International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Research Article

Association Of Serum Ferritin Levels With Febrile Seizures In Children: A Case-Control Study

Dr Nagaraj[1], Dr Md Altaf Attar[2], Dr Sumangala Mulagund[3]

[1] Senior resident Dept of pediatrics YIMS yadgir
[2]Assistant professor Dept Of Pediatrics yims yadgir
[3]Senior resident Dept of anesthesiology YIMS yadgir

OPEN ACCESS

Corresponding Author:

Dr Nagaraj
Senior resident Dept of pediatrics
YIMS yadgir

Received: 08-08-2025
Accepted: 24-08-2025
Available online: 11-09-2025

ABSTRACT

Background: Febrile seizures are the most common seizure type in childhood, with iron deficiency proposed as a modifiable risk factor. Serum ferritin, a sensitive indicator of iron stores, may be associated with seizure occurrence and severity.
Objective: To evaluate the association between serum ferritin levels and febrile seizures in children aged 6 months to 5 years.
Methods: A hospital-based case–control study was conducted from April to August 2025 at Yadgir Institute of Medical Sciences, including 25 children with febrile seizures (cases) and 25 age- and sex-matched febrile children without seizures (controls). Serum ferritin was measured using ELISA, along with hematological indices and C-reactive protein (CRP). Statistical analysis was performed using Student's t-test and Chi-square test, with $p < 0.05$ considered significant.
Results: Mean serum ferritin was significantly lower in cases than controls (48.6 ± 18.4 vs. 92.3 ± 25.7 ng/mL, $p < 0.001$). Low ferritin (<30 ng/mL) occurred in 24% of cases and none of the controls ($p = 0.02$). Ferritin levels were lower in complex seizures compared to simple seizures (39.2 ± 19.6 vs. 52.1 ± 17.3 ng/mL, $p = 0.04$) and in seizures lasting >5 minutes ($p = 0.05$). Hemoglobin was also lower in cases ($p = 0.04$), while MCV, hematocrit, and CRP showed no significant differences.
Conclusion: Lower serum ferritin levels are significantly associated with febrile seizures, particularly with complex type and longer duration. Early identification and correction of iron deficiency may help reduce seizure occurrence and severity in at-risk children.

Keywords: *Febrile seizures, serum ferritin, iron deficiency, case–control study, pediatric neurology*

INTRODUCTION

Febrile seizures are the most common type of seizure disorder in childhood, affecting 2–5% of children aged 6 months to 5 years [1]. They are defined by the International League Against Epilepsy (ILAE) as seizures occurring in association with fever (temperature ≥38°C) in the absence of central nervous system infection, metabolic disturbance, or prior afebrile seizures [2]. Febrile seizures are broadly classified into simple (generalized, lasting less than 15 minutes, and not recurring within 24 hours) and complex (focal, prolonged, or recurrent within 24 hours) [3].

The etiology of febrile seizures is multifactorial, with genetic predisposition, environmental triggers, and biochemical factors playing significant roles [4]. Iron deficiency has been proposed as one of the modifiable risk factors. Iron is essential for myelination, neurotransmitter synthesis (dopamine, serotonin, γ-aminobutyric acid), and oxygen transport to the brain [5]. Deficiency may lower the seizure threshold by impairing neurotransmission and cerebral oxygenation [6]. Serum ferritin, an intracellular iron storage protein, reflects total body iron stores and is considered the most sensitive laboratory indicator of iron deficiency [7]. However, ferritin is also an acute-phase reactant and can be elevated in infections and inflammation, complicating its interpretation in febrile illnesses [8]. Several studies have evaluated the

relationship between serum ferritin and febrile seizures, but the results have been inconsistent — some report significantly lower ferritin levels in febrile seizure patients compared to febrile controls [9,10], while others find no such association [11].

Given the potential implications for prevention and management, further exploration in diverse populations is warranted. This study aims to determine the association between serum ferritin levels and febrile seizures in children aged 6 months to 5 years, and to assess whether ferritin levels differ with seizure type and duration.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based case–control study was conducted in the Department of Pediatrics at Yadgir Institute of Medical Sciences, Yadgir, over five months from April 2025 to August 31, 2025. The study aimed to evaluate the association between serum ferritin levels and febrile seizures in children.

