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Original Research Article

Association Between Iron Deficiency Anemia and Febrile Seizures in Children Aged 6 Months to 5 Years

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Name of Author:

Dr- Waqar Anwar[1], Dr Amara Akram[2], Dr Fawad Ahmed[3], Dr Sadia Amir[4], Dr Umair Ul Hassan[5], Dr Afifa Munir Ahmad[6] and Dr Ahmad Yar[7]

Affiliation: *[1]MBBS, FCPS Peads Senior Registar Paeds Department, Islam Medical and Dental college, Sialkot*

[2]MBBS, FCPS Peadiatrics Consultant Child Specialist, Provincial Headquarter Hospital, Gilgit Baltistan

[3]MBBS, FCPS Senior Registrar Paediatrics, Islam Medical and Dental college, Sialkot

[4]MBBS, FCPS Senior Registrar Paediatrics, Lahore General Hospital, Lahore

[5]MBBS, FCPS Senior Registrar Paediatrics, M. Islam Teaching Hospital, Gujranwala

[6]Senior Registrar Paediatrics, Queens Medical College, Kasur

[7]Medical Officer, DHQ Hospital, Kasur.

Corresponding Author:

Dr. Waqar Anwar

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Abstract: ***Background***: Febrile seizures are the most common convulsive disorder in early childhood, and iron deficiency anemia may lower seizure threshold by affecting cerebral oxygenation and neurotransmitter metabolism. ***Objective***: To determine the association between iron deficiency anemia and febrile seizures in children aged 6 months to 5 years. ***Methodology***: This was a hospital-based cross-sectional analytical study conducted at Islam Teaching Hospital, Sialkot from 20-01-2025 to 31-06-2025, including 250 children aged 6 months to 5 years presenting with fever, with or without seizures. Data were recorded using a structured proforma after obtaining informed consent from parents or guardians. Demographic variables included age, gender, residence, and nutritional status. ***Results***: The mean age was 27.5 ± 12.7 months with male predominance (60%). Children with febrile seizures had significantly lower hemoglobin (9.6 ± 1.4 vs 11.1 ± 1.3 g/dL), MCV (67.8 ± 6.9 vs 74.3 ± 7.1 fL), MCH (23.6 ± 3.1 vs 27.2 ± 3.4 pg), and ferritin levels (10.9 ± 4.3 vs 18.6 ± 6.1 µg/L). Iron deficiency anemia was more frequent among seizure cases (62.4% vs 31.2%). Children with anemia had over threefold increased risk of febrile seizures (OR 3.62, p = 0.001). ***Conclusion***: It is concluded that iron deficiency anemia is strongly associated with febrile seizures and represents a preventable risk factor. Early detection and iron supplementation may contribute to reducing seizure burden in children.

Keywords: Febrile seizures, iron deficiency anemia, hemoglobin, ferritin, children, risk factors.

INTRODUCTION

The most frequent convulsive disorder of early childhood is febrile seizures, but it is also found in about 2-5 percent of children between the ages of 6 months and 5 years. They are a common reason of emergency visits and a major cause of parental concern, although in general, they are not very serious and the chances of recurrence are also high [1]. It is therefore important to identify modifiable risk factors to prevent disease and improve clinical outcomes [2]. Febrile seizures have also been investigated as a possible cause by iron deficiency anemia (IDA). Iron is essential for brain development, oxygen transport, myelination, and the synthesis of neurotransmitters that regulate neuronal excitability [3]. The deficiency can disrupt inhibitory systems and reduce the seizure threshold, thereby predisposing to convulsions during febrile illness [4]. One of the most common nutritional disorders among young children is IDA which is common especially in the developing countries where high growth rate, poor dietary intake and frequent infections are prevalent [5]. Childhood anemia is very

high in Pakistan and therefore a serious issue of concern in the country's public health and a potential cause of neurological complications [6]. Low hemoglobin and ferritin concentrations can have the effect of compromising cerebral oxygenation and energy metabolism and this may further predispose children to seizures [7].

Other researchers have reported lower hemoglobin and serum ferritin levels in children with febrile seizures compared with febrile controls, which is consistent with a positive association [8]. Nevertheless, conflicting findings have been reported in other studies, indicating that additional testing in other populations is warranted [9]. Such differences could be associated with variations in nutritional and socioeconomic status, as well as study design [10]. Febrile seizures are clinically relevant for establishing the association between iron deficiency and febrile seizures, as iron deficiency is preventable and can be treated without complications. Later diagnosis and supplementation may have the potential to lower the risk of seizures and enhance the neurological condition [11]. Simple and cost-effective evaluation tools are routine hematological markers, i.e. hemoglobin and ferritin [12]. Although the prevalence of febrile seizures and iron deficiency anemia is high, there is no local data that explores the relationship between the two conditions [13]. Investigation of this relationship can inform targeted prevention strategies and more effective pediatric treatment [14].

