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FREQUENCY OF IRON DEFICIENCY ANEMIA IN CHILDREN PRESENTING WITH FEBRILE SEIZURES–A CROSS-SECTIONAL STUDY

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Abstract

Objective: *This study aimed to determine the frequency of iron deficiency anemia (IDA) in children with febrile seizures and investigate its association with febrile convulsions.* **Materials and Methods:** *A cross-sectional study was conducted with 360 children aged 6 months to 5 years presenting with febrile seizures. Demographic data and blood samples were collected for iron-related assessments. Data analysis included descriptive statistics and chi-square tests.* **Results:** *Among the study population, 18.9% (68) of the children had iron deficiency anemia. No significant associations were found between gender, milk-feeding practices, or post-treatment status and iron deficiency anemia. However, a significant association was observed between low-income households and iron deficiency anemia, with a prevalence of 25.2%.* **Conclusion:** *Iron deficiency anemia occurs in a notable proportion of children with febrile seizures. Socioeconomic factors, specifically low-income households, were associated with a higher prevalence of iron deficiency anemia. Early detection and intervention for iron deficiency anemia in children with febrile seizures may help reduce the risk of seizure recurrence and associated complications. Public health strategies targeting low-income households can play a crucial role in improving iron status and preventing iron deficiency anemia in this population.*

Keywords: *Children, prevalence, Febrile seizures, Iron deficiency anemia, Socioeconomic factors*

INTRODUCTION

Febrile seizures are the most common type of seizure in young children, typically occurring between the ages of 6 and 60 months. They are characterized by seizures that are associated with febrile illnesses and usually do not have evidence of central nervous system infections or acute electrolyte abnormalities. Febrile seizures have an incidence rate ranging from 2% to 5% in the pediatric population (1). These seizures have peak incidence rate between 14 and 18 months of age (2). Febrile seizures can be categorized into two types (Fig. 1): simple febrile seizures, which are brief and generalized, and complex febrile seizures, which are longer in duration (>15 minutes), recur within 24 hours, or have focal features (3).

Iron is an essential nutrient that plays a crucial role in various physiological processes, including the transport of oxygen to tissues such as the brain (4). Iron also has importance in the metabolism of neurotransmitters and various enzymes, such as aldehyde oxidases and monoamine oxidases (4). The deficiency of iron has been associated with behavioral disorders, mental retardation, and impaired immune function (4). Neurological symptoms such as irritability, short attention span, learning deficits, sleep disturbance, and weak memory have also been reported in children with iron deficiency . Iron deficiency can lead to neurological complications, including papilledema, pseudotumor cerebri, and 6th nerve palsy, as well as behavioral disturbances (5).

The relationship between iron deficiency and febrile seizures has been the subject of investigation, but findings have been inconsistent throughout previous studies. Some studies have reported a higher prevalence of iron deficiency, with or without anemia, in children with febrile seizures (6). For example, a study by Millichap and colleagues found that iron deficiency, defined as serum ferritin <30 ng/ml, was significantly more prevalent in children with febrile seizures compared to controls (7, 8). Another study by Hartfield and colleagues found an association between iron deficiency anemia and the risk of febrile

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seizures (9). However, other studies have not found a significant association between iron deficiency and febrile seizures (6). Febrile seizures were defined as seizures that occurred in children aged 6 to 60 months, characterized by a body temperature of 38°C or higher, in the absence of central nervous system infections or acute electrolyte abnormalities. A history of prior afebrile seizures was also an exclusion criterion (10). Anemia was defined as a hemoglobin concentration more than 2 standard deviations below the mean reference value for age- and sex-matched healthy populations. According to the World Health Organization (WHO), iron deficiency anemia in children between 6 months and 5 years of age was identified as a hemoglobin level below 11 g/dl. Iron deficiency was determined based on serum iron levels below 50 µg/l, total iron binding capacity (TIBC) above 450 µg/l, and serum ferritin levels below 12 mg/l in children up to 5 years of age (11). The classification of febrile seizures is shown in Fig. 1.

