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Frequency of Iron Deficiency Anemia in 6–60 Months Old Children Presenting with Febrile Seizure

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ABSTRACT

Objective: To determine the proportion of iron deficiency anemia (IDA) among children aged 6–60 months presenting with febrile seizures.

Methodology: This cross-sectional study was conducted in the Department of Pediatrics, Ayub Teaching Hospital, Abbottabad, Pakistan, from Jan to December, 2024. Children with febrile seizures were evaluated for IDA using hemoglobin (Hb), mean corpuscular volume (MCV), and serum ferritin levels. Data were collected after obtaining informed written consent from parents/guardians.

Results: Among 116 children with febrile seizures, 60 (51.7%) were aged 6–30 months and 56 (48.3%) were 31–60 months, with a mean age of 28 ± 17.01 months. The mean Hb level was 8 ± 1.46 g/dL, mean MCV was 65 ± 11.13 fL, and mean serum ferritin was 21 ± 2.87 ng/mL. Of the total participants, 68 (58.6%) were males and 48 (41.4%) were females. Iron deficiency was observed in 77 children (66.4%).

Conclusion: This study demonstrates a strong association between iron deficiency anemia and febrile seizures in children. Early detection and management through iron supplementation and dietary modifications may help reduce the incidence of febrile seizures, as IDA is a modifiable risk factor.

Keywords: Iron deficiency, Anemia, Febrile seizure.

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Introduction

Febrile seizures (FS) are the most common neurological disorder in children ranging from 6 months to 60 months age, with an incidence of 2 to 5 percent. The infections are associated with a fever of at least 38°C (100°F) and without CNS infection, metabolic disturbance, or other underlying causes.[1] The peak incidence occurs around 18 months, and the exact pathophysiology is unknown, but it has been determined both by genetic and environmental factors.[2] While FS are usually regarded as benign and self-imitating, they are a cause of considerable anxiety to parents and caregivers, and they frequently result in unnecessary emergency visits and hospitalizations. [3]

Iron deficiency anemia (IDA), the most common nutritional deficiency in children, is one of the contributing factors looked at for predisposing the case of FS.[4] Numerous neurological functions, including myelin production, neurotransmitter metabolism, and brain energy regulation, depend on iron. Because iron deficiency impairs their function, iron deficiency may lower the seizure threshold.[5] Research has shown that children with IDA may not only be at greater possibility of developing FS but also may experience longer seizure duration, increased recurrence rates and more complex seizure kinds.[6]

In fact, IDA is a not uncommon problem, especially in the case of children, especially in conditions of developing countries.[7] Iron deficiency is a major public health issue as studies in Pakistan indicate that around 65% of children suffer iron deficiency.[8] Investigation of the possibility of the association between IDA and FS in

this region is of high clinical importance since the burden of IDA and FS is very high.[9] There is however a debate regarding the relationship between IDA and FS. On the contrary, strong association has been demonstrated in some studies and suggested that iron deficiency may paradoxically rise the seizure threshold to cause conflicting interpretations in others.[10]

There have been attempts to explore the possibility of a link between iron deficiency anemia (IDA) and febrile seizures (FS) in children and the results have been disparate. On the other hand, some studies claim that IDA elevates the risk of FS as it affects neuronal metabolism and neurotransmitter activity while others report inconsistency or vice versa. Nevertheless, a low serum ferritin level is a potential predictor that an insufficient amount of iron stores may lead to enhanced seizure susceptibility during febrile episodes. An understanding of this relationship is important because early identification and management of IDA may in some way reduce the incidence or extent of FS in children. [11]

With such high prevalence of both FS and IDA in our region, this study is intended to find out the frequency of IDA in children who present with FS in our hospital. Since FS is a preventable and treatable condition where dietary modifications and iron supplementation can reduce risk, FS could be identified as a potential risk factor for FS and can help in developing preventive strategies.

Early intervention and correction of IDA may help to reduce incidence and severity of FS and thus improve neurologic outcomes and reduce parental anxiety. The findings of this study about the association between IDA and FS in our local population will offer valuable insights to clinical practice and public health intervention.

Methodology

This cross-sectional study was conducted over a six-month period, from January 2024 to June 2024, to determine the incidence of iron deficiency anemia (IDA) among patients with febrile seizures presenting to the Department of Pediatrics, Ayub Teaching Hospital, Abbottabad. Based on an expected prevalence of 74% for IDA in febrile seizure (FS) patients, with a 95% confidence level and an absolute precision of 8%, the required sample size was calculated using WHO sample size calculation software. The final sample size was 116, and participants were recruited using a non-probability consecutive sampling technique.

The study included children aged 6 to 60 months both sexes with febrile seizures, and excluded children with seizures due to other metabolic disturbances, intracranial infection, children with anemia other than iron deficiency, children with epilepsy and afebrile seizures.

Ethical approval was obtained from the hospitals ethical committee before initiating data collection and informed written consent obtained from the child's parent or guardian explaining the use of data in the research only. Patient details were recorded on a structured proforma and after they were confirmed to have a case of febrile seizure, a blood sample was collected and referred to the hospital laboratory for hemoglobin, mean corpuscular volume (MCV) and serum ferritin levels. The trainee had taken the results and recorded them.

Quantitative variables such as age, hemoglobin level, MCV level, and serum ferritin level were described predicatively by the mean and standard deviation of the sample collected data did which were entered into and analyzed using SPSS version 18.

Categorical variables, such as gender and presence of iron deficiency anemia, were computed, frequencies and percentages. Anemia prevalence among age and gender groups was post stratified chi square tested at a level of significance of 5% in order to determine statistical differences.

