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Original Research Article

Association of iron deficiency anemia with febrile seizures in pediatric patients

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ABSTRACT

Background: Febrile seizures are the most common seizure disorder in children, occurring in 2-5% of those aged 6 months to 5 years. Although usually benign, they cause significant parental anxiety. This study aimed to evaluate the association of iron deficiency anemia with febrile seizures in pediatric patients.
Methods: A hospital-based prospective case-control study was conducted in the department of pediatrics, American international institute of medical sciences, Udaipur, from March 2023 to August 2024. A total of 100 children aged 6 months-5 years were enrolled, including 50 with febrile seizures (cases) and 50 age-matched febrile children without seizures (controls). Hematological parameters (Hb, MCV, MCH, MCHC, RDW and ferritin) and serum electrolytes (Na^+, K^+ and Ca^{2+}) were measured.
Results: The mean hemoglobin level was significantly lower in cases (9.18±1.86 g/dL) compared to controls (10.65±1.12 g/dL; p=0.001). Other red cell indices and ferritin were lower in cases but not statistically significant. Electrolyte levels were comparable in both groups. Hospitalization was required more frequently among cases (60%) than controls (8%; p<0.001). Complex seizures (62%) were more common than simple seizures (38%), and nearly half (46%) had recurrent episodes.
Conclusions: The study demonstrates a significant association between low hemoglobin and febrile seizures, reinforcing IDA as an important, modifiable risk factor. Routine screening and correction of anemia in early childhood may reduce the incidence and recurrence of febrile seizures.

Keywords: Febrile seizures, Iron deficiency anemia, Hemoglobin, Children

INTRODUCTION

Febrile seizures are the most common type of seizure disorder in children, occurring in 2-5% of those aged between 6 months and 5 years.[1] They are defined as seizures associated with fever without evidence of intracranial infection, metabolic disturbance, or prior afebrile seizures.[2] Although generally benign, febrile seizures are a major cause of parental anxiety due to their sudden onset and dramatic presentation.

The etiology of febrile seizures is multifactorial and includes genetic predisposition, environmental factors, and nutritional deficiencies. Among these, iron deficiency anemia has emerged as an important risk factor. Iron is essential for normal neurological functioning, playing a key role in myelination, neurotransmitter metabolism, and enzymatic processes.[3] Its deficiency may impair oxygen transport to the brain and alter synaptic transmission, thereby lowering the seizure threshold.

Several studies have demonstrated a strong association between iron deficiency anemia and febrile seizures. Bhat et al reported that the prevalence of anemia was significantly higher among children with febrile seizures compared to febrile controls.[4] Similarly, Sit et al found that children with febrile seizures were six times more likely to be iron deficient, with low serum ferritin as a major determinant.[5] Kumar et al also observed significantly lower hemoglobin and ferritin levels in

seizure patients, suggesting that anemia is an independent risk factor for febrile seizures.[6]

On the other hand, some studies have shown contradictory results. Talebian and Momtazmanesh observed a lower incidence of anemia in febrile seizure cases compared to controls.[7] Soheilipoor et al also reported higher rates of anemia among febrile children without seizures, raising questions about the consistency of this association.[8] Despite these variations, meta-analyses have confirmed that iron deficiency anemia is significantly linked with febrile seizures, with nearly double the risk observed in affected children.[9]

This study aimed to evaluate the association of iron deficiency anemia with febrile seizures in pediatric patients.

METHODS

Study design and population

This study was designed as a prospective case-control study conducted in the department of pediatrics, American international institute of medical sciences, Udaipur, Rajasthan. The study was carried out over a period extending from March 2023 to August 2024.

A total of 100 children were included using a convenience sampling method. Out of these, 50 children aged between 6 months and 5 years presenting with febrile seizures were enrolled as cases, while 50 age-matched febrile children without seizures served as controls.

