (TIBC), and transferrin saturation, which were compared between the two groups. **Results:** During the study period, a total of 80 patients between the age of 6 months and 60 months were enrolled. The study group included 40 cases and 40 controls. The mean age of the cases were 26.77±6.25 months and 27.52±8.36 months in controls. The majority of FS were noted in the 6 to 24 months age group, which included near about 50% of the study subjects. Upper Respiratory Infection (URI) was the most common cause of febrile illness in our study. The mean temperature (measured from axilla) in the case group during the FS attack was 100.71 ± 1.63 °F which was significantly higher compared to the control group which was 98.32 ± 1.85. **Conclusion:** Febrile seizures are the most prevalent kind of convulsive episodes in youngsters. While FS often presents as a harmless and temporary disease, it may induce significant levels of worry and apprehension in parents. Our findings indicate that gender, peak body temperature, underlying cause of fever, and microcytic hypochromic anaemia are significant risk factors for the incidence of the first febrile seizure episode.
Keywords: Febrile Seizure, Iron Deficiency, Anemia

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INTRODUCTION

Febrile seizure is the predominant convulsive condition in children, affecting around 2% to 5% of children aged 3 to 60 months. The underlying mechanisms of FS are still not well understood [1]. FS, or febrile seizure, is believed to be a reaction of the developing brain to fever that occurs at different ages. Research conducted on animal models has shown that as the brain matures, there is an increase in neuronal excitability, which may contribute to the occurrence of FS[1]. This hypothesis is substantiated by the observation that the majority (65 to 85%) of febrile seizures occur in children between the ages of 6 months and 3 years, with the highest occurrence at 18 months[2-4]. Recent research have shown that iron shortage may increase the incidence of febrile seizures, since these seizures are more prevalent in children under the age of two, and iron deficiency anaemia is also frequent in children of the same age. Haemoglobin contains iron, which is essential for the transportation of oxygen to several organs, including the brain[5-9]. Iron deficiency impairs the metabolism of some neurotransmitters[10, 11]. The concept that iron deficiency may contribute to the occurrence of convulsions is supported by several lines of data. Nevertheless, the conducted investigations have shown contradictory findings. Several investigations have shown that individuals with iron deficiency have a considerably increased occurrence of febrile convulsions compared to the control group[12-15]. In contrast, several authors have shown that anaemic children have a lower probability of experiencing febrile seizures compared to children who have not had febrile seizures. Additionally, they have found that iron deficiency may serve as a preventive mechanism against convulsions by raising the threshold for experiencing them. Additional research has shown that iron deficiency does not have any influence on febrile seizures in children[16- 19]. As the connection between iron deficiency and febrile seizure has not been established, it is possible to consider chance or other unidentified variables as potential causes[20-22].

MATERIAL AND METHODS

The study population consisted of 80 patients aged 6 to 60 months admitted in the Department of Pediatrics. 40 children with febrile seizures and 40

controls with febrile illness only were included in the study. The parents of all patients provided written informed consent for inclusion in the study, which was approved by the Institutional Ethics Committee. The febrile seizure group (n = 40) included patients with seizure accompanied by fever ≥38 °C without central nervous system infection or metabolic disorders. The control group (n = 40) was selected randomly from among children admitted for febrile illnesses, such as gastroenteritis, otitis media, or respiratory tract infections, without seizure around the same time with the cases. Patients with chronic cardiovascular, renal, rheumatological or malignant diseases, and hemoglobinopathies, or other blood disorders were excluded from the study as they were more likely to have anemia. Patients with central nervous system diseases such as developmental delay, motor disabilities, and mental or cognitive defects were also excluded as they could have nutritional deficiency that may affect the results of the study. All of the febrile seizure patients and controls received appropriate diets for their ages without feeding problems. The febrile seizure and control groups were comparable in age, gender distribution, and clinical characteristics of febrile illness. Routine hematologic investigation was performed at the emergency department or 1st day of admission. The laboratory results regarding blood indices and iron status were analyzed using complete blood count (CBC), serum iron, plasma ferritin, total iron binding capacity (TIBC), and transferrin saturation, which were compared between the two groups. Anemia was defined as a hemoglobin (Hb) level of 2 standard deviations below the normal values for age, i.e., Hb < 10.5 g/dL for ages 6–24 months and < 11.5 g/dL for ages 2–5 years. Iron deficiency was defined as serum iron < 22 μg/dL, plasma ferritin < 30 ng/mL, or transferrin saturation < 16% [23, 24]. Children with a history of a febrile seizures, any antiepileptic drug medication, central nervous system infection, neurological deficit, or developmental delay were excluded from the study.

The collected data were analyzed using SPSS 25.0 statistical software. Descriptive statistics and Chi-square test was used for analysis of qualitative variables. Univariate analysis of all variables affecting febrile seizures were considered statistically significant with $P < 0.05$.

RESULTS

During the study period, a total of 80 patients between the age of 6 months and 60 months were enrolled. The study group included 40 cases and 40 controls. The mean age of the cases were 26.77±6.25 months and 27.52±8.36 months in controls. The majority of FS were noted in the 6 to 24 months age group, which included near about 50% of the study subjects. Upper Respiratory Infection (URI) was the most common cause of febrile illness in our study. The mean temperature (measured from axilla) in the case group during the FS attack was 100.71 ± 1.63 °F which was significantly higher compared to the control group which was 98.32 ± 1.85 (p-value =0.26) [Table 1].

Table 1: various parameters across the cases and the control group

	Case		Control		P value
Gender	**Number=40**	**Percentage**	**Number=40**	**Percentage**	**0.12**
Male	22	55	21	52.5	
Female	18	45	19	47.5	
Age in months					0.36
6-24	20	50	18	45	
24-48	15	37.5	17	42.5	
48-60	5	12.5	5	12.5	
Etiology of fever					0.17
URTI	30	75	3	7.5	
UTI	5	12.5	2	5	
Others	5	12.5	35	87.5	
Mean maximum temperature (deg F)	100.71 ± 1.63		98.32 ± 1.85		0.26

Table 2: Abnormal laboratory findings in patients with febrile seizures in comparison to the control groups

Parameters	Cases	Controls	P value
Red blood cell indices			
Hb (g/dl)	6.11±1.36	10.05±2.25	
MCV (fL)	60.25±4.33	79.96±5.58	
MCH (pg/cell)	22.65±2.96	30.36±3.39	0.02
RDW (%)	18.89±2.58	15.99±1.69	

DISCUSSION

In the present study, maximum mean temperature, upper respiratory and urinary tract infection as cause of fever, low mean hemoglobin 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[21]. 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[22]. 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[22-25]. In our study, the mean maximum temperature was 100.71°F in cases and 98.32°F in controls. 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[26]. In the study group URTI was the most common cause of fever, followed by UTI and other infections like otitis media, gastroenteritis. Various studies reported similar findings with URI, gastroenteritis and UTI as most common cause of fever[27, 28].Literature reports that 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[11]. Jensen FE reported that prematurity and difficult labour is the major risk factors[1]. Statistically significant lower mean hemoglobin, MCV, MCH and higher RDW values in patients compared to controls. Similar results were observed by Jones T et al.[6], 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. In another study, Vaswani et al., observed that low serum ferritin level is a risk factor for first febrile seizure[25].

CONCLUSION

Febrile seizures are the most prevalent kind of convulsive episodes in youngsters. While FS often presents as a harmless and temporary disease, it may induce significant levels of worry and apprehension in parents. Our findings indicate that gender, peak body temperature, underlying cause of fever, and microcytic hypochromic anaemia are significant risk factors for the incidence of the first febrile seizure episode.

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