

The association between iron profile studies and febrile seizures in age group 6 months - 5 years

Prajakta Joshi¹, Asmita Singh¹, Preeti Jain²

ABSTRACT

Abstract: Children with febrile seizures often demonstrate lower hemoglobin levels, reduced serum ferritin, and altered iron indices compared with febrile children without seizures. These findings suggest that iron deficiency may act as a modifiable risk factor by lowering seizure threshold during febrile illnesses. Hence, this study was undertaken to assess the association between iron profile and febrile seizures in children aged 6 months to 5 years. This was a cross-sectional observational study carried at department of Paediatrics. Total 200 study participants were enrolled in this study with mean age was 27.57 ± 16.25 months. Most of the study participants who developed febrile seizures belonged to the 25–60 months. About 120 (60%) were males and 80 (40%) were females. Family history of febrile seizure was present in 38 (19%) and about 28 (14%) had recurrence of seizure during same illness. About 152 (76%) were found to be iron deficient, while only 48 (24%) had normal iron status. Moderate anemia was the most common hematological finding seen in 74 (37%) study participants followed by mild anemia in 52 (26%). There was statistically highly significant association between serum Iron level and Serum ferritin level with the occurrence of febrile seizure ($p < 0.01$). There was no association found between MCV, TIBC, Transferrin saturation and duration of seizure during febrile seizure episode. Based on the findings of this study, it can be concluded that iron deficiency anemia is significantly associated with febrile seizures in children aged 6 months to 5 years.

Key-words: Febrile seizure, Iron deficiency anaemia, Serum ferritin, Serum iron

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2.*Corresponding Author: Preeti Jain – MBBS MD Pathology, HOD and Senior Consultant and DNB Teacher, Grade 1, Department of Pathology, BDBA Hospital, Kandivali (W), Mumbai 400067, Ph. 8779065509, hodpathologybdba@gmail.com; 1. Prajakta Joshi – MBBS MD Paediatrics, Senior Consultant and DNB Teacher, Grade 1, Department of Paediatrics, BDBA Hospital, Kandivali (W), Mumbai 400067, Ph. 9768331224, docpraj@gmail.com; 3. Asmita Singh – MBBS, Junior Resident Paediatrics, Department of Paediatrics, BDBA Hospital, Kandivali (W), Mumbai 400067, Ph. 8108422627, asmitasingh1802@gmail.com

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INTRODUCTION

Febrile seizures are the most common seizure disorder occurring during childhood and constitute one of the most frequent neurological emergencies encountered in pediatric practice. Febrile seizures defined as seizures associated with fever, usually with a body temperature of 38°C or above, occurring in children between 6 months and 5 years of age in the absence of central nervous system infection, acute metabolic disturbances, or prior afebrile seizures. Although febrile seizures are generally benign and self-limiting, their sudden onset often produces significant fear and emotional stress among parents and caregivers, frequently resulting in emergency medical consultations and hospitalization.^{1,2,3} Febrile seizures are broadly classified into simple febrile seizures and complex febrile seizures based on clinical presentation and duration. Simple febrile seizures are generalized tonic-clonic in nature, last for less than 15 minutes, and occur only once within a 24-hour period during a febrile illness. In contrast, complex febrile seizures are characterized by one or more of the following features: focal onset or focal neurological manifestations, seizure duration exceeding 15 minutes, or recurrence within 24 hours during the same febrile episode.¹

Globally, febrile seizures affect approximately 2–5% of children, making them a major pediatric health concern. Higher prevalence has been reported in Asian countries, ranging from approximately 5–10%, suggesting the influence of genetic susceptibility, environmental factors, infectious disease patterns, and healthcare-related variables. Family history of febrile seizures or epilepsy is considered an important predisposing factor.² In India, precise national prevalence data regarding febrile seizures are limited; however, due to large pediatric population and high infectious disease burden in India, febrile seizures remain an important public health concern.³

Recurrence is an important clinical aspect of febrile seizures. Approximately 30–35% of children experience recurrence after their first

febrile seizure episode. Although the majority of children recover completely without long-term neurological sequelae, recurrent febrile seizures may cause repeated hospital visits and significant psychosocial stress to families.⁴

