

**A Study to Assess the Relationship between Iron Deficiency Anaemia and Febrile Convulsion in Children: An Analytical Study**Sunil Kumar Singh<sup>1</sup>, Anil Kumar<sup>2</sup><sup>1</sup>Senior Resident, Department of Pediatrics, GMCH, Bettiah, Bihar, India<sup>2</sup>Professor and HOD, Department of Pediatrics, GMCH, Bettiah, Bihar, India

Received: 08-09-2023 / Revised: 12-10-2023 / Accepted: 21-12-2023

Corresponding Author: Dr. Sunil Kumar Singh

Conflict of interest: Nil

**Abstract****Aim:** The aim of the present study was to assess the relationship between iron deficiency anaemia and febrile convulsion in children hospitalized at the tertiary care centre.**Methods:** This prospective, case-control study was conducted in department of Paediatrics, Study duration was of 8 months. After applying inclusion and exclusion criteria, total of 100 children were included in present study with 50 cases in each group.**Results:** Maximum children belonged to the age group of 6 months to 1 year in both the groups, followed by age group of 1-2 year in both the groups. Children above 3 years in both groups were 8% in cases. Iron deficiency anaemia was more prevalent in cases (56%) as compared to controls (28%). Iron deficiency was diagnosed by hematological investigations of Hb less than 11 g/dl, HCT less than 33%, MCV less than 74 fl, MCH less than 24 pg, MCHC less than 32%, SI less than 50 µg/dl, SF less than 12 µg/dl, TIBC more than 400 µg/dl, and transferring saturation less than 15%10. We compared various hematological indices among cases and controls. We also find significant p value for MCV and MCHC among cases and controls.**Conclusion:** The present study concluded that that iron deficiency anemia is strongly correlated with febrile convulsion probably through increasing the threshold of convulsion in patients with iron deficiency. Iron deficiency anaemia is easily correctable and preventable, most common micronutrient deficiency. Early detection and prompt correction may help in reducing febrile seizures incidence in children below 5 years of age.**Keywords:** Anemia, Febrile Seizures, Iron.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

**Introduction**

Febrile seizures are the commonest cause of seizures in children, occurring in 2-5% of children. [1] Complications like aspiration can occur during each episode of seizures. [2-5] Febrile seizure episodes are agonizing to the parent and child and can cause psychological trauma to both. [6] Iron deficiency is the commonest micronutrient deficiency worldwide, and is a preventable and treatable condition. Iron is needed for brain energy metabolism, for metabolism of neurotransmitters and for myelination. Thus, iron deficiency may alter the seizure threshold of a child. [8,9] Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition. [10,11]

By definition, Febrile Seizures (FS) are the seizures that occur between the ages of six months to 60 months with a temperature of 38°C (100.4°F) or higher, that is not the result of Central Nervous System (CNS) infection or any metabolic

imbalance, and that occurs in the absence of a history of prior afebrile seizure. [12] Iron deficiency has non haematological systemic effects. Both iron deficiency and IDA are associated with impaired neurocognitive function in infancy and also increased risk of seizures, strokes, breath-holding spells in children and exacerbation of restless leg syndrome. [13] Many of the nervous system enzymes are iron-dependent because of their activities. Iron deficiency inhibits the metabolism of certain neurotransmitters including monoamine and aldehyde oxidase. [14,15] And thus, it may alter the seizure threshold of a child. [13]

It has been determined that, iron depletion has a negative effect on neurocognitive function and supplementing iron reduces breath-holding spells, on the other hand, fever can exaggerate the negative effect of anaemia on the brain. Considering the above features, IDA as a risk factor for FS is probable. [16] Iron is an important

nutrient that acts as a cofactor for several enzymes in the body, as well as playing roles in the production and function of neurotransmitters, hormones, and DNA (deoxyribonucleic acid) duplication. Iron is also essential for enzymes involved in neurochemical reactions, such as myelin formation, metabolism of some neurotransmitters, and brain energy metabolism. [17] Studies conducted on the role of iron deficiency in febrile convulsion have yielded completely conflicting results. In some of these studies, iron deficiency has been identified as a risk factor [18], while in others it has been stated that iron deficiency increases the threshold of neuron excitation and thus can play a protective role against febrile convulsion. [19]

The aim of the present study was to assess the relationship between iron deficiency anaemia and febrile convulsion in children hospitalized at the tertiary care centre.

### Materials and Methods

This prospective, case-control study was conducted in Department of Paediatrics, GMCH, Bettiah, Bihar, India. Study duration was of 8 months. After applying inclusion and exclusion criteria, total of 100 children were included in present study with 50 cases in each group.

#### The children aged 6 months to 5 years were categorized into two groups:

1. The case group: It included 30 children with first attack of FS.
2. The control group: It included 30 febrile children but without seizures at the same age.