Inclusion criteria

Children aged 6 months to 5 years, fever ≥38°C with or without seizures, febrile seizures diagnosed according to WHO guidelines were included in the study.[2]

Exclusion criteria

Evidence of central nervous system (CNS) infection or the congenital CNS malformations, history of epilepsy or atypical febrile seizures, known metabolic disorders (other than anemia), previously diagnosed hematological malignancies or bleeding disorders, children already receiving iron supplementation, critically ill or unstable patients at the presentation were excluded from the study.

Ethical considerations and data collection

The study was approved by the institutional ethics committee of American international institute of medical sciences, Udaipur, and written informed consent was obtained from parents or guardians in accordance with the Declaration of Helsinki. All participants underwent laboratory investigations including complete blood count (hemoglobin, MCV, MCH, MCHC and RDW), serum ferritin for iron stores, and serum electrolytes (sodium, potassium, calcium) when required. Anemia was defined as hemoglobin <11 g/dL, and iron deficiency anemia was considered when low hemoglobin was associated with reduced serum ferritin levels.

Statistical analysis

All collected data were entered into Microsoft excel and analyzed using SPSS version 20.0 software. Continuous variables were expressed as mean and standard deviation or median with interquartile range, depending on the distribution. Categorical data were presented as frequencies and percentages. Comparisons between cases and controls were performed using the Chi-square test or Fisher's exact test for categorical variables and the independent t test or Mann-Whitney U test for continuous variables. A $p<0.05$ considered statistically significant.

RESULTS

Table 1 shows that majority of cases were between 25-36 months (32%) and 37-48 months (26%), while a higher proportion of controls were in the 6-12 months group. Males predominated among cases (58%). Rural and urban distribution was equal across both groups. Hospitalization was significantly more common among cases (60%) compared to controls (8%). Table 2 show among children with febrile seizures, complex seizures were more frequent (62%) than simple seizures (38%). Nearly half (46%) experienced recurrent seizures. Ear discharge, cough, and cold were the commonest fever triggers.

Table 3 show children with febrile seizures had significantly lower hemoglobin levels compared to controls, indicating a strong association between anemia and seizure occurrence. Other red cell indices (MCV, MCH, MCHC, RDW and ferritin) were lower in cases but did not reach statistical significance. Electrolyte levels, including sodium, potassium, and calcium, were comparable between the two groups.

Table 1: Socio-demographic and clinical characteristics of study participants, (n=100).

Variables	Cases (n=50)	Controls (n=50)	P value
Age group (months)			
6-12	4.0%	26.0%	
13-24	18.0%	20.0%	
25-36	32.0%	14.0%	0.515
37-48	26.0%	18.0%	
49-60	20.0%	22.0%	

Continued.

Variables	Cases (n=50)	Controls (n=50)	P value
Sex			
Male	58.0%	50.0%	0.422
Female	42.0%	50.0%	
Socio-economic status			
High	22.0%	28.0%	0.487
Middle	22.0%	28.0%	
Low	56.0%	44.0%	
Hospitalization required	60.0%	8.0%	<0.001
Family history of seizures	42.0%	40.0%	0.839

Table 2: Clinical profile of febrile seizure cases, (n=50).

Variables	Cases
Type of seizure	
Simple	38.0%
Complex	62.0%
Recurrence of seizures	
Yes	46.0%
No	54.0%
Triggers of fever	
Cold	18.0%
Cough	20.0%
Ear discharge	24.0%
Urinary tract infection	8.0%
Others	30.0%

Table 3: Hematological and biochemical parameters of cases and controls.

