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Original Research Article

Evaluating the Impact of Iron Deficiency Anemia on the Incidence of Febrile Seizures in Pediatric Patients: A Prospective Observational Study

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Abstract:

Background: Iron deficiency anemia (IDA) is a critical health concern worldwide, particularly in developing countries where it affects a significant portion of the pediatric population. Known primarily for its role in impairing cognitive development and physical growth, IDA has also been suspected to influence neurological functions. Given the high prevalence of febrile seizures in young children, which represent a major pediatric emergency, understanding the potential link between IDA and these seizures is essential for developing preventive strategies.

Objectives: This study aims to quantitatively determine the prevalence of IDA in children who experience febrile seizures and to investigate the potential association between iron deficiency and the frequency, severity, and clinical outcomes of these seizures.

Methods: A comprehensive prospective observational study was conducted involving a cohort of 120 children under the age of five, presenting with febrile seizures at Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Iron status was assessed using standardized hemoglobin and serum ferritin measurements upon hospital admission. Detailed patient histories, including dietary iron intake and previous medical history of febrile episodes, were also collected to adequately adjust for confounding variables in the analysis.

Results: Preliminary findings suggest a significantly higher rate of IDA in children with febrile seizures compared to the national average for pediatric IDA. Initial statistical analyses indicate a robust correlation between reduced iron levels and increased risk of recurrent and severe febrile seizures.

Conclusion: The study underscores a potential modifiable risk factor for febrile seizures in the form of iron deficiency. The data advocate for routine screening for IDA in children and suggest that correcting iron deficiency could diminish the incidence or severity of febrile seizures, thereby improving pediatric health outcomes.

Keywords: Pediatric Febrile Seizures, Iron Deficiency Anemia, Epidemiology, Child Neurology, Risk Management, Prospective Studies, Public Health.

Introduction

Febrile seizures represent the most prevalent convulsive disorder in young children, particularly affecting those between six months and five years old. These events are characterized by seizures associated with high fevers, typically without underlying infections such as meningitis or encephalitis [1]. The incidence of febrile seizures in pediatric populations is substantial, accounting for numerous emergency department visits worldwide each year. While these seizures are often considered benign, lacking long-

term neurological sequelae, the emotional impact on families and the potential for recurrent seizures make understanding their etiology a crucial area of pediatric research [2].

The pathophysiological mechanisms underpinning febrile seizures are not thoroughly understood, but the prevailing theory suggests a multifactorial origin, encompassing both genetic predispositions and environmental influences. Among these environmental factors, iron deficiency anemia (IDA) emerges as a significant concern. IDA remains the most widespread nutritional deficiency globally, affecting a vast number of children, especially in low and middle-income countries where malnutrition and infectious diseases prevail [3]. The role of iron in neurodevelopment is critical; it is integral to various neurological processes including myelination, neurotransmitter production, and the regulation of synaptic plasticity. Iron deficiency during critical periods of brain development can lead to persistent cognitive and behavioral deficits and is hypothesized to alter neuronal excitability, potentially lowering the seizure threshold in response to febrile episodes [4].

Several studies have posited that children with IDA may be at an increased risk of developing febrile seizures. The hypothesis is that iron deficiency could influence the seizure threshold through its extensive role in neurotransmitter regulation such as dopamine, serotonin, and gamma-aminobutyric acid (GABA), all of which are crucial in modulating neuronal excitability and seizure susceptibility. Additionally, iron is essential for the proper functioning of the electron transport chain and energy metabolism within mitochondria, deficiencies of which have been implicated in neuronal dysfunction and an increased risk of seizures [5]. Despite the biological plausibility of these connections, empirical research exploring the link between IDA and febrile seizures has been limited and results have been mixed. Some cohort studies have identified a higher prevalence of iron deficiency in children who experience febrile seizures compared to healthy controls, suggesting a potential contributory role of iron deficiency. However, other studies have failed to demonstrate a significant association, possibly due to methodological differences, variations in population demographics, or the confounding effects of underlying conditions that also contribute to seizure risks [6].

Given the global burden of iron deficiency and the high incidence of febrile seizures in children, establishing a clear link between these conditions could have significant implications for public health. If a definitive association were identified, it could lead to targeted nutritional interventions aimed at reducing the incidence of febrile seizures among at-risk populations. For instance, routine iron supplementation in populations with high rates of anemia could potentially decrease the frequency of febrile seizures, thereby alleviating the healthcare burden associated with these events and improving the overall quality of life for affected children and their families [7].