Study Population

A total of 50 children aged 6 months to 5 years were enrolled, comprising 25 cases and 25 controls.

- Cases: Children presenting with febrile seizures (simple or complex) as per the International League Against Epilepsy (ILAE) definition, i.e., a seizure accompanied by fever (≥38°C) without evidence of intracranial infection, metabolic disturbance, or history of afebrile seizures.
- Controls: Age- and sex-matched febrile children without seizures, attending the outpatient department or admitted for febrile illness during the same period.

Inclusion Criteria

Cases:

1. Children aged 6 months–5 years with a first or recurrent febrile seizure.
2. Fever onset within 24 hours of seizure episode.

Controls:

1. Children aged 6 months–5 years with febrile illness but no seizure history.

Exclusion Criteria (for both groups)

1. Evidence of central nervous system infection (meningitis, encephalitis).
2. Known neurological disorders or developmental delay.
3. Chronic systemic illness (e.g., thalassemia, chronic kidney disease).
4. Children already on iron supplementation or diagnosed with iron deficiency anemia under treatment.
5. Recent blood transfusion (within 3 months).

Sample Size and Sampling Technique

The sample size was fixed at 50 children, with 25 in each group, based on feasibility and study duration. Cases were selected consecutively from pediatric emergency/admission units, while controls were selected from febrile children visiting the outpatient department, matched for age (±6 months) and gender.

Data Collection

After obtaining written informed consent from parents/guardians, a detailed clinical history was recorded, including:

- Demographic details (age, sex)
- Presenting complaints
- Fever duration and grade
- Seizure characteristics (type, duration, number of episodes)
- Past medical history

A thorough general and systemic examination was performed.

Laboratory Investigations

Blood samples (3 mL) were collected under aseptic precautions within 24 hours of admission for:

1. Serum ferritin – measured using an enzyme-linked immunosorbent assay (ELISA) method.
2. Complete blood count – for hemoglobin, hematocrit, mean corpuscular volume (MCV), and red cell indices.
3. C-reactive protein (CRP) – to account for the acute phase reaction influence on ferritin levels.

All laboratory analyses were conducted in the institutional central laboratory, following standard operating procedures.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 21.1. Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's *t*-test.

Categorical variables were presented as frequencies and percentages, and compared using Chi-square or Fisher's exact test. A *p*-value of <0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

Table 1: Age and Gender Distribution

Age Group	Cases (n=25)	Controls (n=25)	Total (n=50)	p-value
6–12 months	6 (24.0%)	5 (20.0%)	11 (22.0%)	0.89
13–24 months	10 (40.0%)	9 (36.0%)	19 (38.0%)	
25–36 months	5 (20.0%)	6 (24.0%)	11 (22.0%)	
37–60 months	4 (16.0%)	5 (20.0%)	9 (18.0%)	
Mean ± SD (months)	24.8 ± 11.2	25.6 ± 10.9	—	0.81
Male	15 (60.0%)	14 (56.0%)	29 (58.0%)	0.78
Female	10 (40.0%)	11 (44.0%)	21 (42.0%)	

Table 2: Fever Profile

Parameter	Cases (n=25)	Controls (n=25)	p-value
Mean temperature (°C)	38.9 ± 0.6	38.7 ± 0.5	0.21
Duration before admission (hours)	10.8 ± 4.2	11.4 ± 4.5	0.58
Viral etiology suspected	16 (64.0%)	15 (60.0%)	0.77
Bacterial etiology suspected	9 (36.0%)	10 (40.0%)	

Table 3: Type of Febrile Seizure in Cases

Seizure Type	Number (n=25)	Percentage
Simple	18	72.0%
Complex	7	28.0%

Table 4: Recurrence of Febrile Seizures

Recurrence Status	Number (n=25)	Percentage
First episode	20	80.0%
Recurrent episode	5	20.0%