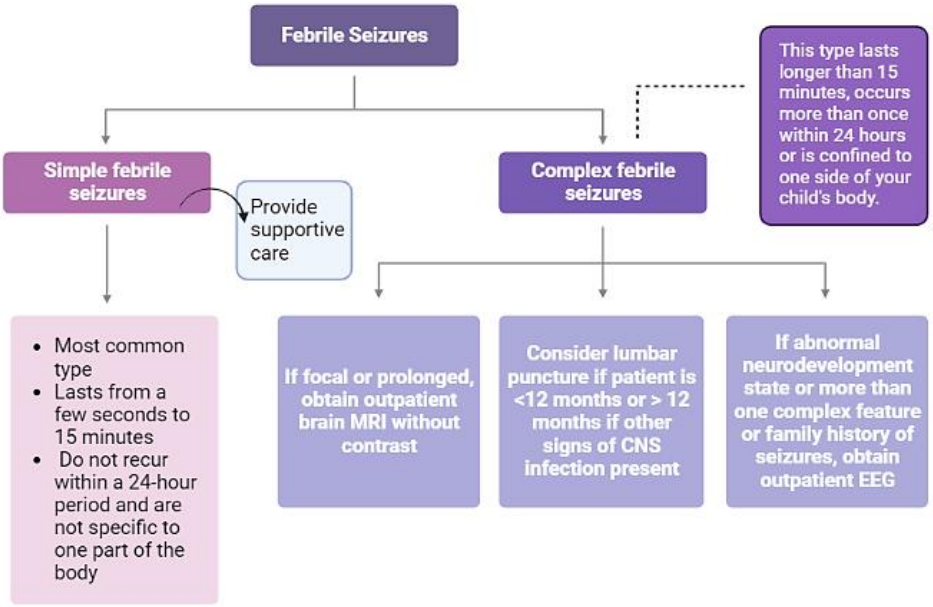

Fig. 1. An overview of the classification of febrile seizures

The prevalence of febrile seizures varies between different regions and populations. For example, a recent study carried out in South Korea has revealed a noteworthy finding regarding the prevalence of febrile seizures. According to the study's findings, the 5-year prevalence of febrile seizures in the South Korean population was determined to be approximately 6.92%. This prevalence rate is notably higher compared to the mean prevalence of 2-5% which has been commonly observed in children worldwide (12). The findings of this study shed light on a potential variation in the incidence of febrile seizures in the South Korean population, highlighting the importance of regional and demographic factors that may influence the prevalence of this medical condition. Development of febrile seizures in children with iron deficiency anemia is shown in Fig. 2.

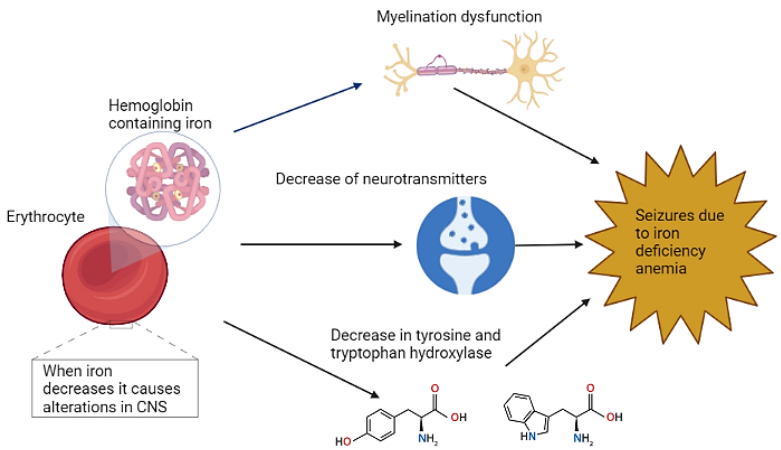

Fig. 2. Development of febrile seizures in children with iron deficiency anemia

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Given the conflicting findings regarding the association between iron deficiency and febrile seizures, as well as the potential neurological implications of iron deficiency, further investigation is warranted. The findings of this study are expected to contribute to our understanding of the frequency of iron deficiency anemia in children presenting with febrile seizures and the potential association between these two conditions.

MATERIALS AND METHODS

STUDY DESIGN

This study employed a cross-sectional design to collect data from a specific point in time. Data collection took place in the Outpatient Department of Children's Hospital at PIMS, Islamabad, providing a suitable environment for the recruitment and examination of participants. The study was conducted over a period of 6 months after receiving ethical approval. To ensure a representative sample, a sample size of 360 cases was calculated based on a 95% confidence level, an 8% margin of error, and an expected prevalence of iron deficiency anemia of 47.05% among children with febrile seizures. Non-probability consecutive sampling was employed to enroll participants who met the selection criteria.