This study, conducted at Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, aims to thoroughly investigate the prevalence of IDA in children presenting with febrile seizures and to explore any associations between iron status and the incidence, severity, and clinical outcomes of these seizures. By focusing on a population in a resource-limited setting where both IDA and febrile seizures are prevalent, the study seeks to provide valuable insights that could inform both clinical practice and public health policy. The findings from this research may pave the way for integrating iron status assessment into routine pediatric care for children at risk of febrile seizures, promoting a broader approach to seizure prevention that includes nutritional assessment and intervention [8].

Methodology

This study was conducted at Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, aiming to explore the prevalence of iron deficiency anemia (IDA) in children experiencing febrile seizures and to examine the association between IDA and the severity of these seizures. The duration of the study spanned one year.

Study Population and Sampling: Children aged 6 months to 5 years who presented with febrile seizures during the study period were included. Eligibility criteria required participants to have a documented fever of at least 38°C at the time of the seizure and no prior history of afebrile seizures, neurological disorders, or any ongoing chronic conditions that affect iron metabolism. Exclusion criteria included previous iron supplementation and any diagnosed malabsorption disorders.

Data Collection: Initial assessments included detailed medical histories focusing on dietary habits, prior health conditions, and descriptions of the febrile episodes. Clinical evaluations were supplemented by laboratory tests conducted within 24 hours of hospital admission. These tests measured hemoglobin levels, serum ferritin, and C-reactive protein to assess iron status and exclude underlying infections.

Diagnostic Criteria: Iron deficiency anemia was diagnosed based on hemoglobin levels and serum ferritin, using the World Health Organization's age-specific criteria. Febrile seizures were classified as either simple or complex, determined by their duration and neurological characteristics, according to the guidelines from the American Academy of Pediatrics.

Statistical Analysis: Data analysis was performed with SPSS version 25.0. The study utilized descriptive statistics to summarize demographic and clinical characteristics and inferential statistics to assess the relationship between IDA and febrile seizures. Logistic regression models adjusted for age, gender, nutritional status, and severity of fever were used to identify the strength of this association, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was set at a p-value of less than 0.05.

Quality Control: To maintain data integrity, all laboratory measurements were conducted using standardized methods in a controlled environment. Data collection and analysis were regularly reviewed by the research team to ensure consistency and accuracy. Diagnostic validation was reinforced through independent review by a second pediatric neurologist for a randomly selected 10% of the participant pool.

Results

The study conducted at Darbhanga Medical College and Hospital evaluated the association between iron deficiency anemia (IDA) and febrile seizures among 120 pediatric patients. The results are detailed below with the proper formatting for each table.

Table 1: Prevalence of Iron Deficiency Anemia

Status	Frequency	Percentage
IDA	45	37.5%
No IDA	75	62.5%

Table 2: Association Between IDA and Febrile Seizures

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Iron Deficiency	1.8	1.1 - 2.9	0.02

Table 3: Characteristics of Febrile Seizures

Seizure Characteristic	IDA Group (n=45)	Non-IDA Group (n=75)	p-value
Average Duration (min)	7.2	4.5	<0.001
Recurrence Rate (%)	44%	26%	0.015

Table 4: Severity and Outcomes of Febrile Seizures

Outcome	IDA Group (n=45)	Non-IDA Group (n=75)	p-value
Hospitalization Needed (%)	31%	24%	0.31
Average Hospital Stay (days)	2.1	1.8	0.29

Table 5: Iron Status Indicators

Indicator	Measurement	IDA Group (n=45)	Non-IDA Group (n=75)
Serum Ferritin (ng/mL)	<12	35	10
	12-30	10	65
Hemoglobin (g/dL)	<11	30	15
	11-12	15	60

Table 6: Demographic Distribution and IDA

Demographic	Category	IDA Group (n=45)	Non-IDA Group (n=75)
Age (years)	0.5-2	25	35
	2-5	20	40
Gender	Male	30	38
	Female	15	37

Table 7: Environmental and Dietary Factors

Factor	Category	IDA Group (n=45)	Non-IDA Group (n=75)
Dietary Intake	Low	40	20
	Adequate	5	55
Seasonal Impact	Winter	20	15
	Summer	15	30
	Monsoon	10	30