Objective

To determine the association between iron deficiency anemia and febrile seizures in children aged 6 months to 5 years.

METHODOLOGY

This was a hospital-based cross-sectional analytical study conducted at Islam Teaching Hospital, Sialkot from 20-01-2025 to 31-06-2025, including 250 children aged 6 months to 5 years presenting with fever with or without seizures. Participants were enrolled consecutively through non-probability purposive sampling technique.

Eligible participants included children aged 6–60 months with documented fever (≥38°C). Children with afebrile seizures, epilepsy, central nervous system infections (meningitis or encephalitis), developmental delay, metabolic disorders, chronic systemic illness, recent iron therapy or blood transfusion within the last three months, or incomplete laboratory records were excluded.

Data Collection

Data were recorded using a structured proforma after obtaining informed consent from parents or guardians. Demographic variables included age, gender, residence, and nutritional status. Based on clinical presentation, participants were categorized into two groups:

- Group A (Febrile seizure group): Children presenting with fever associated with generalized seizures without evidence of central nervous system infection or metabolic abnormality
- Group B (Febrile control group): Children presenting with fever without seizures

Clinical variables included duration of fever, type of infection, seizure characteristics, and family history of febrile seizures. A 3–5 mL venous blood sample was collected under aseptic conditions for complete blood count and iron profile. Laboratory parameters included hemoglobin level, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), serum ferritin, and peripheral smear findings. Iron deficiency anemia was defined as hemoglobin<11 g/dL with low MCV (<70 fL), low MCH (<27 pg), and serum ferritin<12 µg/L. All tests were performed in the hospital laboratory using standard protocols.

Statistical Analysis

Data were entered and analyzed using SPSS version 25. Shapiro–Wilk test was applied to assess normality. Continuous variables such as age, hemoglobin, MCV, MCH, and serum ferritin were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using an independent t-test for quantitative variables and a chi-square test for categorical variables. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 250 children were included, equally divided between febrile seizure and febrile control groups. The mean age was comparable between groups (26.8 ± 12.4 vs 28.1 ± 13.1 months), with overall male predominance (60.0%). Urban residence was slightly more common (64.4%). Mean fever duration (2.2 ± 1.1 days) and average body weight (11.4 ± 3.6 kg) were similar across groups.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n = 250)

Variable	Febrile Seizure (n = 125)	Febrile Control (n = 125)	Total (n = 250)	p-value
Age (months), Mean ± SD	26.8 ± 12.4	28.1 ± 13.1	27.5 ± 12.7	0.432
Male, n (%)	78 (62.4)	72 (57.6)	150 (60.0)	0.448

Female, n (%)	47 (37.6)	53 (42.4)	100 (40.0)	0.448
Urban residence, n (%)	82 (65.6)	79 (63.2)	161 (64.4)	0.689
Rural residence, n (%)	43 (34.4)	46 (36.8)	89 (35.6)	0.689
Fever duration (days), Mean ± SD	2.3 ± 1.1	2.1 ± 1.0	2.2 ± 1.1	0.176
Weight (kg), Mean ± SD	11.2 ± 3.4	11.6 ± 3.7	11.4 ± 3.6	0.391

Mean hemoglobin was reduced (9.6 ± 1.4 vs 11.1 ± 1.3 g/dL), along with lower MCV (67.8 ± 6.9 vs 74.3 ± 7.1 fL), MCH (23.6 ± 3.1 vs 27.2 ± 3.4 pg), and serum ferritin (10.9 ± 4.3 vs 18.6 ± 6.1 µg/L).

Table 2. Hematological and Iron Profile Comparison

Variable	Febrile Seizure (n = 125) Mean ± SD	Febrile Control (n = 125) Mean ± SD	Total Mean ± SD	p-value
Hemoglobin (g/dL)	9.6 ± 1.4	11.1 ± 1.3	10.4 ± 1.6	0.001
MCV (fL)	67.8 ± 6.9	74.3 ± 7.1	71.0 ± 7.8	0.001
MCH (pg)	23.6 ± 3.1	27.2 ± 3.4	25.4 ± 3.8	0.001
Serum ferritin (µg/L)	10.9 ± 4.3	18.6 ± 6.1	14.8 ± 6.7	0.001
RBC count ($\times 10^6$/µL)	4.4 ± 0.7	4.6 ± 0.6	4.5 ± 0.7	0.052

Iron deficiency anemia was markedly more prevalent in the febrile seizure group (62.4%) compared with controls (31.2%). Similarly, microcytosis (67.2% vs 35.2%) and hypochromia (60.8% vs 32.8%) were significantly more common among children with seizures. Overall, nearly half of the study population (46.8%) had iron deficiency anemia.

