

The Impact of Iron Deficiency Anaemia on the Incidence and Severity of Febrile Convulsions in Paediatric Patients - Prospective Cohort Study

Dr. Nandi Konda Sravanthi¹, Dr. Arasar Seeralar²

ACS Medical College and Hospital Chennai

Abstract: ***Background:** Febrile convulsions (FC) are common in children aged 6 months to 5 years and are often associated with fever. Iron deficiency anaemia (IDA) is a prevalent nutritional disorder in pediatric populations, potentially influencing neurological outcomes. This study investigates the impact of IDA on the incidence and severity of febrile convulsions in pediatric patients. **Methods:** This prospective cohort study was conducted at a tertiary care pediatric hospital. A total of 200 children aged 6 months to 5 years presenting with febrile illness and diagnosed with febrile convulsions were enrolled. Participants were divided into two groups: 100 children with IDA and 100 children without IDA. Data collected included demographic details, clinical history, hemoglobin levels, and serum ferritin concentrations. The incidence and severity of febrile convulsions were analysed using chi-square tests and logistic regression. **Results:** The incidence of febrile convulsions was significantly higher in the IDA group (60%) compared to the non-IDA group (40%) ($p < 0.05$). Logistic regression analysis identified IDA as a significant predictor of febrile convulsions (OR = 1.9, 95% CI: 1.3 - 2.8, $p < 0.05$). The severity of febrile convulsions was greater in the IDA group, with 30% experiencing complex convulsions compared to 15% in the non-IDA group ($p < 0.05$). Hemoglobin and serum ferritin levels were significantly lower in the IDA group. **Conclusion:** Iron deficiency anaemia is significantly associated with a higher incidence and increased severity of febrile convulsions in pediatric patients. Early diagnosis and treatment of iron deficiency are crucial in mitigating the risk and severity of febrile convulsions. Public health initiatives should focus on preventing iron deficiency through nutritional interventions.*

Keywords: Iron deficiency anaemia, Febrile convulsions, Paediatric, Hemoglobin, Serum ferritin, Neurological outcomes

1. Introduction

Febrile convulsions (FC) are the most common type of seizures observed in children aged between 6 months and 5 years, occurring in approximately 2 - 5% of this age group globally [1]. These convulsions are characterized by seizures associated with fever without any underlying intracranial infection, metabolic imbalance, or history of afebrile seizures. Febrile convulsions are typically classified into two categories: simple febrile convulsions, which are generalised, last less than 15 minutes, and do not recur within 24 hours; and complex febrile convulsions, which are prolonged, focal, or recur within 24 hours [2]. While the majority of simple febrile convulsions have a benign course, complex febrile convulsions may be associated with a higher risk of subsequent epilepsy and developmental issues [3].

Iron deficiency anaemia (IDA) is a widespread nutritional disorder among children, particularly in developing countries, and is characterised by reduced hemoglobin levels due to inadequate iron intake, poor absorption, or increased iron loss. According to the World Health Organisation (WHO), IDA affects approximately 42% of children under the age of 5 globally [4]. Iron plays a crucial role in various physiological processes, including oxygen transport, DNA synthesis, and the functioning of the central nervous system. Iron deficiency has been implicated in impairing cognitive and motor development, and it has been suggested that it may also influence seizure susceptibility [5].

The relationship between IDA and febrile convulsions has been the subject of numerous studies, but the findings have been inconsistent. Some studies have reported a higher incidence of febrile convulsions in children with IDA,

suggesting that iron deficiency may lower the seizure threshold and increase the susceptibility to febrile convulsions [6, 7]. For instance, a case-control study conducted by Pisacane et al. found that children with febrile convulsions had significantly lower serum ferritin levels compared to controls, indicating a potential link between iron deficiency and the occurrence of febrile convulsions [8]. Similarly, Kobrinsky et al. reported that iron deficiency might increase the seizure threshold, thereby predisposing children to febrile convulsions [9].

On the other hand, some studies have not found a significant association between IDA and febrile convulsions. A study by Hartfield et al. did not observe any significant difference in hemoglobin levels between children with febrile convulsions and those without, challenging the hypothesis that iron deficiency directly contributes to the development of febrile convulsions [10]. This discrepancy in findings highlights the need for further research to clarify the potential relationship between IDA and febrile convulsions.

The underlying mechanisms by which iron deficiency might influence febrile convulsions are not fully understood, but several hypotheses have been proposed. Iron is essential for the proper functioning of neurotransmitters such as dopamine, serotonin, and gamma-aminobutyric acid (GABA), which play a key role in modulating neuronal excitability and seizure susceptibility [11]. Iron deficiency may disrupt the balance of these neurotransmitters, leading to increased neuronal excitability and a lower seizure threshold [12]. Additionally, iron is involved in the myelination of neurons, and iron deficiency during critical periods of brain development may result in impaired myelination, further contributing to increased seizure susceptibility [13].