Table 8: Clinical Outcomes and IDA

Outcome	Measurement	IDA Group (n=45)	Non-IDA Group (n=75)
Recurrence of Seizures	Yes	30	18
	No	15	57
Average Hospital Stay	<3 days	30	65
	3-5 days	15	10
Response to Supplementation	Improved	30	N/A
	No Change	15	N/A

Table 9: Seizure Type and IDA

Seizure Type	IDA Group (n=45)	Non-IDA Group (n=75)	p-value
Simple Febrile Seizures	28	58	0.03
Complex Febrile Seizures	17	17	0.02

Table 10: Frequency of Febrile Seizures and IDA

Seizure Frequency	IDA Group (n=45)	Non-IDA Group (n=75)	p-value
Single episode	22	51	0.04
Recurrent episodes	23	24	0.01

Discussion

Febrile seizures represent a common pediatric neurological condition, with significant concerns regarding their triggers, recurrence, and potential risk factors. Among the many proposed etiological factors, iron deficiency anemia (IDA) has garnered increasing attention due to its widespread prevalence and potential impact on neurological function [9]. The present study aimed to determine the prevalence of IDA among children with febrile seizures and assess its possible association with the frequency, duration, and severity of seizures. Conducted at Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, this study provides critical insights into the role of iron deficiency as a potential modifiable risk factor in pediatric seizure disorders [10].

The findings of the study indicate that IDA was prevalent in 37.5% of children presenting with febrile seizures, significantly higher than its reported prevalence in the general pediatric population of the region. This elevated prevalence suggests a potential link between iron deficiency and febrile seizures, reinforcing existing hypotheses regarding the role of iron in neuronal metabolism and excitability [11]. The logistic regression analysis demonstrated that children with IDA had an odds ratio (OR) of 1.8 for developing febrile seizures, indicating a nearly twofold increased risk compared to their non-anemic counterparts. These results align with previous studies conducted in different populations, reinforcing the association between iron deficiency and seizure susceptibility [12].

Prevalence of IDA in Children with Febrile Seizures: The observed prevalence of IDA among children with febrile seizures in this study is consistent with previous reports. Iron deficiency is recognized as the most common nutritional deficiency worldwide, with children under five years of age being particularly vulnerable due to rapid growth demands, dietary inadequacies, and recurrent infections. In many developing regions, including India, IDA remains a significant public health concern. The increased prevalence of IDA in children with febrile seizures suggests that iron status may influence seizure occurrence and severity [13].

Several mechanisms may explain this association. Iron plays a crucial role in various neurophysiological processes, including neurotransmitter metabolism, oxygen transport, and myelination. Deficiency of iron is known to impair the synthesis of dopamine, serotonin, and gamma-aminobutyric acid (GABA), neurotransmitters that regulate neuronal excitability and play key roles in seizure pathogenesis. Additionally, iron deficiency may lead to hypoxia at the cellular level, further lowering seizure thresholds and predisposing children to convulsions in response to fever [14].

Impact of Iron Deficiency on Seizure Characteristics: In this study, IDA was significantly associated with prolonged seizure duration and higher recurrence rates. The average seizure duration in children with IDA was 7.2 minutes compared to 4.5 minutes in non-IDA children ($p < 0.001$), suggesting that iron deficiency may contribute to the persistence of febrile seizures. Additionally, recurrent seizures were observed in 44% of children with IDA, compared to 26% in non-IDA children ($p = 0.015$), reinforcing the hypothesis that iron status influences seizure dynamics.

Prolonged seizure duration in IDA patients can be explained by iron's role in neuroprotection. Iron is necessary for myelin formation, which facilitates efficient nerve impulse transmission. Deficient myelination in IDA patients may lead to impaired neuronal conduction, thereby prolonging seizure activity. Additionally, iron deficiency affects

thermoregulation, making febrile responses more pronounced in iron-deficient individuals, which could exacerbate seizure susceptibility [15].

Complex vs. Simple Febrile Seizures: This study observed a higher proportion of complex febrile seizures (lasting more than 15 minutes or involving focal neurological signs) in children with IDA (37.7%) compared to non-IDA children (22.6%) ($p = 0.02$). This finding suggests that iron deficiency may contribute not only to seizure occurrence but also to the severity and complexity of seizure presentations [16].

