



A CROSS SECTIONAL CASE CONTROL STUDY ON ROLE OF IRON DEFICIENCY ANEMIA IN FEBRILE SEIZURES -

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Abstract

Background: Febrile seizures (FS) are the most common convulsive disorder in children aged 6–60 months. Iron deficiency anaemia (IDA) has been proposed as a potential risk factor, yet the precise relationship remains debated. This study aimed to evaluate the role of IDA in FS by comparing haematological parameters between children with and without febrile seizures.

Methods: A hospital-based cross-sectional comparative study was conducted on 100 children (6–60 months). Group I (n=50) comprised children with febrile seizures and Group II (n=50) comprised febrile children without seizures. Haematological parameters — Haemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), and Serum Ferritin — were compared between the two groups. Chi-square test and Pearson's correlation were used for statistical analysis.

Results: Anaemia (Hb <11 g/dL) was present in 76% of Group I vs. 44% of Group II (p=0.001, OR=3.97). Low MCV (<70 fL) was found in 64% vs. 38% (p=0.009, OR=2.86). Low MCH (<27 pg) was present in 84% vs. 64% (p=0.02, OR=2.92). Serum ferritin <30 ng/mL was found in 68% vs. 24% (p=0.00001, OR=6.58). No statistically significant association was found between IDA parameters and seizure recurrence.

Conclusion: Iron deficiency anaemia is a significant and potentially modifiable risk factor for febrile seizures in children. Early detection and timely correction of IDA may help prevent febrile seizures in this age group. Routine screening for IDA is recommended in all children presenting with febrile seizures.

Keywords: *Iron deficiency anaemia; Febrile seizures; Children; Serum ferritin; Haemoglobin; Paediatrics*

1. Introduction

Febrile seizures (FS) are the most common seizure disorder in children, occurring in 2–5% of the paediatric population between 6 and 60 months of age. While generally considered benign, they cause significant parental anxiety and impose a burden on healthcare resources. Understanding the modifiable risk factors associated with febrile seizures is therefore of considerable clinical importance.

Iron deficiency anaemia (IDA) is one of the most prevalent nutritional deficiencies worldwide and disproportionately affects children in developing countries. Iron plays a critical role in neurotransmitter synthesis, myelination, and neuronal energy metabolism. A deficiency of iron may alter the threshold for neuronal excitability and predispose susceptible children to seizures in the setting of fever. Several case-control studies have explored the relationship between IDA and FS with varying results. Some investigators have found a significantly higher prevalence of IDA in children with febrile seizures compared to febrile controls, while others have failed to demonstrate a significant association. Two systematic reviews and meta-analyses have concluded that IDA is a predisposing factor for febrile convulsions, particularly in regions with a moderate-to-high prevalence of anaemia. Despite this growing body of evidence, no prospective comparative study had been performed in the Telangana region of India, where both the prevalence of IDA and febrile seizures are expected to be high given the regional epidemiological profile. This study was therefore undertaken to determine the haematological profile — Haemoglobin, MCV, MCH, and Serum Ferritin — in children with febrile seizures admitted to a tertiary care hospital in Hyderabad, and to compare these parameters with febrile children without seizures, thereby evaluating the role of iron deficiency in febrile seizures.

2. Patients and Methods

2.1 Study Design and Setting

This was a hospital-based cross-sectional comparative study conducted in the Department of Paediatrics at Owaisi Hospital and Princess Esra Hospital, Deccan College of Medical Sciences, Hyderabad — the largest tertiary care centre in the state of Telangana. The study was conducted from January 2019 to June 2020. Ethical clearance was obtained from the Institutional Review Board of Deccan College of Medical Sciences.

2.2 Study Population and Sample Size

Children between 6 and 60 months of age admitted during the study period were enrolled. The prevalence of febrile seizures was estimated at 2–5% in this age group. Using the lowest prevalence (2%) with a 95% confidence interval and an allowable absolute error of 3%, the minimum sample size was calculated as 86; this was rounded up to 100 after adding a 10% attrition margin ($N = 94.6 \approx 100$).

The study population was divided into two equal groups:

- Group I (Cases, $n=50$): Children with febrile illness and seizures.
- Group II (Controls, $n=50$): Children with febrile illness but without seizures.