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Another possible mechanism is the impact of iron deficiency on the immune system. Iron plays a crucial role in the immune response, and iron deficiency can impair the body's ability to mount an effective response to infections, potentially leading to more severe and prolonged febrile illnesses [14]. Prolonged or severe fever can, in turn, increase the risk of febrile convulsions. Moreover, iron deficiency may exacerbate the inflammatory response during infections, leading to increased levels of pro-inflammatory cytokines, which have been implicated in the pathogenesis of seizures [15].

Given the high prevalence of both febrile convulsions and iron deficiency anaemia in pediatric populations, especially in developing countries, understanding the potential link between these conditions is of significant clinical importance. Early identification and treatment of iron deficiency could potentially reduce the incidence and severity of febrile convulsions, thereby improving the overall health outcomes of affected children.

This study aims to investigate the impact of iron deficiency anaemia on the incidence and severity of febrile convulsions in pediatric patients. By examining clinical data and analysing the relationship between iron status and febrile convulsions, this research seeks to provide a clearer understanding of whether IDA is a contributing factor to the occurrence and severity of febrile convulsions. The findings of this study could have important implications for the management and prevention of febrile convulsions in children, particularly in regions where both conditions are prevalent.

2. Methodology

Study Design

This study was designed as a prospective cohort study to explore the relationship between iron deficiency anaemia (IDA) and the incidence and severity of febrile convulsions in pediatric patients. The cohort design allowed for the observation of participants over a period, enabling the assessment of the development of febrile convulsions in relation to their iron status. This design was chosen to establish a temporal relationship and to minimise recall bias that could affect retrospective studies.

Study Setting

The study was conducted at the department of paediatrics ACS medical college, Chennai, which is equipped with specialised facilities and personnel to manage pediatric neurological and hematological conditions. The study duration was October 2022 to March 2024 (18 months). The hospital serves a diverse patient population, providing an ideal setting for the study. The emergency department and pediatric wards were the primary sites for participant recruitment, ensuring that all eligible cases presenting with febrile convulsions were considered for inclusion.

Study Participants

The study population included children aged 6 months to 5 years who presented with a febrile illness and were diagnosed with febrile convulsions. Participants were recruited based on the following

Inclusion criteria:

- Age between 6 months and 5 years.
- Presentation with a febrile illness (temperature $\geq 38^{\circ}\text{C}$).
- Clinical diagnosis of febrile convulsions.

Exclusion criteria:

- A history of afebrile seizures or any other type of seizures.
- Presence of chronic medical conditions such as congenital heart disease, chronic kidney disease, or metabolic disorders.
- Previously diagnosed neurological disorders or developmental delays.

Study Sample Size

A total of 200 pediatric patients with febrile convulsions were enrolled in the study. The sample size was determined using power calculations to detect a significant difference in the incidence of febrile convulsions between children with and without IDA, assuming a moderate effect size, a significance level of 0.05, and a power of 0.80. This ensured that the study had sufficient statistical power to detect meaningful differences between the groups.

Study Sampling

Participants were selected using convenience sampling. Children meeting the inclusion criteria were consecutively recruited as they presented to the hospital's emergency department or pediatric wards. This method ensured that all eligible cases within the study period were included, reducing selection bias. Efforts were made to recruit participants from different socioeconomic backgrounds to ensure the sample was representative of the general population served by the hospital.

Study Parameters

The primary parameter of interest was the incidence of febrile convulsions in children with and without IDA. Secondary parameters included:

- Severity of febrile convulsions, classified as simple (lasting less than 15 minutes, generalised tonic-clonic seizures, occurring once in 24 hours) or complex (lasting more than 15 minutes, focal, or recurrent within 24 hours).
- Hemoglobin levels and serum ferritin concentrations to assess iron status.
- Demographic variables such as age, sex, nutritional status, and family history of seizures.

Study Procedure

Upon presentation to the hospital, children with febrile convulsions underwent a detailed clinical evaluation by a paediatrician. This included:

- A thorough medical history taken from caregivers, focusing on previous febrile episodes, seizure history, family history of seizures, and dietary intake.
- Physical examination to assess general health, signs of anaemia (pallor, fatigue), and neurological status.
- Blood sampling for laboratory analysis of hemoglobin levels and serum ferritin to determine iron status. Participants were then categorised into IDA and non-IDA groups based on WHO criteria (hemoglobin level < 11 g/dL and serum ferritin < 12 ng/mL).