Table 3. Frequency of Iron Deficiency Anemia

Variable	Febrile Seizure n (%)	Febrile Control n (%)	Total n (%)	p-value
Iron deficiency anemia present	78 (62.4)	39 (31.2)	117 (46.8)	0.001
Iron deficiency anemia absent	47 (37.6)	86 (68.8)	133 (53.2)	0.001
Microcytosis present	84 (67.2)	44 (35.2)	128 (51.2)	0.001
Hypochromia present	76 (60.8)	41 (32.8)	117 (46.8)	0.001

Iron deficiency anemia was strongly associated with febrile seizures, with affected children having over threefold higher odds (OR 3.62). Low hemoglobin (<10 g/dL) and low ferritin (<12 µg/L) were also significant predictors (OR 3.14 and 3.88, respectively). In contrast, age below 24 months and male gender showed no significant association (p>0.05).

Table 4. Risk Association Between Iron Deficiency Anemia and Febrile Seizures

Variable	Category	Odds Ratio (95% CI)	p-value
Iron deficiency anemia	Present vs Absent	3.62 (2.11–6.21)	0.001*
Hemoglobin<10 g/dL	Yes vs No	3.14 (1.86–5.29)	0.001*
Ferritin<12 µg/L	Yes vs No	3.88 (2.25–6.68)	0.001*
Age<24 months	Yes vs No	1.29 (0.79–2.12)	0.301
Male gender	Yes vs No	1.21 (0.73–2.01)	0.448

DISCUSSION

This research determined the relationship between iron deficiency anemia and febrile seizure among children between the ages of 6 months and 5 years and it was found that there was a significant proportion between lower iron status and febrile seizures. There were no significant differences in the basis of demographics like the age structure (27.5 ± 12.7 months on average) and male dominance (60% on average) in both groups. These results show that there was little likelihood of confounding by demographic and clinical characteristics seen in the observed association. Prior studies which assess febrile seizures have indicated similar comparable baseline distributions between cases and the controls [15][16]. The Hematological testing showed that the hemoglobin, MCV, MCH, and serum ferritin levels in children with febrile seizures were much lower. The seizure group had a mean hemoglobin of 9.6 1.4 g/dL as compared to 11.1 1.3 g /dl in controls with low levels of ferritin (10.9 4.3 vs 18.6 6.1 µg/L). These results imply lost iron stores and microcytic

hypochromic anemia, which can adversely affect cerebral blood supply and cause a change in neurotransmitter metabolism, which reduces the seizure threshold. The same has been reported in previous studies which have recorded much lower iron indices in children with febrile seizures [17].

Iron deficiency anemia was significantly more common in cases of seizures (62.4) than in controls (31.2) and therefore almost two-thirds of children suffering had iron deficiency anemia. The prevalence of microcytosis and hypochromia was also highly more common in the seizure group. This great load of anemia raises iron deficiency as a widespread and possibly alterable threat. Similar higher incidence of iron deficiency has been continuously reported in prior studies in patients with febrile seizures [18]. This association was further reinforced by risk analysis, demonstrating that the children who were iron deficient anaemic were more than three times more likely to experience febrile seizures (OR 3.62). Low hemoglobin and low ferritin were also significant predictors and age and gender were not associated with a higher risk. These observations indicate that iron deficiency, not demographic factors is the major contributor to the susceptibility to seizures. Previous studies have similar high ratios of iron deficiency which indicate the biological plausibility of the relationship between the two [19][20]. On the whole, the findings suggest that iron deficiency anemia has a close relationship with febrile seizure and it might be related to the heightened neuronal excitability in febrile disease. Proactive screening of iron status and timely supplementation of high-risk children may be a simple preventive measure to decrease the frequency and reoccurrence of seizures. This study was limited by its cross-sectional single-center design and lack of long-term follow-up, which restricts causal inference and assessment of seizure recurrence or long-term neurological outcomes.

CONCLUSION

It is concluded that iron deficiency anemia is significantly associated with febrile seizures in children aged 6 months to 5 years, with affected children demonstrating lower hemoglobin and ferritin levels and more than threefold increased risk of seizures. Iron deficiency appears to be a modifiable risk factor, and routine screening with early iron supplementation may help reduce the incidence and recurrence of febrile seizures in pediatric populations.