Anemia was defined as Hb <11 g/dl. Iron deficiency anemia (IDA) is the most common nutritional deficiency worldwide and remains a major public health problem, particularly in infants and young children. It is characterized by reduced hemoglobin synthesis due to inadequate iron availability, resulting in diminished oxygen-carrying capacity of blood. According to WHO classification: Mild anemia corresponds to a hemoglobin level of 10.0–10.9 g/dl, Moderate anemia corresponds to hemoglobin level 7.0–9.9 g/dl and Severe anemia correspond to hemoglobin level less than 7.0 g/dl. Children between 6 months and 5 years of age are especially vulnerable because of rapid growth, increased iron requirements, inadequate dietary intake, recurrent infections, and poor nutritional practices. Since this age group overlaps with the peak age of febrile seizure occurrence, iron deficiency anemia has emerged as a clinically important factor requiring further evaluation.⁵

India carries one of the highest burdens of childhood anemia globally. According to the National Family Health Survey (NFHS-4), 58.6% of children aged 6–59 months in India are anemic, highlighting the widespread nature of this nutritional deficiency. The coexistence of high anemia prevalence and frequent febrile illnesses in Indian children creates an important clinical scenario in which iron deficiency may significantly influence seizure susceptibility.⁶

Iron also plays a vital role in neurotransmitter metabolism and neuronal signaling. It is required for the synthesis and proper functioning of neurotransmitters such as dopamine, serotonin, norepinephrine, and gamma-aminobutyric acid (GABA), all of which are essential for maintaining normal neuronal excitability. Deficiency of iron may impair neurotransmitter synthesis, alter synaptic transmission, and disturb the balance between

excitatory and inhibitory pathways in the brain. Additionally, iron deficiency may reduce cerebral oxygen delivery and impair energy metabolism, thereby increasing neuronal irritability and lowering seizure threshold. These mechanisms provide biological plausibility for the association between iron deficiency and seizure susceptibility in children.

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Over the past decade, increasing attention has been directed toward understanding the relationship between iron deficiency anemia and febrile seizures. Several observational studies and recent systematic reviews have suggested that children with febrile seizures often demonstrate lower hemoglobin levels, reduced serum ferritin, and altered iron indices compared with febrile children without seizures. These findings suggest that iron deficiency may act as a modifiable risk factor by lowering seizure threshold during febrile illnesses. However, some studies have reported conflicting results, indicating that the association remains incompletely understood and may vary across different populations.⁸

In addition to the presence of iron deficiency, the severity of iron deficiency anemia may also influence seizure susceptibility. Evaluating not only the presence but also the severity of iron deficiency is therefore important in understanding its relationship with febrile seizures. This may help identify high-risk children who may benefit from early screening and timely intervention.^{8,9}

Since iron deficiency is preventable and treatable, early detection and correction may help reduce seizure susceptibility and improve clinical outcomes. Hence, this study was undertaken to assess the association between iron profile studies and febrile seizures in children aged 6 months to 5 years attending a tertiary care hospital.

Methodology: This was a cross-sectional observational study carried at department of paediatrics, tertiary care hospital, Bharat Ratna Dr. Babasaheb Ambedkar municipal general hospital, Kandivali (w), Mumbai from Dec 2024 to Aug 2025. Approval from the institutional

ethics committee was obtained. The sample size was calculated using a single proportion formula: $n = \frac{\left[Z \frac{\alpha}{2} \right] p(1-p)}{d^2}$, at 95% confidence level. In the study conducted by Nigade RM et al, the proportion of children with febrile seizures and iron deficiency anemia was found to be 85.88%.¹⁰ This value was taken for sample size calculation. Adding 10% to adjust for non-response and dropouts, the final sample size was 200 study subjects. All pediatric patients aged 6 months to 5 years presenting with simple febrile seizures associated with fever were enrolled in this study by convenient sampling. Written informed consent was obtained from the parents or relatives after explaining the procedure in their vernacular language. Patients with a history of chronic illnesses, polycythemia, afebrile seizures, known cases of epilepsy, those having any signs of central nervous system infection, hematologic disorder, breath holding spells or with any neurodevelopmental problem (e.g. Cerebral palsy, prematurity, hemiplegia, neurodegenerative disorder) were excluded. After obtaining informed written consent from parents, data was collected using a structured and pre-tested questionnaire. A detailed history was taken, followed by clinical and physical examination. After stabilization, venous blood samples were collected under aseptic precautions and sent to the pathology department for hematological investigations. To diagnose iron deficiency, the following investigations were performed: Hemoglobin Estimation (Hb), MCV (Mean Corpuscular Volume), Serum Iron (Sr. Iron), Total Iron Binding Capacity (TIBC) and serum Ferritin. The reference range was for MCV ≥ 75 fL, Serum Iron 50–120 $\mu\text{g/DL}$, TIBC 250–400 $\mu\text{g/dL}$, Ferritin 12–200 ng/mL and Transferrin Saturation 20–50%. According to WHO classification: Mild anemia corresponds to a hemoglobin level of 10.0–10.9 g/dl, Moderate anemia corresponds to hemoglobin level 7.0–9.9 g/dl and Severe anemia correspond to hemoglobin level less than 7.0 g/dl.