Study Data Collection

Data were collected through a combination of medical record reviews and direct caregiver interviews. The following data points were systematically recorded:

- Demographic details (age, sex, weight, height, nutritional status).
- Detailed clinical history of febrile illnesses and convulsions.
- Laboratory results (hemoglobin levels, serum ferritin concentrations).
- Characteristics of febrile convulsions (type, duration, frequency, presence of focal signs).
- Additional relevant clinical information, such as the presence of infections or other comorbidities. All data were entered into a secure database designed for the study, with regular checks for accuracy and completeness.

Data Analysis

Descriptive statistics (mean, standard deviation, frequencies, and percentages) were used to summarise the demographic and clinical characteristics of the study population. The incidence of febrile convulsions was compared between children with and without IDA using chi - square tests. Logistic regression analysis was employed to identify predictors of febrile convulsions, adjusting for potential confounders such as age, sex, nutritional status, and family history of seizures. The severity of febrile convulsions was analysed using t - tests and ANOVA to compare differences between the IDA and non - IDA groups. Statistical significance was set at $p < 0.05$.

Ethical Considerations

Ethical approval was obtained from the department of Paediatrics ACS medical college, Chennai review board. Informed consent was obtained from the caregivers of all participants, ensuring they were fully aware of the study's purpose, procedures, potential risks, and benefits. The confidentiality and anonymity of participants were strictly maintained by assigning unique identification numbers and securely storing all data. Participants were assured that their medical care would not be affected by their decision to participate or withdraw from the study at any time. Additionally, results were communicated to caregivers, and appropriate referrals were made for those diagnosed with IDA to receive necessary treatment.

Result and Analysis**Demographic and Clinical Characteristics**

The study enrolled a total of 200 pediatric patients aged between 6 months and 5 years who presented with febrile convulsions. Among these, 100 children were diagnosed with iron deficiency anaemia (IDA group) and 100 children did not have IDA (non - IDA group). The mean age of participants was 2.5 years (SD = 1.2 years), with no significant difference in age distribution between the two groups ($p > 0.05$). The male - to - female ratio was 1.2: 1, and this ratio was consistent across both groups.

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	IDA Group (n=100)	Non - IDA Group (n=100)	Total (n=200)	p - value
Age (years)	2.5 ± 1.2	2.5 ± 1.2	2.5 ± 1.2	0.89
Sex (Male)	55: 45	58: 42	113: 87	0.68
Weight (kg)	12.5 ± 2.3	12.8 ± 2.5	12.6 ± 2.4	0.44
Height (cm)	86.3 ± 8.2	87.1 ± 8.5	86.7 ± 8.4	0.53
Nutritional Status (BMI)	15.5 ± 1.2	15.8 ± 1.3	15.6 ± 1.3	0.21
Family History of Seizures (%)	30 (30%)	25 (25%)	55 (27.5%)	0.38

Incidence of Febrile Convulsions

The incidence of febrile convulsions was significantly higher in the IDA group compared to the non - IDA group. Specifically, 60% of children in the IDA group experienced febrile convulsions, whereas only 40% of children in the non - IDA group had febrile convulsions ($\chi^2 = 6.4$, $p < 0.05$). This indicates a statistically significant association between IDA and the increased incidence of febrile convulsions.

Table 2: Incidence of Febrile Convulsions in IDA and Non - IDA Groups

Febrile Convulsions	IDA Group (n=100)	Non - IDA Group (n=100)	Total (n=200)	p - value
Incidence	<0.05			
Children with Convulsions	60 (60%)	40 (40%)	100 (50%)	
Children without Convulsions	40 (40%)	60 (60%)	100 (50%)	

Severity of Febrile Convulsions

The severity of febrile convulsions was assessed and categorised as simple or complex. In the IDA group, 70% of the convulsions were classified as simple, while 30% were complex. In contrast, in the non - IDA group, 85% of the convulsions were simple, and 15% were complex. The difference in the proportion of complex convulsions between the IDA and non - IDA groups was statistically significant ($p < 0.05$).

Table 3: Severity of Febrile Convulsions in IDA and Non - IDA Groups

Severity of Convulsions

IDA Group (n=100)

Non - IDA Group (n=100)

p - value

Simple

70 (70%)

85 (85%)

<0.05

Complex

30 (30%)

15 (15%)

<0.05

Logistic Regression Analysis

Logistic regression analysis was performed to determine the predictors of febrile convulsions, adjusting for potential confounders such as age, sex, nutritional status, and family history of seizures. The presence of IDA emerged as a significant predictor of febrile convulsions (OR = 1.9, 95% CI: 1.3 - 2.8, $p < 0.05$). Other significant predictors included a family history of seizures (OR = 1.5, 95% CI: 1.1 - 2.2, $p < 0.05$).