INCLUSION AND EXCLUSION CRITERIA

Children between 6 months and 5 years of age, irrespective of gender, who were presented with febrile seizures as defined previously, were included in the study. Exclusion criteria encompassed atypical febrile seizures, afebrile seizures, evidence of central nervous system infection, chronic neurodevelopmental problems, previous diagnoses of other hematological disorders, bleeding or coagulation disorders, hematological malignancies, current iron supplementation, or any serious illness.

DATA COLLECTION PROCEDURE

To collect data, a total of 360 children meeting the inclusion criteria were consecutively enrolled from the Pediatric Medicine Outpatient Department at PIMS, Islamabad. Prior informed consent was obtained from the parents or guardians of the participants. Demographic information, including the child's name, age, gender, and duration of febrile fits, was recorded. Subsequently, blood samples were collected using sterile techniques and a 3cc disposable syringe, performed by a trained staff nurse. In the present study, meticulous handling of the collected samples was of paramount importance to ensure accurate results. These samples were systematically dispatched to the hospital laboratory for a comprehensive assessment of serum iron, ferritin, and TIBC (Total Iron Binding Capacity) levels. The diagnosis of iron deficiency anemia was made based on specific criteria, including low serum iron levels, elevated TIBC, ferritin levels below 12 mg/L, and hemoglobin levels below 11 g/dL. These diagnostic parameters were considered in the absence of any concurrent medical conditions that could influence the accuracy of these measurements. All data collected during the study were diligently recorded in a standardized proforma to maintain the integrity of the information. All data were carefully recorded in a proforma. Ethical approval and parental consent were obtained prior to initiating the study.

DATA ANALYSIS

Data obtained from the study were entered into a statistical software package, such as SPSS version 20, for analysis. Quantitative variables, including age, weight, serum iron, ferritin, and TIBC levels, were presented as means with standard deviations (SD). Qualitative variables, such as gender and the presence of iron deficiency anemia, were expressed as frequencies and percentages. Stratification was performed based on age, gender, and febrile seizure characteristics. Post-stratification, the chi-square test was applied to compare the frequency of iron deficiency anemia in the different stratified groups. A p-value of ≤0.05 was considered statistically significant.

Furthermore, descriptive statistics were employed to summarize the demographic characteristics of the participants and the prevalence of iron deficiency anemia. The mean and SD were calculated for continuous variables, while frequencies and percentages were determined for categorical variables. Subgroup analyses were conducted to explore potential associations between iron deficiency anemia and specific demographic or clinical factors.

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Ethical considerations were carefully observed throughout the study. Informed consent was obtained from the parents or guardians of the participating children, and the study protocol was approved by the ethical review board. Confidentiality of the collected data was strictly maintained, ensuring the privacy and anonymity of the participants.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

The study encompassed a cohort of 360 children, demonstrating an equitable distribution of gender. Females constituted 49.7% (179), and males comprised 50.3% (181) of the participant pool. The children were categorized based on their milk-feeding practices, revealing 47.5% (171) as breastfed and 52.5% (189) as formula-fed. The mean age of the participants was 25.67 months.

PREVALENCE OF IRON DEFICIENCY ANEMIA

Among the study participants, 18.9% (68) exhibited iron deficiency anemia, while the majority, 81.1% (292), did not manifest signs of iron deficiency (Fig. 3).

