

Association between Iron Deficiency Anemia and Febrile Convulsions in Paediatric Patients: A Prospective Case Control Study

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Abstract

Background: Febrile seizure is among the most common convulsion disorders in children, in the first five years of life.

- It affects about 2% to 5% of all children between 6 to 60 months of age; coinciding with the peak age of incidence of Iron deficiency anemia.
- Some of the recent studies have reported that iron deficiency could be a risk factor for febrile seizure because febrile seizure 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.
- Iron deficiency reduces the metabolism of some neurotransmitters.

Aims & Objectives: This study aims to determine the association between iron status and febrile seizures in children aged 6 months to 60 months of age.

Material & Methods: In this prospective case-control study, we evaluated 50 children aged 6 to 60 months in two 25 persons group.

• Cases consisted of 25 children with diagnosis of febrile seizures and controls group consisted of 25 children with febrile illness without convulsions, who were admitted at the Paediatric Intensive Care Unit and Paediatric wards at Shadan Institute of Medical Sciences, Hyderabad from November 2020 to April 2022.

• Both groups were reviewed to determine the iron status using Hemoglobin concentration, Mean corpuscular volume, Mean corpuscular hemoglobin, serum ferritin, serum iron, TIBC and serum transferrin to make the diagnosis of Iron deficiency anemia.

Results: The 2 groups were compared and no significant difference was found with regards to age, gender and disease causing the febrile illness.

- Iron deficiency anemia was found in 48% (12 children) of the cases and 20% (5 children) of the controls group.
- This indicates a statistically significant association between iron deficiency anemia and febrile seizures.

Conclusion: Iron deficiency anemia is more frequent among children with febrile seizures than with febrile illness alone.

Introduction

Febrile seizures (FS) are seizures that occur in children between the ages of 6 months and 60 months, with body temperature of 38°C or higher not resulting from Central Nervous System (CNS) infection or any metabolic imbalance without any prior afebrile seizures. This condition occurs in 2-5% of the children who are neurologically healthy. A simple febrile seizure is a primary generalized, usually tonic-clonic attack associated with fever, not recurrent within a 24-hour period and lasting for a maximum of 15 min. A complex febrile seizure is more prolonged (>15 min), is focal, and /or reoccurs within 24 hour. Another condition which has longer duration of more 30 minutes of seizure attack is called status Epilepticus. The precise cause of febrile seizure is not known, but several genetic and environmental factors have been implicated. The maximum age of febrile seizure occurrence is 14-18 months, which overlaps with the maximum prevalence of Iron Deficiency Anaemia (IDA). IDA is the most common nutritional deficiency in the world. Iron is an important micronutrient which is used by roughly all the cells in the human body. Iron is used as cofactor for metabolism of many neurotransmitters, monoamine and aldehyde oxidase in the brain. The metabolism of these neurotransmitters will be affected in the patient with iron deficiency leading to decrease in these neurotransmitters, which may decrease the threshold for seizure. Fever can worsen the negative effects of low serum ferritin on the brain and trigger seizure. Different factors have been considered for febrile seizures, including familial (genetic) factors, prenatal factors, present acute illness, the highest degree of fever and finally anemia. Iron deficiency anemia (IDA), as the most common type of anemia during infancy and childhood, occurs usually between 9-24 months of age and this period coincides with the peak incidence of

FS. It has been determined that iron depletion has negative effect on neurocognitive functions of children and supplemental iron can reduce breath holding spells. On the other hand, fever can exaggerate the negative effect of anemia on brain. Considering the age of prevalence of IDA and FS 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 aldehydase), a relationship between IDA and FS is probable.

Objective

With respect to the high prevalence of febrile seizures and IDA in children and considering the fact that IDA is a probable risk factor for febrile seizure occurrence, this study was conducted to determine the association between iron deficiency anemia and febrile seizure. As iron deficiency anemia is preventable and treatable, it will help in the prevention and management of febrile seizures.

Methods:

In this prospective case-control study, we evaluated 50 children aged 6 to 60 months in two 25 persons group. Cases consisted of 25 children with diagnosis of febrile seizures and controls group consisted of 25 children with febrile illness without convulsions, who were admitted at the Paediatric Intensive Care Unit and Paediatric wards at Shadan Institute of Medical Sciences, Hyderabad from November 2020 to April 2022. Both groups were reviewed to determine the iron status using Hemoglobin concentration, Mean corpuscular volume, Mean corpuscular hemoglobin, serum ferritin, serum iron, TIBC and serum transferrin to make the diagnosis of Iron deficiency anemia. Iron deficiency was defined as per the WHO criteria as hemoglobin less than 11 g/dl, mean corpuscular volume (MCV) less than 72 fl, mean corpuscular hemoglobin (MCH) less

than 25 pg, mean corpuscular hemoglobin concentration (MCHC) less than 30 g/dl, total iron-binding capacity more than 210 µg/dl, transferrin saturation less than 15%, red cell distribution width (RDW) of more than 15%, and serum ferritin less than 30 µg/l.