2.3 Inclusion and Exclusion Criteria

Children aged 6–60 months presenting with febrile illness with or without seizures were included if their parents/guardians provided written informed consent. Children with central nervous system infections, developmental delay or neurological deficit, protein-energy malnutrition, those already on iron therapy or regular blood transfusion, and those whose guardians declined consent were excluded.

2.4 Data Collection and Laboratory Investigations

Demographic data, seizure characteristics (type, number of episodes), nature of the febrile illness, family history of epilepsy or febrile seizures, temperature at admission, and nutritional status were recorded on a structured proforma. Blood samples were collected at admission. Haemoglobin, MCV, and MCH were measured by automated analyser, and Serum Ferritin was measured by chemiluminescence method.

2.5 Operational Definitions

Iron deficiency anaemia was defined as the coexistence of: (1) Haemoglobin <11 g/dL in children under 5 years, or <11.5 g/dL in older children; (2) MCV <70 fL; (3) MCH <27 pg; and (4) Serum ferritin <30 μ g/dL (a higher cut-off was applied given that serum ferritin is an acute-phase reactant whose level rises in inflammatory conditions including fever).

2.6 Statistical Analysis

Data were entered and analysed using Microsoft Excel 2010 and Epi Info 7.2.0. Continuous variables are reported as mean $\pm$ SD. Categorical variables are presented as frequency and percentage. The Student's t-test was used for intergroup comparison of continuous variables. Pearson's Chi-square test was used to assess associations between categorical variables. Odds ratios with 95% confidence intervals were calculated. A p-value of <0.05 was considered statistically significant.

3. Results

3.1 Demographic Characteristics

Both groups were comparable in terms of age and sex distribution (Table 1). In Group I, the largest age cohort was 12–23 months (46%), followed by 6–11 months (34%), 24–35 months (14%), 36–47 months (4%), and 48–60 months (2%). Similarly, in Group II, 12–23 months was the most common age group (44%). Males predominated in both groups: 68% in Group I and 64% in Group II.

Table 1. Age Distribution of Study Population

Age (months)	Group I – Freq.	Group I – %	Group II – Freq.	Group II – %
6–11	17	34	13	26
12–23	23	46	22	44
24–35	7	14	6	12
36–47	2	4	4	8
48–60	1	2	3	6
Total	50	100	50	100

3.2 Socio-Economic Status

The majority of children in Group I (42%) and Group II (30%) belonged to Kuppaswamy socio-economic class IV, reflecting the predominantly lower-middle and lower socio-economic strata served by the institution.

3.3 Seizure Characteristics

Among Group I, 86% had simple febrile seizures and 14% had complex febrile seizures. A single episode of seizure was recorded in 64%, while 36% had multiple episodes. A past history of febrile seizures was present in 34%, and a positive family history of febrile seizures was documented in 10%.

3.4 Diagnosis in Control Group

The predominant diagnosis in Group II was pneumonia (54%), followed by urinary tract infection (24%), viral fever (16%), enteric fever (4%), and septicaemia (2%).

3.5 Haematological Parameters

All four haematological parameters studied showed a statistically significant association with febrile seizures (Table 2).

Table 2. Comparison of Haematological Parameters between Groups

Parameter	Group I (%)	Group II (%)	Chi-square	P value	Odds Ratio (95% CI)
Hb <11 g/dL	76%	44%	X ² =10.67	0.001*	3.97 (1.7–9.63)
MCV <70 fL	64%	38%	X ² =6.76	0.009*	2.86 (1.27–6.29)
MCH <27 pg	84%	64%	X ² =5.198	0.02*	2.92 (1.13–7.95)
Serum Ferritin <30 ng/mL	68%	24%	X ² =19.48	0.00001*	6.58 (2.7–16.42)

* Statistically significant ($p < 0.05$)

Anaemia (Hb <11 g/dL) was present in 76% of Group I compared to 44% of Group II, a highly significant difference ($p=0.001$, OR=3.97). Children in the febrile seizure group were nearly four times more likely to be anaemic than febrile controls. The prevalence of low MCV (<70 fL) was significantly higher in Group I (64%) than Group II (38%) ($p=0.009$, OR=2.86), indicating a microcytic pattern more prevalent in seizure cases.