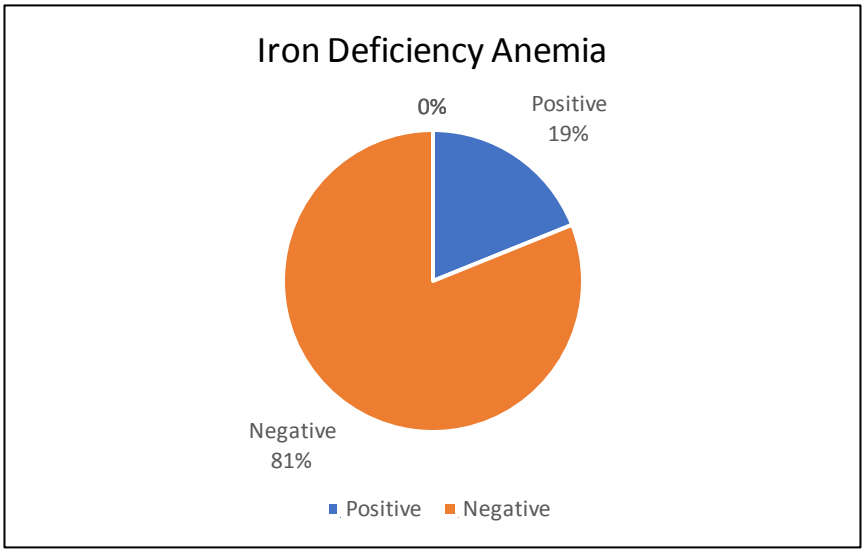

Fig. 3. Frequency of iron deficiency anemia among children with Febrile Seizures

POST-TREATMENT STATUS

Post-treatment outcomes indicated that 33.1% (119) of the children were cured, 0.3% (1) deceased, 45% (162) showed improvement, and 21.7% (78) remained in a stable condition.

INCOME STATUS AND IRON DEFICIENCY ANEMIA

Examining the income status of families, 26.9% (97) belonged to high-income households, 36.4% (131) to low-income households, and 36.7% (132) to middle-income households (Table I).

Table I. Key demographic and health characteristics of the study population showing gender distribution, milk feeding practices, iron deficiency anemia, post-treatment status, and income status

Factor	Categories	N	%
Gender	Female	179	49.7%
	Male	181	50.3%
Milk Fed	Breast Fed	171	47.5%
	Formula Fed	189	52.5%
Iron deficiency anemia	Positive	68	18.9%
	Negative	292	81.1%
Post-treatment status	Cured	119	33.1%
	Died	1	0.3%
	Improved	162	45%
	Stationary	78	21.7%
Income Status	High	97	26.9%
	Low	131	36.4%
	Middle	132	36.7%

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ASSOCIATION ANALYSIS

Table II presents a detailed breakdown of iron deficiency anemia concerning gender, milk-feeding practices, and income.

GENDER

No statistically significant difference in the frequency of iron deficiency anemia was observed between males and females. The p-value for this factor was 0.626.

MILK-FEEDING PRACTICES

No significant difference in the frequency of iron deficiency anemia was noted between breastfed and formula-fed children. The p-value for this factor was 0.246.

Post-Treatment Status: No significant association between different outcomes and the frequency of iron deficiency anemia was identified. The p-value for this factor was 0.813.

INCOME STATUS

A significant association was observed between income status and the prevalence of iron deficiency anemia. The condition was more prevalent in low-income groups (25.2%, n=33) compared to high-income (12.4%, n=12) and middle-income groups (17.4%, n=23). The p-value for this factor was 0.043, indicating a statistically significant difference among income groups.

Table II. Relationship of Iron Deficiency Anemia with Various Factors in Children with Febrile Seizures

Factor	Categories	Iron Deficiency Anemia				P -value
		Positive		Negative		
		n	%	n	%	
Gender	Female	32	17.9%	147	82.1%	0.626
	Male	36	19.9%	145	80.1%	
Milk Fed	Breast Fed	28	16.4%	143	83.6%	0.246
	Formula Fed	40	21.2%	149	78.8%	
Post-treatment status	Cured	23	19.3%	96	80.7%	0.813
	Died	0	0%	1	100%	
	Improved	28	17.3%	134	82.7%	
	Stationary	17	21.8%	61	78.2%	
Income Status	High	12	12.4%	85	87.6%	0.043
	Low	33	25.2%	98	74.8%	
	Middle	23	17.4%	109	82.6%	

DISCUSSION

Iron is an essential nutrient crucial for the proper growth and development of children. Its deficiency can have significant detrimental effects on various organs, resulting in anemia, abnormal growth, behavioral changes, mental retardation, altered thermoregulation, impaired physical performance, and compromised immune function (13). Moreover, insufficient iron levels have been associated with neurological symptoms such as behavioral changes, poor attention span, and learning deficits in children, indicating a potential link between iron insufficiency and other neurological disturbances, including febrile seizures (14). Several studies have investigated the relationship between iron deficiency and febrile seizures in children, providing valuable insights into this association (15-17) all reported iron deficiency as a potential risk factor for febrile seizures.