#### Exclusion criteria:

Children with atypical FS, afebrile seizures, any signs of CNS infection, any chronic neurodevelopment problems, previous diagnosis of other hematological problems, bleeding or

coagulation disorders, hematological malignancy, on iron supplementation, and any serious illness. A written informed consent was taken from parents, prior to participation in present study. After admission, all children were thoroughly examined to exclude children with a previous history of epilepsy, developmental delay, neurological deficit, and CNS infection. Demographic details, clinical details such as body temperature upon admission, cause of fever, duration between initiation of fever and convulsion, family history of febrile convulsion, and details of the seizure history including duration, frequency, and type of seizure (simple or complex) were recorded for all children. Diagnostic criteria for simple FS included seizures associated with fever and the seizures were generalized, short duration (<15 min), no recurrence of seizures within 24 h, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizures. Blood investigations carried out to diagnose iron deficiency included hemoglobin (Hb) level, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), serum ferritin level (SF), serum iron level (SI), total iron-binding capacity (TIBC), and transferrin saturation of children. Other explanatory variables such as urine routine, stool routine and chest x- ray which can be the potential confounders were also included in the study and considered for analysis. Data were entered and analysed using SPSS software. Nominal data were expressed as frequency and percentage. Numerical data were expressed as mean, SD and were compared using Student's t-test. P values of less than 0.05% were considered significant, and P values of less than 0.01% were considered highly significant.

### Results

**Table 1: Age distribution among case and control**

Age in years	Febrile Seizures (Cases)	Febrile Illness without seizures (Controls)
6 months to 1 year	21 (42%)	20 (40%)
1 to 2 years	17 (34%)	22 (44%)
2 to 3 years	6 (12%)	6 (12%)
3 to 4 years	4 (8%)	0
4 to 5 years	2 (4%)	2 (4%)
<b>Total</b>	<b>50</b>	<b>50</b>

Maximum children belonged to the age group of 6 months to 1 year in both the groups, followed by age group of 1-2 year in both the groups. Children above 3 years in both groups were 8% in cases.

**Table 2: Prevalence of iron deficiency anaemia**

Groups	Febrile Seizures (Cases)	Febrile Illness without seizures (Controls)
Iron deficiency anaemia	28 (56%)	14 (28%)
No iron deficiency anaemia	22 (44%)	36 (72%)

Iron deficiency anaemia was more prevalent in cases (56%) as compared to controls (28%).

**Table 3: Incidence of Iron deficiency anemia in cases and controls**

Parameters	Cases	Controls	P Value
Hb (<11 g/dl)	28 (56%)	13 (26%)	0.007
HCT (< 33%)	8 (16%)	7 (14%)	0.68
SF (< 12 µg/dl)	26 (52%)	18 (36%)	0.02
MCV (< 74 fl)	18 (36%)	12 (24%)	0.18
MCHC (<32 %)	8 (16%)	5 (10%)	0.36
PS MCHC	23 (46%)	12 (24%)	0.017

Iron deficiency was diagnosed by hematological investigations of Hb less than 11 g/dl, HCT less than 33%, MCV less than 74 fl, MCH less than 24 pg, MCHC less than 32%, SI less than 50 µg/dl, SF less than 12 µg/dl, TIBC more than 400 µg/dl, and transferring saturation less than 15%10. We compared various hematological indices among cases and controls. We also find significant p value for MCV and MCHC among cases and controls.

### Discussion

Febrile convulsion (FC) is the most common disorder in the nervous system of children and 2-5% children affected every year. Febrile convulsion is defined as convulsion resulting from fever. It occurs in children of 6 months to 6 (full six) years of age, is accompanied by fever higher than 38°C, and does not involve symptoms of central nervous system infections or any other background causes. [20] Studies identified various risk factors for febrile seizures, including developmental delay, discharge from a neonatal unit after 28 days, day-care attendance, viral infections, family history of febrile seizures, certain vaccinations, and nutritional deficiencies, including iron and zinc, mothers who smoke or consume alcoholic beverages. [21,22]

Maximum children belonged to the age group of 6 months to 1 year in both the groups, followed by age group of 1-2 year in both the groups. Children above 3 years in both groups were 8% in cases. Iron deficiency anaemia was more prevalent in cases (56%) as compared to controls (28%). Age for peak incidence of febrile seizure is 14 to 18 months, which overlaps with that of iron deficiency anaemia which is from 6 to 24 months.<sup>22</sup> Considering the age prevalence of iron deficiency anaemia and febrile convulsion which are the same, the role of iron in the metabolism of neurotransmitter (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehydoxidase), the function of hemoglobin in conveying oxygen to the brain and since fever can exacerbate symptoms that result from anaemia, a relationship between iron deficiency anaemia and febrile convulsions is probable. [23,24]

Kumari et al [25] performed a study on 308 children aged 6 months to 3 years old and found 63.6% of the case group suffered from iron deficiency in comparison with 24.7% of the control

group. They concluded that iron deficiency was an important risk factor in simple febrile convulsion. In a study by Vaswani et al [26] had 68% of the cases were iron deficient compared with 30% of the controls. Iron deficiency was diagnosed by hematological investigations of Hb less than 11 g/dl, HCT less than 33%, MCV less than 74 fl, MCH less than 24 pg, MCHC less than 32%, SI less than 50 µg/dl, SF less than 12 µg/dl, TIBC more than 400 µg/dl, and transferring saturation less than 15%10. We compared various hematological indices among cases and controls. We also find significant p value for MCV and MCHC among cases and controls. S. ferritin being an acute phase reactant, low levels in the setting of fever makes it a more reliable indicator. Although RDW is an indicator of iron status our study did not have significant difference in RDW in cases and controls. Derakhshanfar et al<sup>27</sup> found that the level of iron deficiency and iron deficiency anemia in the control group were significantly higher than those in the case group, and concluded that the risk of febrile convulsion in children suffering from iron deficiency was less than the risk in other children.