Results:

- The 2 groups were compared and no significant difference was found with regards to age, gender and disease causing the febrile illness.
- Iron deficiency anemia was found in 48% (12 children) of the cases and 20% (5 children) of the controls group.
- This indicates a statistically significant association between iron deficiency anemia and febrile seizures.

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data. Odds ratio was estimated to determine the strength of association between Iron deficiency anemia and Febrile convulsions.

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Table 1: Association between Iron deficiency Anemia and Febrile Convulsions

		Cases		Controls	
		Count	%	Count	%
Iron deficiency Anemia	Present	12	48%	5	20%
	Absent	13	52%	20	80%
Total		25		25	

$\chi^2 = 4.367$, $df = 1$, $p = 0.036^*$

Odds Ratio = 3.692 [95% CI 1.052 to 12.96]

In the study among cases, 48% had Iron deficiency Anemia and among controls, 20% had iron deficiency Anemia. There was significant association between Iron deficiency Anemia and Febrile convulsions.

Odds ratio was 3.692 i.e. Subjects with Iron deficiency Anemia had 3.692 times higher risk for Febrile convulsions compared to Subjects without Iron deficiency Anemia.

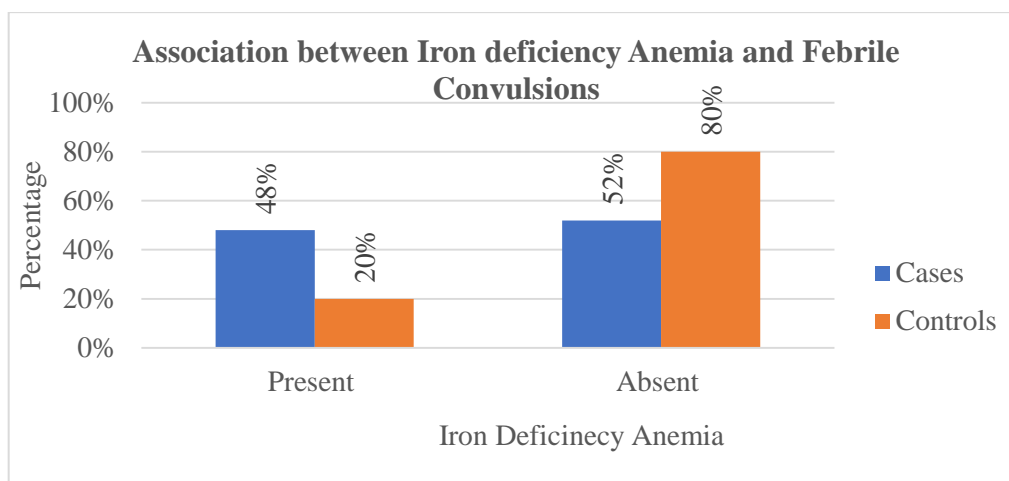


Figure 1: Bar diagram showing Association between Iron deficiency Anemia and Febrile Convulsions

Discussion:

The mean age of onset in present study is 18 months which is comparable to the other studies. Alfredo Piscane et al found the mean age for FS was 15 months. Separate studies done by Vasvani RK et al, Waruiru C et al and Azhar S Daoud et al also found that FS peaks at 18 months. Naveed-ur-Rehmann et al found mean age was 22.97 ± 9.52 months. Ellenberg et al found the average convulsion age to be 23.3 months. Amir Salari et al found average age of 39 ± 15.92 months. There was a preponderance of male in present study for the febrile seizure group. Regardless of the era of the study or particulars of the design; boys have consistently emerged with higher frequency of febrile seizures. Incidence ratios of boys: girls have ranged from 1.1:1 to 2:1. The shorter the duration of recognized fever, the higher the chances of recurrence. For those with FS within an hour of onset, the recurrence risk at 1 yr was 46%, compared with 39% for those with prior fever lasting 1 to 24 hrs and 15% for those with more than 24 hrs of recognized fever before the FS. In present study, being a urban hospital, no significant difference is noted in incidence among children of low socioeconomic and high socioeconomic status. Upper respiratory tract infection is the commonest trigger of febrile seizure in present group of children and no statistical difference could be made out with the control group, as per different etiology.

This is in keeping with Nelson and Ellenberg (1978), Millichap et al (2006) and Kyong KL et al. Chevrie and Aicardi et al (1975) reported URTI in 72% of the cases and Azhar S Daoud et al from Jordan, reported URTI as the commonest triggering factor, diagnosed in 53% of cases, which is comparable to present study. However the etiology of febrile convulsion varies from country to country due to different infection profile.

Conclusion:

- Iron deficiency anemia is more frequent among children with febrile seizures than with febrile illness alone.

- Findings suggest that low hemoglobin concentration and low serum ferritin maybe risk factors for development of febrile seizures; hence screening for iron deficiency anemia should be considered in children presenting with febrile seizures.

So clinicians need to be vigilant about iron deficiency anemia while providing care to children with febrile seizure

Recommendations:

We recommend evaluation for iron status of every child who present with simple febrile seizures and treat it, if iron deficiency is diagnosed such that the incidence of simple febrile seizures can be decreased.

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