Data were entered in MS excel. Data were analyzed using statistical package for the social

sciences (SPSS software, version 21). Results were expressed as frequency and percentage, and mean $\pm$ standard deviation (sd) or median values, as appropriate. Cross-tabulation and chi-square test were used to assess the relationship and association between various variables. All results were considered statistically significant if $p < 0.05$.

Results: Total 200 study participants were enrolled in this study with mean age was 27.57 ± 16.25 months. Most of the study participants

who developed febrile seizures belonged to the 25–60 months. About 120 (60%) were males and 80 (40%) were females. Family history of febrile seizure was present in 38 (19%) and about 28 (14%) had recurrence of seizure during same illness. About 152 (76%) were found to be iron deficient, while only 48 (24%) had normal iron status. Moderate anemia was the most common hematological finding seen in 74 (37%) study participants followed by mild anemia in 52 (26%). (Table 1)

Table 1: Distribution of study participants according to Clinico-social parameter

Clinico-social parameter		Frequency	Percentage
Age group	6 – 12	40	20
	13 – 24	70	35
	25 – 60	90	45
Gender	Male	120	60
	Female	80	40
Family History of Febrile Seizure	Present	38	19
	Absent	162	81
Recurrence during same illness	Yes	28	14
	No	172	86
Iron Status	Iron Deficient	152	76
	Normal Iron Status	48	24
Hemoglobin Level (g/dL)	Normal (≥ 11)	48	24
	Mild Anemia (10-10.9)	52	26
	Moderate Anemia (7-9.9)	74	37
	Severe Anemia (< 7)	26	13

Table 2 shows, there was statistically highly significant association between serum Iron level and Serum ferritin level with the occurrence of febrile seizure ($p < 0.01$). There was no

association found between MCV, TIBC, Transferrin saturation and duration of seizure with occurrence of febrile seizure.

Table 2: Association between different haemological parameter in iron deficiency and febrile seizure

Patients with Febrile Seizure		Normal Iron Status (n=48)	Iron Deficient (n=152)	p Value
MCV	< 75 fL (microcytosis)	31 (64.58%)	0 (0%)	0.01
	≥ 75 fL (normal)	17 (35.42%)	152 (100%)	
Serum Iron (< 50 μ g/dL)	< 50 μ g/dL	30 (62.50%)	104 (68.42%)	0.01
	50–120 μ g/dL	18 (37.50%)	48 (31.58%)	
TIBC (> 400 μ g/dL)	250–400 μ g/dL	12 (25%)	26 (17.11%)	0.22
	> 400 μ g/dL	36 (75%)	126 (82.89%)	
Ferritin	< 12 ng/mL	30 (62.50%)	104 (68.42%)	0.006

	12–200 ng/mL	18 (37.50%)	48 (31.58%)	
Transferrin Saturation	20–50%	11(22.92%)	21 (13.82%)	0.1338
	<20%	37 (77.08%)	131 (86.18%)	
Duration of seizure	<10 minutes	38 (79.17%)	116 (76.32%)	0.6824
	≥10 minutes	10 (20.83%)	36 (23.68%)	

DISCUSSION

Febrile seizure (FS) is the most common seizure disorder in childhood, occurring in 2–5% of children under five years worldwide and up to 10% in some Asian regions. In our study, the majority of children were in the 25–60 months age group, followed by the 13–24 months age group. Age is one of the most important epidemiological determinants of febrile seizures. Febrile seizures are predominantly seen in children between 6 months and 5 years because this period represents a critical phase of brain maturation. The immature brain is more vulnerable to hyperthermia-induced neuronal discharge due to incomplete maturation of inhibitory pathways and enhanced excitatory neurotransmission. Papageorgiou V et al. (2015) ¹¹ reported that febrile seizures occurred most commonly between 2 and 5 years of age, closely matching the findings of this study. Some studies have reported slightly earlier age peaks. Freedman DA et al. (2020) ¹² noted a relatively higher frequency in children below 24 months. Such variation may be attributed to differences in nutritional status, genetic predisposition, environmental exposures and healthcare accessibility across populations.