Low MCH (<27 pg) was found in 84% of Group I vs. 64% of Group II ($p=0.02$, OR=2.92). The association remained statistically significant.

The most striking finding was that of serum ferritin: 68% of children in Group I had serum ferritin <30 ng/mL, compared to only 24% in Group II ($p=0.00001$, OR=6.58). This nearly seven-fold odds ratio represents the strongest haematological predictor of febrile seizures in this study.

3.6 Association with Seizure Recurrence

When the haematological parameters were analysed specifically against seizure recurrence (first episode vs. past history of febrile seizures) within Group I, no statistically significant association was found for any of the four parameters (Hb: $p=0.9$; MCV: $p=0.47$; MCH: $p=0.4$; serum ferritin: $p=0.11$). This suggests that while IDA predisposes to the occurrence of febrile seizures, it does not independently influence their recurrence.

4. Discussion

This study demonstrated a statistically significant association between iron deficiency anaemia and febrile seizures in children aged 6–60 months. All four haematological markers — Hb, MCV, MCH, and serum ferritin — were significantly lower in children with febrile seizures compared to febrile controls, consistent with a pattern of iron deficiency. The most compelling finding was the serum ferritin result. With an odds ratio of 6.58 (95% CI 2.7–16.42, $p<0.00001$), children with low serum ferritin were over six times more likely to have febrile seizures than those with normal ferritin levels. This aligns closely with findings from Jang et al., who reported an odds ratio of 6.18 for serum ferritin <30 ng/mL in a prospective South Korean case-control study, and from Rashid et al., who found low serum ferritin in 11 of 29 febrile seizure cases but none among 25 febrile controls.

The biological plausibility of this association is supported by the role of iron in neurological function. Iron is essential for the synthesis of dopamine, serotonin, and GABA — neurotransmitters that regulate neuronal excitability. Iron is also critical for myelination and energy-dependent ion transport. Deficiency of iron may lower the seizure threshold, making the febrile brain more susceptible to convulsions. The observation that serum ferritin — the earliest and most sensitive marker of iron depletion — shows the strongest association supports the hypothesis that pre-anaemic iron deficiency, rather than established anaemia, may be the key pathophysiological factor.

Our finding that anaemia was present in 76% of febrile seizure cases (vs. 44% in controls, OR=3.97) is comparable to the 58% vs. 39% rates reported by Hussain et al. and the 65.52% vs. 31.03% rates from Sahar et al. Minor discrepancies may reflect differences in the diagnostic cut-off values for Hb, the age distribution of study populations, and regional dietary iron intake.

The absence of a significant relationship between IDA and seizure recurrence in our study is consistent with findings from Kumar et al. and others. This suggests that iron deficiency may lower the initial threshold for a seizure but does not specifically govern the propensity for recurrence, which is likely governed by other neurological and genetic factors.

A limitation of this study is the cross-sectional design, which precludes causal inference. It is possible that the stress response of a seizure episode may itself lower serum iron or ferritin transiently, although ferritin is generally elevated in inflammatory states, making this bias conservative. The relatively small sample size is another limitation. Future work should include a prospective design with randomisation to iron supplementation to test whether correction of IDA reduces the incidence of first febrile seizures.

5. Conclusion

This study confirms that iron deficiency anaemia is a significant and potentially modifiable risk factor for febrile seizures in children aged 6–60 months. All key haematological indices — haemoglobin, MCV, MCH, and serum ferritin — were significantly lower in children with febrile seizures than in febrile controls. The odds of febrile seizures were nearly 6.6 times higher in children with low serum ferritin. Iron deficiency does not appear to independently influence seizure recurrence. Given that IDA is highly prevalent in the paediatric population of developing nations and is readily treatable, early screening and timely correction of iron deficiency may represent an effective, low-cost intervention to reduce the burden of febrile seizures in this age group.

Routine serum ferritin estimation is recommended in all children presenting with a first febrile seizure, and iron supplementation should be considered where deficiency is confirmed.

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