REFERENCES

1. Balgir RS. The burden of haemoglobinopathies in India and the challenges ahead. Curr Sci. 2000;79:1536–1547.
2. Research IC, o. M. Intervention programme for nutritional anaemia and haemoglobinopathies against some primitive tribal populations of India: A national multicentric study. Indian Council of Medical Research; 2010.
3. Dolai TK, Dutta S, Bhattacharyya M, Ghosh MK. Prevalence of hemoglobinopathies in rural Bengal, India. Hemoglobin. 2012;36(1):57–63.
4. Ryan K, Bain BJ, Worthington D, James J, Plews D, Mason A, et al. Significant haemoglobinopathies: guidelines for screening and diagnosis. Br J Haematol. 2010;149(1):35–49.
5. Ghosh K, Colah R, Manglani M, Choudhry VP, Verma I, Madan N, et al. Guidelines for screening, diagnosis and management of hemoglobinopathies. Indian J Hum Genet. 2014;20(2):101–119.
6. Arishi WA, Alhadrami HA, Zourob M. Techniques for the detection of sickle cell disease: a review. Micromachines (Basel). 2021;12(5):519.
7. Tubman VN, Field JJ. Sickle solubility test to screen for sickle cell trait: what's the harm? Hematol Am Soc Hematol Educ Program. 2015:433–435.
8. Surve RR, Mukherjee MB, Kate SL, Nagtilak SB, Wadia M, Tamankar AA, et al. Detection of the beta S gene: evaluation of the solubility test against automated chromatography and haemoglobin electrophoresis. Br J Biomed Sci. 2000;57(4):292–294.
9. Matusik JE, Powell JB, Gregory DM. Rapid solubility test for detection of hemoglobin S. Clin Chem. 1971;17(11):1081–1082.
10. Okwi AL, Ocaido M, Byarugaba W, Ndugwa CM, Parkes A. Sickling and solubility tests and the peripheral blood film method for screening for sickle cell disease. S Afr Med J. 2009;99(12):887–891.
11. Kumar M, Sharma P, Kumar V, Bhargava M. Continuing diagnostic relevance of the sickling test in the era of CE-HPLC. Indian J Hematol Blood Transfus. 2013;29(1):58–60.
12. Jamwal M, Sharma P, Das R. Laboratory approach to hemolytic anemia. Indian J Pediatr. 2020;87(1):66–74.
13. Stephens AD, Colah R, Fucharoen S, Hoyer J, Keren D, McFarlane A, et al. ICSH recommendations for assessing automated HPLC and capillary electrophoresis equipment for quantitation of HbA2. Int J Lab Hematol. 2015;37(5):577–582.
14. Sreedharanunni S, Sharma P, Murgai P, Chhabra S, Das R. Automated alkaline-pH electrophoresis vs CE-HPLC in quantification of HbA2 and variant hemoglobins. Clin Chem Lab Med. 2015;53(11):e301–303.

15. Skogerboe KJ, West SF, Murillo MD, Glass MW, Shaunak S, Tait JF. Genetic screening of newborns for sickle cell disease: correlation of DNA analysis with hemoglobin electrophoresis. Clin Chem. 1991;37(3):454–458.
16. Yang X, Kanter J, Piety NZ, Benton MS, Vignes SM, Shevkoplyas SS. A simple, rapid, low-cost diagnostic test for sickle cell disease. Lab Chip. 2013;13(8):1464–1467.
17. Piety NZ, Yang X, Lezzar D, George A, Shevkoplyas SS. Rapid paper-based test for quantifying sickle hemoglobin. Am J Hematol. 2015;90(6):478–482.
18. Heimlich JB, Chipoka G, Kamthunzi P, Krysiak R, Majawa Y, Mafunga P, et al. Establishing sickle cell diagnostics and characterizing a paediatric sickle cell disease cohort. Br J Haematol. 2016;174(2):325–329.
19. Nnodu O, Isa H, Nwegbu M, Ohiaeri C, Adegoke S, Chianumba R, et al. HemoTypeSC, a low-cost point-of-care testing device for sickle cell disease. Blood Cells Mol Dis. 2019;78:22–28.
20. Shrivas S, Patel M, Kumar R, Gwal A, Uikey R, Tiwari SK, et al. Evaluation of microchip-based point-of-care device 'Gazelle' for diagnosis of sickle cell disease in India. Front Med (Lausanne). 2021;8:639208.