Out of 200 children, 120 (60%) were males and 80 (40%) were females in present study. Gender differences in febrile seizure occurrence have been observed in multiple studies, with most reporting a slight male predominance. Although the exact mechanism remains unclear, several biological and environmental factors may contribute to this distribution. Sharif MR et al. (2015) ¹³ and Krishnan R et al. (2018) ¹⁴ similarly observed a higher proportion of males compared to females. The higher prevalence in males may be related to genetic susceptibility, sex-related hormonal influences,

and immunological differences affecting response to fever. However, some studies have shown nearly equal gender distribution, indicating that gender alone may not independently determine febrile seizure risk.

Study was found that all children have simple febrile seizure, family history of febrile seizures was present in 28 (14%) children and absent in 172 (86%). Recurrence during the same illness was observed in 28 (14%) children. Family history is a well-established risk factor and indicates genetic predisposition. Several genes involved in ion channel regulation and neuronal excitability have been implicated in febrile seizure susceptibility. The predominance of simple febrile seizures in this study indicates that most seizure episodes were clinically benign and self-limiting.

In the study, 48 (24%) children had normal hemoglobin levels, 52 (26%) had mild anemia, 74 (37%) had moderate anemia, and 26 (13%) had severe anemia. Moderate anemia was the most common hematological abnormality. Köksal AO et al. (2016) ¹⁵ reported significantly lower hemoglobin levels among children with febrile seizures. Jang HN et al. (2019) ¹⁶ found a significant association between anemia and febrile seizures. Madavi D et al. (2021) ¹⁷ reported that moderate to severe anemia was associated with increased seizure recurrence. Moderate and severe anemia may contribute to neuronal instability by causing chronic cerebral hypoxia and impaired neurotransmitter function. Iron deficiency additionally worsens this by affecting myelination and synaptic transmission.

After analysis it was found that, there was statistically highly significant association between serum Iron level and Serum ferritin level with the occurrence of febrile seizure (p

<0.01). There was no association found between MCV TIBC, Transferrin saturation and duration of seizure during febrile seizure episode.

Assessment of iron profile provides a more accurate evaluation of iron status than hemoglobin alone. While less hemoglobin reflects overt anemia, parameters such as serum ferritin, serum iron, TIBC, and transferrin saturation help identify early iron deficiency before severe anemia develops. Iron deficiency may therefore exist even in children with near-normal hemoglobin values. Köksal AO et al. (2016)¹⁵ demonstrated significantly lower serum iron and ferritin levels in children with febrile seizures compared to controls. Jang HN et al. (2019)¹⁶ similarly reported reduced ferritin and serum iron levels with elevated TIBC among affected children. Zheng SF et al. (2019)¹⁷ also found that altered iron indices were strongly associated with febrile seizures. International studies further support these findings. Elkafafy M et al. (2021)¹⁸ reported significantly lower ferritin and transferrin saturation in febrile seizure patients. Chaudhary BR et al. (2021)¹⁹ also found a strong correlation between low iron stores and febrile seizures. Iron plays a central role in neuronal metabolism.

We also found that, 152 (76%) children were found to be iron deficient, while only 48 (24%) had normal iron status. This was one of the most important findings of this study and strongly supports the hypothesis that iron deficiency is associated with febrile seizures. The prevalence of iron deficiency in the study population was remarkably high. Sharif MR et al. (2015)²⁰ reported significantly higher

prevalence of iron deficiency among children with febrile seizures compared to controls. Elkafafy M et al. (2021)¹⁸, Chaudhary BR et al. (2021)¹⁹, Awais M et al. (2022)²¹, and Hussain A et al. (2023)²² also demonstrated strong positive associations between iron deficiency and febrile seizures. The study strongly supports iron deficiency as an important modifiable risk factor for febrile seizures. Bakkannavar S et al. (2024)²³ and Sulviani R et al. (2023)²⁴ further strengthened the evidence that iron deficiency significantly increases susceptibility to febrile seizures and may influence seizure severity. Since iron deficiency is both identifiable and treatable, early screening and timely correction of iron deficiency in high-risk children may help reduce the burden, recurrence, and severity of febrile seizures. Therefore, routine evaluation of iron status should be considered in children presenting with febrile seizures.

Conclusion: It is concluded that iron deficiency anemia is significantly associated with febrile seizures in children aged 6 months to 5 years. A high proportion of children with febrile seizures had anemia, microcytosis, and abnormal iron profile parameters including low serum iron and low ferritin level. Increasing severity of anemia was associated with higher seizure frequency. Since iron deficiency is a preventable and treatable condition, early identification and timely management of iron deficiency in children may reduce the incidence, severity, and recurrence of febrile seizures. Therefore, routine screening for anemia and iron deficiency should be considered in all children presenting with febrile seizures, especially in high-risk populations.

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