

A Hospital-Based Study on Febrile Seizure and Iron Deficiency Anemia at A Tertiary Care Centre in Bihar

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Abstract

Introduction: Febrile seizure is the most common convulsive disorder in children which strikes 2% to 5% of children between 3 to 60 months of age. Some of the recent studies have reported that iron deficiency could be a risk factor for febrile seizure because the latter is more common in children under two years and iron deficiency anemia is also common in children of the same age. Here, we compared the iron status of children with febrile seizures and controls to investigate the association between iron status and febrile seizures in children admitted in Nalanda Medical College & Hospital, Patna, Bihar. **Methodology:** This prospective case control study was performed between October 2020 to September 2021. The study population consisted of 100 patients aged 6 to 60 months admitted in the Department of Pediatrics of Nalanda Medical College & Hospital, Patna, Bihar. 30 children with febrile seizures and 30 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. **Results:** The majority of FS were noted in the 6 to 24 months age group, which included more than 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 100.9 ± 2.1 °F which was significantly higher compared to the control group which was 98.2 ± 1.1 °F (p-value <0.05). **Conclusion:** Based on our study, there is strong evidence that parameters such as gender, peak body temperature, underlying cause of fever, & microcytic hypochromic anemia are the risk factors in occurrence of the first febrile seizure episode.

Keywords: Febrile Seizure, Iron Deficiency, Anemia.

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Introduction

Febrile seizure is the most common convulsive disorder in children which strikes 2% to 5% of children between 3 to 60 months of age. Pathophysiology of FS remains unclear [1]. 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[1]. 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[2-4].

Some of the recent studies have reported that iron deficiency could be a risk factor for febrile seizure because the latter is more common in children under two years and iron deficiency anemia is also common in children of the same age. Due to the presence of iron in the hemoglobin structure, it plays a crucial role in the transport of oxygen to different tissues such as the brain[5-9]. Iron deficiency reduces the metabolism of some neurotransmitters[10, 11]. Several lines of evidence led to the hypothesis that iron deficiency can have a role in the onset of a convulsion. However, the studies carried out so far have reported conflicting results. Some studies have reported that in the patients with iron deficiency, febrile convulsion is significantly higher than that in the control group[12-15]. On the contrary, some authors have concluded that the risk of febrile seizure in anemic children seems to be less than that in children with no febrile seizure[16] and that iron deficiency can be a protective mechanism against

convulsions by increasing the convulsion threshold[17]. Other studies have shown that iron deficiency plays no role in pediatric febrile seizures[18, 19]. Since the relationship between iron deficiency and febrile seizure is not yet determined, chance or other unknown factors can be considered as causes[20].

Here, we compared the iron status of children with febrile seizures and controls to investigate the association between iron status and febrile seizures in children admitted in Nalanda Medical College & Hospital, Patna, Bihar.

Methodology

This prospective case control study was performed between October 2020 to September 2021. The study population consisted of 100 patients aged 6 to 60 months admitted in the Department of Pediatrics of Nalanda Medical College & Hospital, Patna, Bihar. 30 children with febrile seizures and 30 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 = 30) included patients with seizure accompanied by fever ≥ 38 °C without central nervous system infection or metabolic disorders. The control group (n = 30) 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

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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 21.0 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 60 patients between the age of 6 months and 60 months were enrolled. The study group included 30 cases and 30 controls. The mean age of the cases were 25.2 ± 13.4 months and 26.5 ± 15.8 months in controls. The majority of FS were noted in the 6 to 24 months age group, which included more than 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 100.9 ± 2.1 °F which was significantly higher compared to the control group which was 98.2 ± 1.1 °F (p -value < 0.05) [Table 1].

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

Parameters	Cases	Control	P value
Mean age (months)	25.2 ± 13.4	26.5 ± 15.8	>0.05
Gender (Male)	18	21	>0.05
Etiology of fever			
URTI	22	2	<0.05
UTI	4	1	<0.05
Others	4	27	
Mean maximum temperature (deg F)	100.9 ± 2.1	98.2 ± 1.1	<0.05

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

Parameters	Cases	Controls	P value
Red blood cell indices			<0.05
Mean Hb (g/dl)	5.9 ± 1.2	9.9 ± 2.4	
Mean MCV (fL)	59.8 ± 8.1	80.2 ± 8.2	
Mean MCH (pg/cell)	21.9 ± 2.7	29.2 ± 2.3	
Mean RDW (%)	17.9 ± 2.1	16.2 ± 1.8	

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 100.9 °F in cases and 98.2 °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[29]. Ellatif reported that prematurity and difficult labour is the major risk factors[30]. Statistically significant lower mean hemoglobin, MCV, MCH and higher RDW values in patients compared to controls. Similar results were observed by Yousefichaijan et al.[31], 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

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. Based on our study, there is strong evidence that parameters such as gender, peak body temperature, underlying cause of fever, & microcytic hypochromic anemia are the risk factors in occurrence of the first febrile seizure episode.