Parameters	Cases (n=50)	Controls (n=50)	P value
Hemoglobin (g/dL)	9.18±1.86	10.65±1.12	0.001
MCV (fL)	73.16±6.12	74.97±5.91	0.509
MCH (pg)	23.83±1.71	25.54±1.63	0.396
MCHC (%)	30.42±1.91	31.09±2.20	0.431
RDW (%)	14.83±1.74	15.15±1.63	0.345
Plasma ferritin (ng/mL)	31.71±9.82	34.72±8.51	0.115
Serum sodium (mEq/L)	134.79±2.86	135.40±2.82	0.297
Serum potassium (mEq/L)	4.22±0.45	4.26±0.46	0.693
Serum calcium (mg/dL)	9.48±0.57	9.48±0.62	0.999

DISCUSSION

The present study was undertaken to evaluate the association of iron deficiency anemia with febrile seizures in children aged 6 months to 5 years. Our findings demonstrated that anemia was significantly more prevalent among children with febrile seizures compared to febrile children without seizures. Hemoglobin levels were also significantly lower in cases, although differences in other red cell indices such as MCV, MCH, MCHC, RDW, and plasma ferritin did not reach statistical significance.

Electrolyte disturbances including sodium, potassium, and calcium were not significantly different between the groups. These results highlight anemia, particularly low hemoglobin levels, as an important risk factor for febrile seizures.

Our findings are consistent with earlier reports which indicated a high prevalence of anemia among children with febrile seizures. Sahib et al similarly found a significant association between low hemoglobin and febrile seizures, reporting that children with seizures were nearly twice as likely to be anemic compared to controls.[10] Bhat et al also reported that the prevalence of iron deficiency anemia was five times higher among febrile seizure patients.[4] These results strengthen the evidence that iron deficiency anemia is a modifiable risk factor in seizure pathogenesis.

The biological plausibility of this association lies in the critical role of iron in neuronal function. Iron deficiency affects neurotransmitter metabolism, myelination, and oxidative metabolism, all of which contribute to neuronal hyperexcitability.[3] Sit et al further demonstrated that serum ferritin levels were significantly lower in seizure

patients, suggesting that iron deficiency impairs neuronal thresholds for excitability and increases seizure susceptibility.[5] Similarly, Kumar et al found both hemoglobin and ferritin levels to be consistently reduced among febrile seizure patients, irrespective of fever intensity, indicating that iron deficiency independently contributes to seizure risk.[6]

Interestingly, some studies have reported contrasting findings. Talebian and Momtazmanesh noted a lower incidence of anemia in seizure patients compared to controls.[7] Soheilipoor et al also reported that anemia was more common among febrile children without seizures than those with seizures.[8] These inconsistencies may be explained by differences in anemia definitions, regional nutritional backgrounds, or small sample sizes. Despite these variations, meta-analyses such as that conducted by Kwak et al have confirmed a significant association between iron deficiency anemia and febrile seizures, with pooled odds ratios showing nearly double the risk.[9]

The present study did not observe significant differences in plasma ferritin levels between cases and controls, although mean values were lower in the seizure group. This aligns with the findings of Ghosal, who reported that while hemoglobin levels may not differ substantially, indices like MCV, MCH, and ferritin are more reliable indicators of iron deficiency in febrile seizure populations.[11]

Moreover, Alatwani et al emphasized that iron deficiency may also influence the recurrence and complexity of febrile seizures, highlighting the importance of early detection and treatment.[12]

In contrast, serum electrolyte levels in our study did not differ significantly between cases and controls. While previous studies have suggested that hyponatremia may lower seizure thresholds in febrile illnesses, our results indicate that anemia rather than electrolyte imbalance is a stronger determinant of seizure susceptibility.[13-15] This finding is consistent with reports by Kumar et al who concluded that anemia and hyponatremia may both play roles, but anemia demonstrated a stronger and more consistent association.[16,17]

CONCLUSION

Overall, the findings of this study reinforce that iron deficiency anemia is an important, modifiable risk factor for febrile seizures. Correcting anemia in early childhood could play a key role in reducing the incidence and recurrence of febrile seizures.

Public health measures such as routine screening for anemia, iron supplementation, and improved nutrition strategies for children may therefore help in lowering the burden of this condition, particularly in regions with high prevalence of childhood anemia.

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