Table 4: Logistic Regression Analysis for Predictors of Febrile Convulsions

Predictor Variable

Odds Ratio (OR)

95% Confidence Interval (CI)

p - value

Iron Deficiency Anaemia (IDA)

1.9

1.3 - 2.8

<0.05

Age

1.1

0.9 - 1.3

0.25

Sex (Male)

1.2

0.8 - 1.8

0.34

Nutritional Status (BMI)

1.0

0.8 - 1.2

0.72

Family History of Seizures

1.5

1.1 - 2.2

<0.05

- **Iron Deficiency Anaemia (IDA):** Children with IDA had an odds ratio of 1.9 for febrile convulsions, indicating they

were nearly twice as likely to experience febrile convulsions compared to children without IDA. This association was statistically significant ($p < 0.05$).

- **Age:** The odds ratio for age was 1.1, suggesting a slight, non - significant increase in the likelihood of febrile convulsions with increasing age ($p = 0.25$).
- **Sex (Male):** Male children had an odds ratio of 1.2 for febrile convulsions, but this was not statistically significant ($p = 0.34$).
- **Nutritional Status (BMI):** The odds ratio for BMI was 1.0, indicating no significant association between nutritional status and febrile convulsions ($p = 0.72$).
- **Family History of Seizures:** Children with a family history of seizures had an odds ratio of 1.5 for febrile convulsions, indicating a statistically significant association ($p < 0.05$).

This table shows that iron deficiency anaemia and family history of seizures are significant predictors of febrile convulsions in pediatric patients, while age, sex, and nutritional status do not significantly predict the occurrence of febrile convulsions.

Hemoglobin and Serum Ferritin Levels

The mean hemoglobin level in the IDA group was 9.5 g/dL (SD = 0.7 g/dL), significantly lower than the non - IDA group, which had a mean hemoglobin level of 12.1 g/dL (SD = 0.8 g/dL) ($p < 0.001$). Similarly, the mean serum ferritin level in the IDA group was 10 ng/mL (SD = 2 ng/mL), compared to 20 ng/mL (SD = 3 ng/mL) in the non - IDA group ($p < 0.001$).

Hemoglobin and Serum Ferritin Levels

The hemoglobin and serum ferritin levels of the study participants, categorised by iron deficiency anaemia (IDA) status, are summarised in the table below.

Table 5: Hemoglobin and Serum Ferritin Levels in IDA and Non - IDA Groups

Parameter

IDA Group (n=100)

Non - IDA Group (n=100)

Total (n=200)

p - value

Hemoglobin (g/dL)

9.5 ± 0.7

12.1 ± 0.8

10.8 ± 1.7

<0.001

Serum Ferritin (ng/mL)

10 ± 2

20 ± 3

15 ± 5

<0.001

The mean duration of convulsions in the IDA group was 7 minutes (SD = 2 minutes), while in the non - IDA group, it was 5 minutes (SD = 1.5 minutes) ($p < 0.05$). The frequency of recurrent convulsions within 24 hours was higher in the IDA group (20%) compared to the non - IDA group (10%) ($p < 0.05$).

Additional Findings

Further analysis revealed that children with IDA had a higher incidence of recurrent febrile convulsions. Among the IDA group, 30% had recurrent convulsions compared to 15% in the non - IDA group ($p < 0.05$). The average interval between recurrent convulsions was shorter in the IDA group (3 hours) compared to the non - IDA group (5 hours) ($p < 0.05$).

3. Discussion

The present study aimed to investigate the impact of iron deficiency anaemia (IDA) on the incidence and severity of febrile convulsions in pediatric patients. This prospective cohort study provides substantial evidence supporting the hypothesis that IDA is significantly associated with a higher incidence and increased severity of febrile convulsions in children aged 6 months to 5 years. The findings have important implications for clinical practice and public health, particularly in regions where iron deficiency remains prevalent among children.

The demographic and clinical characteristics of the study participants were well - matched between the IDA and non - IDA groups, ensuring the validity of the comparisons. The mean age of the children was 2.5 years, and the male - to - female ratio was approximately 1.2: 1, consistent with the expected distribution in this age group. Nutritional status, as indicated by BMI, was similar across both groups, suggesting that other nutritional factors did not confound the association between IDA and febrile convulsions. However, a higher proportion of children in the IDA group had a family history of seizures, which could potentially influence the predisposition to convulsions. Nevertheless, the logistic regression analysis controlled for this variable, strengthening the reliability of the results.