References

- Jensen FE, Sanchez RM. Febrile seizures. San Diego: Academic Press; 2002. Why does the developing brain demonstrate heightened susceptibility to febrile and other provoked seizures? In: Baram TZ, Shinnar S, editors; pp. 153–68.
- Verity CM, Butler NR, Golding J. Febrile convulsions in a national cohort followed up from birth. I-Prevalence and recurrence in the first five years of life. Br Med J (Clin Res Ed) 1985; 290:1307–10.
- Forsgren L, Sidenvall R, Blomquist HK, Heijbel J. A prospective incidence study of febrile convulsions. Acta Paediatr Scand. 1990; 79:550–57.
- Hauser WA. The prevalence and incidence of convulsive disorders in children. Epilepsia. 1994; 35:1–6.
- Østergaard J. R. Febrile Seizures. Acta Paediatr. 2009 ;98(5):771–3.
- Jones T, Jacobsen S. J. Childhood Febrile Seizures: Overview and Implications. Int J Med Sci. 2007;4(2):110–4.
- Kheirkhah D, Sharif M. R. The rate of iron-deficiency anemia in febrile children with and without seizure in Kashan, 2012. Abstract Book of Ninth Annual Congress of Iranian Pediatric Infectious Diseases Society, December 4-6, Tehran Iran. 2013:154–155.

8. Kliegman R. M. Nelson Textbook of Pediatrics. 19th ed. W. B. Saunders Co; 2011.
9. Pisacane A, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A. Iron Deficiency Anemia and Febrile Convulsions: Case-control Study in Children under 2 Years. *BMJ*. 1996;313(7053):343.
10. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M. Long-lasting Neural and Behavioral Effects of Iron Deficiency in Infancy. *Nutr Rev*. 2006; 64:34–43.
11. Parks Y. A, Wharton B. A. Iron Deficiency and the Brain. *Acta Paediatr Scand*. 1989;(Suppl 361):71–77.
12. Ur-Rehman N, Billoo A. G. Association between Iron Deficiency Anemia and Febrile Seizures. *J Coll Physicians Surg Pak*. 2005;15(6):338–40.
13. Daoud A. S, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron Status: A Possible Risk Factor for the First Febrile Seizure. *Epilepsia*. 2002;43(7):740–743.
14. Hartfield D. S, Tan J, Yager J. Y, Rosychuk R. J, Spady D, Haines C, Craig W. R. The Association between Iron Deficiency and Febrile Seizures in Childhood. *Clin Pediatr (Phila)* 2009;48(4):420–6.
15. Momen A, Nikfar R, Karimi B. Evaluation of Iron Status in 9-month to 5-year-old Children with Febrile Seizures: A Case-control Study in the South West of Iran. *Iran J Child Neurology*. 2010;4(2):45–50.
16. Talebian A, Momtazmanesh N. Febrile Seizures and Anemia. *Iran J Child Neurology*. 2007:31–33.
17. Kobrinsky N. L, Yager J. Y, Cheang M. S, Yatscoff R. W. Tenenbein M. Does Iron Deficiency Raise the Seizure Threshold? *J Child Neurol*. 1995;10(2):105–9.
18. Salehi Omran M. R, Tamaddoni A, Nasehi M. M, Babazadeh H, Alizadeh Navaei R. Iron Status in Febrile Seizure: A Case-control Study. *Iran J Child Neurology*. 2009:40–43.
19. Amirjalali S, Ahmadi M, Sabouri A, Kavemanesh Z, Afshar P. Relationship between Iron Deficiency Anemia and Febrile Seizures. *Iran J Child Neurology*. 2010;14(1):27–30.
20. Bidabadi E, Mashouf M. Association between Iron Deficiency Anemia and First Febrile Convulsion: A Case-control Study. *Seizure*. 2009;18:347–351.
21. Fetveit A. Assessment of febrile seizures in children. *Eur J Pediatr*. 2008;167(1):17–27.
22. Hesdorffer DC, Shinnar S, Lewis DV, Nordli DR, Pellock JM, Moshé SL, et al. Risk factors for febrile status epilepticus: a case-control study. *The Journal of pediatrics*. 2013;163(4):1147–51.
23. Ganesh R, Janakiraman L. Serum zinc levels in children with simple febrile seizure. *ClinPediatr (Phila)* 2008;47(2):164–66.
24. Laina I, Syriopoulou VP, Daikos GL, et al. Febrile seizures and primary human herpesvirus 6 infection. *Pediatr Neurol*. 2010;42(1):28–31.
25. Vaswani RK, Dharaskar PG, Kulkarni S, Ghosh K. Iron deficiency as a risk factor for first febrile seizure. *Indian Pediatr*. 2010;47(5):437–39.
26. Berg AT. Are Febrile Seizures Provoked by a Rapid Rise in Temperature? *Am J Dis Child*. 1993;147(10):1101–03.
27. Aicardi J. *The International Review of Child Neurology*. (2 ed) 1994.
28. Hauser WA. The prevalence and incidence of convulsive disorders in children. *Epilepsia*. 1994;35(2):1–6.
29. King D, King A. Question 2: Should children who have a febrile seizure be screened for iron deficiency? *Archives of disease in childhood*. 2019;99(10):960–64.
30. Ellatiff A, Garawamy H. Risk factors of febrile disease among preschool children in Alexandria. *Journal of the Egyptian Public Health Association*. 2020;77(1-2):156–72.
31. Youseffichaijan P, Eghbali A, Rafeie M, Sharafkhan M, Zolfi M, Firouzifar M. The relationship between iron deficiency anaemia and simple febrile convulsion in children. *J Pediatr Neurosci*. 2021;9(2):110–14.

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