In the present study, the prevalence of iron deficiency anemia among patients with febrile seizures was noted to be 18.9% (18), conducted a study that revealed a higher prevalence of iron deficiency anemia

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among individuals with febrile seizures, reporting a rate of 44% (19), found an even higher prevalence of 63.6% (20), reported a prevalence rate of 30%. Similarly Two Authors conducted studies and observed prevalence rates of 31.8% and 29%, respectively (14, 21). These findings highlight the variability in the prevalence of iron deficiency anemia among individuals with febrile seizures across different research investigations.

Similarly, a lower prevalence of iron deficiency anemia in children presenting with febrile seizures has been reported in studies by Khalid et al. (5.3%) (22) and (23), (14.8%). Interestingly, certain studies have reported a potentially protective effect of IDA on FS (24, 25). Richard et al. discovered that severe malnutrition, characterized by reduced levels of albumin and plasma protein, as well as electrolyte imbalances such as hypokalemia, hyponatremia, hypomagnesemia, and hypocalcemia, coupled with vitamin D deficiency, could potentially lower the seizure threshold. This combination of factors may contribute to an increased prevalence of epilepsy, including FS, particularly in developing countries(26).

In the current study, no significant associations were observed between gender, milk-feeding practices, or post-treatment status and iron deficiency anemia. These findings are consistent with some previous studies that did not find a significant relationship between these factors and iron deficiency anemia in the context of febrile seizures. However, it is worth noting that the sample size and study design may have influenced the statistical power to detect such associations. Further research with larger sample sizes and more comprehensive study designs may provide additional insights into these relationships.

One significant finding of this study was the association between low-income households and a higher prevalence of iron deficiency anemia. This finding is in line with the existing literature highlighting the influence of socioeconomic factors on nutritional status. Low-income households may face challenges in accessing a diverse and nutrient-rich diet, leading to an increased risk of iron deficiency anemia (27). Understanding this association can guide interventions and public health strategies targeting vulnerable populations to improve iron status and prevent iron deficiency anemia in children with febrile seizures.

Iron deficiency has been implicated in neurological disturbances and cognitive impairments, highlighting the potential complications for children with febrile seizures. Neurological symptoms such as behavioral changes, poor attention span, and learning deficits have been reported in children with iron deficiency, suggesting a potential link between iron insufficiency and febrile seizures (28). Further research is needed to elucidate the underlying mechanisms and explore the long-term neurological consequences of iron deficiency in this population.

The findings of this study have important clinical implications. Early detection and intervention for iron deficiency anemia in children with febrile seizures may help reduce the risk of seizure recurrence and associated complications. Strategies to improve iron status, such as iron supplementation and dietary interventions, should be considered as part of the management and prevention strategies for febrile seizures. Additionally, public health initiatives targeting low-income households can play a crucial role in reducing the burden of iron deficiency anemia and improving the overall health outcomes of children with febrile seizures.

LIMITATIONS

The cross-sectional design adopted in this study imposes constraints on establishing causal relationships between iron deficiency anemia and febrile seizures. Furthermore, the sample size may have compromised the statistical power, particularly in detecting significant associations related to gender and milk-feeding practices. Subsequent research endeavors incorporating larger sample sizes and longitudinal designs would enhance the robustness of evidence concerning these associations.

CONCLUSION

In summary, the prevalence of iron deficiency poses a substantial concern given its adverse implications for the growth, development, and general well-being of children. Insufficient iron levels can contribute to conditions such as anemia, abnormal growth, compromised immune function, and neurological disturbances. Febrile seizures, a prevalent childhood ailment, have been linked to iron deficiency, prompting various investigations into this relationship.

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Prompt identification, targeted intervention, and effective management of iron deficiency emerge as pivotal measures to mitigate the risk of febrile seizures and their associated complications. Additionally, a holistic approach encompassing nutritional interventions and public health initiatives becomes imperative to ensure optimal iron status and neurodevelopment in children, thereby enhancing their overall health outcomes.

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