Table 5: Serum Ferritin Levels in Cases and Controls

Parameter	Cases (n=25)	Controls (n=25)	p-value
Mean ± SD (ng/mL)	48.6 ± 18.4	92.3 ± 25.7	<0.001*
Median (IQR)	45.0 (35.0–60.0)	90.0 (78.0–105.0)	
Range	20–85	60–130	
Low Ferritin (<30 ng/mL)	6 (24.0%)	0 (0.0%)	0.02*
Normal Ferritin (30–100)	19 (76.0%)	22 (88.0%)	
High Ferritin (>100)	0 (0.0%)	3 (12.0%)	

Table 6: Hematological Parameters

Parameter	Cases (n=25)	Controls (n=25)	p-value
Hemoglobin (g/dL)	10.4 ± 1.2	11.1 ± 1.3	0.04*
Hematocrit (%)	31.6 ± 3.4	33.1 ± 3.1	0.06
MCV (fL)	74.8 ± 5.3	76.2 ± 4.9	0.28
CRP (mg/L)	14.5 ± 5.6	13.8 ± 5.2	0.63

Table 7: Relationship Between Serum Ferritin Levels and Seizure Type

Seizure Type	Mean Ferritin (ng/mL) ± SD	p-value
Simple	52.1 ± 17.3	
Complex	39.2 ± 19.6	0.04*

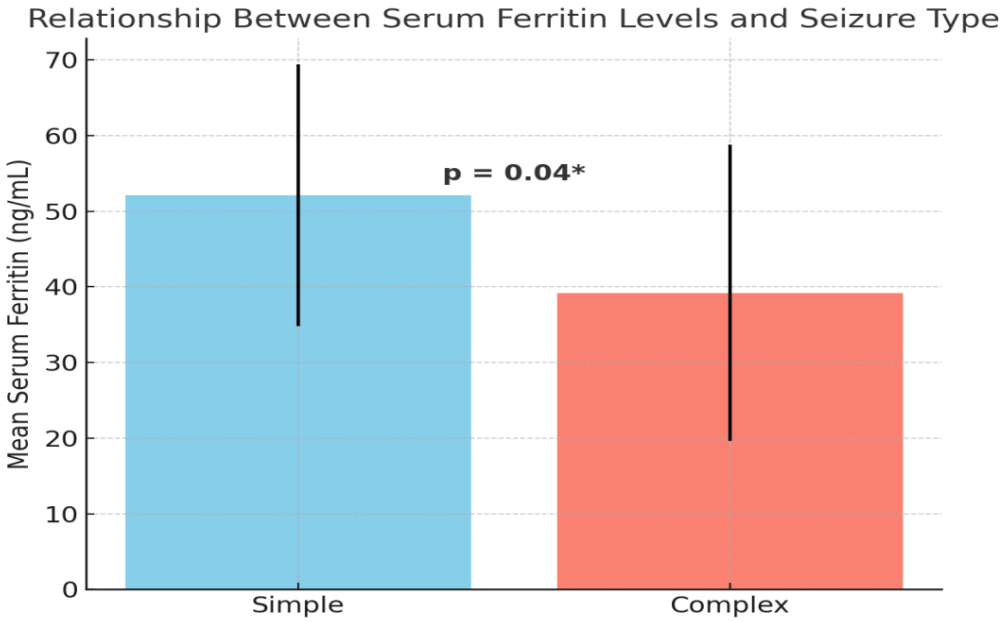

Table 8: Relationship Between Serum Ferritin Levels and Seizure Duration

Duration of Seizure	Mean Ferritin (ng/mL) ± SD	p-value
≤5 minutes	50.8 ± 18.1	
>5 minutes	40.5 ± 19.0	0.05*

DISCUSSION

In this hospital-based case–control study, we observed that children with febrile seizures had significantly lower mean serum ferritin levels compared to age- and sex-matched febrile controls without seizures (48.6 ± 18.4 ng/mL vs. 92.3 ± 25.7 ng/mL, $p < 0.001$). Low ferritin levels (<30 ng/mL) were found in 24% of cases, while none of the controls had ferritin below this threshold. These findings suggest that reduced iron stores may be associated with an increased risk of febrile seizures.