### Conclusion

The present study concluded that that iron deficiency anemia is strongly correlated with febrile convulsion probably through increasing the threshold of convulsion in patients with iron deficiency. Iron deficiency anaemia is easily correctable and preventable, most common micronutrient deficiency. Early detection and prompt correction may help in reducing febrile seizures incidence in children below 5 years of age.

### References

1. Johnston MV. Seizures in childhood. In: Kleigman RM, Behrman RE, Jenson HB, Stanton BP. Nelson Text Book of Pediatrics 18th Edition Philadelphia: Saunders Elsevier; 2007. p.2457-8.
2. American Academy of Pediatrics. Febrile seizures. Pediatrics. 2008; 121:1281-6.
3. American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. Pediatrics. 2004;114:874-7.

4. American Academy of Pediatrics. Committee on Quality improvement, Subcommittee on Febrile Seizures. The long-term management of a child with simple febrile seizures. *Pediatrics*. 1999; 103:1307-9.
5. Lynnet GS, Ingrid ES. Febrile seizures. *BMJ*. 2007; 334:307-11.
6. Waruiru C, Appleton R. Febrile seizures: an update. *Archives of Disease in childhood*. 2004 Aug 1;89(8):751-6.
7. World Health Organization. Iron Deficiency Anemia. Assessment, Prevention and Control. A Guide for Program Managers.
8. Beard J. Iron deficiency alters brain development and functioning. *The Journal of nutrition*. 2003 May 1;133(5):1468S-72S.
9. Batra J, Seth PK. Effect of iron deficiency on developing rat brain. *Indian Journal of Clinical Biochemistry*. 2002 Jul; 17:108-14.
10. Wike WM, Kiser WR. Iron deficiency anaemia and febrile convulsions. Possible confounding factors include lead toxicity.... *BMJ: British Medical Journal*. 1996 Nov 11;313(7066):1205.
11. Prasad AN, Seshia SS. Susceptibility to febrile seizures: more than just a faulty thermostat. *Canadian Journal of Neurological Sciences*. 2009 May;36(3):277-9.
12. NELSON Test Book of Paediatrics 21st edition chapter 611.1 page 3091.
13. Beard JL. Iron deficiency alters brain development and functioning. *J Nutr*. 2003; 133:1468-72.
14. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T, et al. Longlasting neural and behavioral effects of iron deficiency in infancy. *Nutr Rev*. 2006;64(5 Pt 2):34-43.
15. Parks YA, Wharton BA. Iron deficiency and the brain. *Acta Paediatr Scand*. 1989; 361:71-77.
16. Ansun N, Shashi S. Susceptibility of febrile seizures: More than just faulty thermostats. *Canadian J Neurol Sci*. 2009; 36:277-79.
17. Rouault TA, Cooperman S. Brain iron metabolism. In *Seminars in pediatric neurology*. WB Saunders. Sep 1, 2006;13(3):142-148.
18. Leela Kumari P, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures-a case control study. *Indian pediatrics*. 2012 Jan; 49:17-9.
19. Talebian A, Momtazmanesh N, Mosavi SG, Khojasteh MR. Relationship between febrile seizure and anemia.
20. Johnston MV. Seizures in childhood. In: Kleigman RM, Behrman RE, Jenson HB, Stanton BP, editors. *Nelson Text Book of Pediatrics*. 18th ed. Philadelphia: Saunders Elsevier; 2007. p. 2013-2019.
21. Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. *American family physician*. 2012 Jan 15;85(2):149-53.
22. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: Clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics* 2008;121:1281-6.
23. Harris RJ. Iron deficiency anaemia: does it really matter? *Paediatr Child Health* 2007; 17(4):143.
24. Weatherall DJ, Clegg JB. *The thalassaemia syndromes*. 4th ed. London: Blackwell Science; 2001;192:231.
25. Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures: A case control study. *Indian Pediatr* 2012; 49:17-9.
26. Vaswani RK, Dharaskar PG, Kulkarni S, Ghosh K. Iron deficiency as a risk factor for first febrile seizure. *Indian pediatrics*. 2010 May;47:437-9.
27. Derakhshanfar H, Abaskhanian A, Alimohammadi H, ModanlooKordi M. Association between iron deficiency anemia and febrile seizure in children. *Med Glas (Zenica)*. 2012 Mar 9;9(2):239-42.