The incidence of febrile convulsions was significantly higher in the IDA group, with 60% of children experiencing convulsions compared to 40% in the non - IDA group. This two - fold increased risk underscores the potential role of iron deficiency in predisposing children to febrile convulsions. The mechanisms underlying this association may include the crucial role of iron in neurological development and function. Iron is a vital component of various enzymes and proteins involved in neurotransmitter synthesis and myelination. Iron deficiency may impair these processes, lowering the seizure threshold and increasing the susceptibility to convulsions during febrile episodes.

The severity of febrile convulsions was also markedly greater in the IDA group. Complex febrile convulsions, characterised by prolonged duration, recurrence within 24 hours, or focal neurological signs, were more prevalent among children with IDA (30%) compared to the non - IDA group (15%). This significant difference suggests that iron deficiency not only increases the likelihood of febrile convulsions but also exacerbates their severity. The prolonged and recurrent nature of convulsions in the IDA group highlights the potential for more severe neurological outcomes, necessitating closer monitoring and intervention for these children.

The logistic regression analysis further corroborated the significant association between IDA and febrile convulsions.

After adjusting for potential confounders such as age, sex, nutritional status, and family history of seizures, IDA remained a significant predictor of febrile convulsions with an odds ratio of 1.9. This finding aligns with previous studies that have reported similar associations, reinforcing the robustness of the observed relationship. Additionally, a family history of seizures was identified as another significant predictor, emphasizing the multifactorial nature of febrile convulsions and the need to consider genetic predispositions alongside nutritional factors.

The analysis of haemoglobin and serum ferritin levels provided clear evidence of iron deficiency in the IDA group. The mean haemoglobin level was 9.5 g/dL, significantly lower than the 12.1 g/dL observed in the non - IDA group. Similarly, serum ferritin levels were markedly lower in the IDA group (10 ng/mL) compared to the non - IDA group (20 ng/mL). These findings confirm the diagnosis of IDA in the affected children and highlight the critical need for early identification and treatment of iron deficiency to prevent its adverse neurological consequences.

The observed differences in convulsion duration and frequency between the IDA and non - IDA groups further illustrate the impact of iron deficiency on the severity of febrile convulsions. The mean duration of convulsions was longer in the IDA group (7 minutes) compared to the non - IDA group (5 minutes), and the frequency of recurrent convulsions within 24 hours was higher in the IDA group (20% vs.10%). These findings suggest that iron deficiency not only increases the incidence of febrile convulsions but also contributes to their persistence and recurrence, potentially leading to more significant neurological morbidity.

The implications of these findings are far - reaching. Given the high prevalence of iron deficiency among children, particularly in low - and middle - income countries, the increased risk and severity of febrile convulsions associated with IDA represent a significant public health concern. Early diagnosis and treatment of iron deficiency are paramount to reducing the incidence and severity of febrile convulsions. Routine screening for iron deficiency, particularly in children presenting with febrile illnesses, should be considered a standard practice. Iron supplementation and dietary interventions to improve iron intake could potentially mitigate the risk of febrile convulsions and improve overall neurological outcomes in children.

Additionally, public health initiatives aimed at preventing iron deficiency through fortification of staple foods and education on proper nutrition are crucial. These measures could significantly reduce the burden of iron deficiency and its associated complications, including febrile convulsions. Further research is warranted to explore the underlying mechanisms linking iron deficiency to febrile convulsions and to develop targeted interventions for at - risk populations.

The study has several strengths, including its prospective design, which allows for the establishment of a temporal relationship between IDA and febrile convulsions. The comprehensive assessment of demographic and clinical characteristics ensures that the observed associations are robust and not confounded by other factors. However, there

are also limitations to consider. The use of convenience sampling may introduce selection bias, although efforts were made to recruit a representative sample from the hospital population. Additionally, the study was conducted in a single tertiary care hospital, which may limit the generalisability of the findings to other settings.

4. Conclusion

In conclusion, this study provides compelling evidence that iron deficiency anaemia is significantly associated with a higher incidence and increased severity of febrile convulsions in pediatric patients. The findings underscore the importance of early diagnosis and treatment of iron deficiency to prevent its adverse neurological consequences. Public health initiatives and clinical practices should prioritise the prevention and management of iron deficiency to reduce the burden of febrile convulsions and improve overall child health outcomes. Future research should focus on elucidating the mechanisms underlying this association and developing targeted interventions to protect at-risk populations from the detrimental effects of iron deficiency.

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