Our results are consistent with several previous studies. Kumari et al. [9] and Naveed-ur-Rehman et al. [10] both reported significantly lower ferritin levels in febrile seizure cases compared to controls, supporting the hypothesis that iron deficiency lowers the seizure threshold. The biological plausibility lies in iron's role in myelination and neurotransmitter synthesis — deficiency may alter neuronal excitability, predisposing to seizures [5,6].

We also found that ferritin levels were significantly lower in children with **complex febrile seizures** compared to simple seizures (39.2 ± 19.6 ng/mL vs. 52.1 ± 17.3 ng/mL, $p = 0.04$) and in those with seizure duration >5 minutes ($p = 0.05$). This suggests a possible dose–response relationship, where greater iron deficiency is linked with more severe seizure presentations. Similar associations between iron status and seizure complexity have been reported by Hartfield et al. [12] and Pisacane et al. [13].

Interestingly, while hemoglobin levels were also lower in cases than controls ($p = 0.04$), other hematological indices (MCV, hematocrit) and inflammatory marker (CRP) did not differ significantly. This indicates that ferritin, rather than general anemia, may have a more direct association with febrile seizures. Since ferritin is an acute-phase reactant, both groups' febrile state could elevate levels to some extent; yet, the marked difference between cases and controls supports a genuine underlying iron deficiency in the seizure group.

Contradictory results in the literature do exist. For example, Kobrinsky et al. [11] found no association between iron status and febrile seizures, possibly due to differences in population characteristics, nutritional status, or timing of ferritin measurement relative to fever onset.

Limitations of our study include the relatively small sample size and lack of dietary iron assessment. Additionally, as ferritin is influenced by inflammation, even with CRP measurement, some confounding cannot be excluded.

Clinical implications: Early detection and correction of iron deficiency in at-risk children may reduce febrile seizure incidence and severity. Further multicenter studies with larger cohorts and longitudinal follow-up are recommended to clarify causality and assess preventive strategies.

CONCLUSION

This study demonstrates a significant association between lower serum ferritin levels and the occurrence of febrile seizures in children aged 6 months to 5 years. Children with febrile seizures had markedly reduced ferritin compared to age- and sex-matched febrile controls, with the lowest levels observed in complex seizures and longer seizure durations. These findings suggest that iron deficiency may lower the seizure threshold and influence seizure severity. Early screening and correction of iron deficiency could be considered as part of preventive strategies in children at risk for febrile seizures.

REFERENCES

1. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures. Febrile seizures: Clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics*. 2008;121(6):1281–1286.
2. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy. *Epilepsia*. 2017;58(4):522–530.
3. Berg AT, Shinnar S. Complex febrile seizures. *Epilepsia*. 1996;37(2):126–133.
4. Leung AK, Hon KL, Leung TN. Febrile seizures: An overview. *Drugs Context*. 2018;7:212536.
5. Beard JL. Iron deficiency alters brain development and functioning. *J Nutr*. 2003;133(5 Suppl 1):1468S–1472S.
6. Youdim MB, Yehuda S. The neurochemical basis of cognitive deficits induced by iron deficiency in children. *J Neural Transm Suppl*. 2000;60:219–229.
7. Worwood M. Serum ferritin. *CRC Crit Rev Clin Lab Sci*. 1979;10(2):171–204.
8. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker. *Metallomics*. 2014;6(4):748–773.
9. 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(1):17–19.
10. Naveed-ur-Rehman, Billoo AG. Association between iron deficiency anemia and febrile seizures. *J Coll Physicians Surg Pak*. 2005;15(6):338–340.
11. Kobrinsky NL, Yager JY, Cheang MS, et al. Does iron deficiency raise the seizure threshold in children? *J Child Neurol*. 1995;10(2):105–109.
12. Hartfield DS, Tan J, Yager JY, et al. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr (Phila)*. 2009;48(4):420–426.
13. Pisacane A, Sansone R, Impagliazzo N, et al. Iron deficiency anaemia and febrile convulsions: Case-control study in children under two years. *BMJ*. 1996;313(7053):343.