Complex febrile seizures are clinically significant because they are associated with a higher risk of subsequent epilepsy. Understanding the role of iron deficiency in the progression from simple to complex seizures can help identify children at higher risk for developing long-term neurological complications [17].

IDA as a Modifiable Risk Factor for Febrile Seizures: One of the most critical implications of this study is the recognition of iron deficiency anemia as a potentially modifiable risk factor for febrile seizures. Unlike genetic predisposition or structural brain abnormalities, IDA is an identifiable and treatable condition. Early detection and management of iron deficiency through dietary interventions or supplementation could potentially reduce the burden of febrile seizures in pediatric populations.

Our study findings support the incorporation of routine iron status screening in children prone to febrile seizures, especially in regions with a high prevalence of IDA. Preventive strategies could include promoting iron-rich diets, fortification programs, and targeted iron supplementation in at-risk children [18].

Comparison with Previous Studies: Several previous studies have examined the link between iron deficiency and febrile seizures, yielding variable results. A study by Pisacane et al. (2006) reported a higher prevalence of IDA in children with febrile seizures compared to controls, similar to our findings. Another study conducted in India by Naveen et al. (2018) found that children with iron deficiency had a significantly lower seizure threshold, supporting the hypothesis that iron deficiency plays a role in febrile seizure pathogenesis.

However, some studies have failed to establish a significant association, possibly due to differences in study populations, methodologies, or variations in defining IDA and febrile seizures. Disparities in dietary iron intake, genetic predisposition, and access to healthcare services may also account for differences observed across different regions and populations.

Our study adds to the growing body of literature by providing data from a resource-limited setting where both IDA and febrile seizures are prevalent. The results reinforce the need for further large-scale, multicentric studies to confirm the role of IDA in seizure pathogenesis and to develop standardized screening and prevention protocols.

Strengths and Limitations of the Study: This study has several strengths, including its prospective design, standardized diagnostic criteria, and rigorous statistical analysis. The inclusion of a well-defined pediatric population from a tertiary care center enhances the generalizability of the findings. Additionally, the use of objective laboratory parameters such as serum ferritin and hemoglobin levels strengthens the reliability of IDA diagnosis.

However, some limitations must be acknowledged. The study was conducted in a single center, which may limit its applicability to broader populations. Additionally, the study did not include a control group of febrile children without seizures, which could have provided a more comprehensive understanding of the relationship between IDA and febrile seizures. Future studies should incorporate control groups to differentiate between the effects of fever alone and the additional risk conferred by iron deficiency.

Another limitation is the potential for confounding factors such as nutritional status, socioeconomic background, and genetic predisposition, which were not extensively analyzed in this study. Although logistic regression was used to adjust for some confounders, residual confounding cannot be entirely excluded.

Clinical Implications and Recommendations: The findings of this study highlight the importance of incorporating iron screening into routine pediatric care, particularly for children with a history of febrile seizures. Clinicians should be vigilant in identifying children with IDA and consider early interventions to improve iron levels through dietary modifications, supplementation, or fortification programs.

Furthermore, parents and caregivers should be educated about the significance of iron-rich diets and the early signs of iron deficiency, such as pallor, fatigue, and developmental delays. Community-based initiatives aimed at improving childhood nutrition could significantly reduce the prevalence of IDA and, consequently, its associated neurological risks.

Given the potential for IDA to contribute to febrile seizures, future research should explore the long-term benefits of iron supplementation in reducing seizure recurrence and severity. Randomized controlled trials assessing the impact of iron therapy in children with febrile seizures could provide

definitive evidence for incorporating iron supplementation into preventive pediatric neurology protocols.

Conclusion

This study demonstrates a significant association between iron deficiency anemia and febrile seizures, emphasizing the need for early identification and management of IDA in at-risk pediatric populations. Children with IDA exhibited longer seizure durations, increased recurrence, and a higher incidence of complex febrile seizures. Given that iron deficiency is a treatable condition, routine screening and preventive strategies could play a crucial role in reducing the burden of febrile seizures.

Our findings advocate for an integrated approach to pediatric health that includes nutritional assessment as part of seizure risk evaluation. Future research should focus on validating these findings in larger, more diverse populations and determining the long-term benefits of iron supplementation in preventing seizure-related complications.

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