Results

Among 116 patients with febrile seizures, there was a high incidence of iron deficiency anemia (IDA). The mean hemoglobin (Hb) level was 8 g/dL, and the mean corpuscular volume (MCV) was 65 ± 11.13 fL, indicating microcytic anemia. This finding was further supported by serum ferritin levels, which averaged 21 ± 2.87 ng/mL, confirming iron deficiency in a significant proportion of participants. Overall, IDA was present in 66.37% of the study population.

Comparison between age groups (6–30 months and 31–60 months) did not show a statistically significant difference in the prevalence of IDA ($p = 0.945$). Similarly, gender-based analysis revealed no significant association, as the distribution of IDA was comparable between males and females ($p = 0.956$). The relationship between IDA and febrile seizures was assessed using the Chi-square test.

Patients with febrile seizures exhibited somewhat more IDA due to the temptation for a retrospective

epidemiological study, but the lack of a statistically significant association at the 5% significance level insures that causation has not been proven. This implies that while IDA is well described in children with febrile seizures, other contributing factors may also be operative. Meaning that in this cohort, IDA was prevalent among those children and iron deficiency is a modifiable risk factor for which routine screening of children with febrile seizures is needed.

With absence of significant association with age and gender, future studies need to conduct the additional variables, such as nutritional status, socioeconomic factors, and genetic predisposition to understand underlying mechanisms between IDA and febrile seizures.

Table I: Age Distribution of Patients. (n=116)

Age Group	Frequency	Percentage (%)
06-30 Months	60	51.72%
31-60 Months	56	48.27%
Total	116	**100%**

Table II: Descriptive Statistics of Key Variables. (n=116)

Numerical Variable	Mean	Standard Deviation (SD)
Age (months)	28	17.01
Hemoglobin (Hb) Level	8	1.46
MCV Level	65	11.13
Serum Ferritin Level	21	2.87

Table III: Gender Distribution. (n=116)

Gender	Frequency	Percentage
Male	68	58.62%
Female	48	41.37%
Total	116	**100%**

Table IV: Prevalence of Iron Deficiency Anemia. (n=116)

Iron Deficiency Anemia (IDA)	Frequency	Percentage
Yes	77	66.37%
No	39	33.62%
Total	116	**100%**

Table V: Stratification of IDA by Age Group. (n=116)

Age Group	IDA Status	N	Percentage	p-Value
06-30 Months	Yes	40	34.48%	0.945
	No	20	17.24%	
31-60 Months	Yes	37	31.89%	
	No	19	16.37%	

Table VI: Stratification of IDA by Gender. (n=116)

Gender	IDA Status	Frequency	Percentage	p-Value
Male	Yes	45	38.79%	0.956
	No	23	19.82%	
Female	Yes	32	27.58%	
	No	16	13.79%	

Discussion

Numerous studies have examined the connection between iron deficiency anemia (IDA) and febrile seizures (FS), with varying degrees of success. This study showed that iron deficiency anemia was present in 66.37% children with febrile seizures, which makes strong correlation between both these conditions. This finding has been supported by several studies, which also highlight the importance of iron in the neurological function and seizure susceptibility.

A second example of this is that a case control study by Neyazuddin, Nistane. et al looked at children between 6 months and 6 years of age in India. The mean hemoglobin levels in the FS group was significantly lower than control (8.25±1 g/dL vs. 9.86±1.49 g/dL as reported by the study). It also found that serum ferritin levels of the FS group were much smaller than those of the CI group, indicating a strong relationship between febrile seizures and IDA.[12]

In addition, a study performed at Sohag University Hospital in Egypt examined iron status of children with their first febrile seizure. It was found that the mean hemoglobin level was significantly (10.73±1.44) lower in case group compared to control group (11.77±1.24). Additionally, the serum ferritin level was much lower in the FS as compared to that in the control group (13.41±11.71 vs 30.18±8.9), suggesting that IDA may be a risk factor for febrile seizures.[13]

Mohammed Owaiz et al.'s prospective case control study (in Hyderabad) on 50 children (6-60 months) was conducted. When compared with the control group, the study showed that febrile seizures occurred in 48% of children who had IDA and in 20% of children who did not have IDA, suggesting that there is a statistically significant association between febrile seizures and IDA.[14]

Cilli et al. In a retrospective cross sectional study with 100 child aged 6 month to 78 month the prevalence of IDA in the group of FI was 22% while in the control 16%. Although the difference was not statistically significant, the study showed higher prevalence of IDA in children with febrile seizure.[15]

Sulviani R , et al concluded that meta-analysis found that IDA and poor iron indices increase the risk of febrile seizures in the children. Ranging from 1.24 to 1.59, the

odds ratios for modest but significant association were calculated.[16]

A cross sectional descriptive study was conducted by Ahadi et al on 270 children referred to the military hospital for having febrile seizures. Of these 37% of children, according to ferritin indices below 20, abnormal hemoglobin and MCV indices, they felt that iron deficiency may be indeed a risk factor for febrile seizures in children.[17]

Bakkannavar et al. conducted a comprehensive systematic review to discover the associative patterns of IDA with febrile seizures in the children from the age of 5 to 60 months. As part of the review 23 case control studies and a consistent association of IDA and increased community incidence of febrile seizures was shown to emphasise the importance of recognising and managing iron deficiency in this age group. [18]

As stated in the study by Fatima Ashraf et al., 45% of children from 6 months up to 5 years of age with febrile seizures had iron deficiency anemia (IDA), this proves that these two are related. It is important to note that compared to children with an iron deficiency anemia, children with IDA had a higher rate of complicated febrile seizures, implying that iron deficiency may play a role in determining the severity of seizures. These are consistent with previous research that iron screening is necessary in febrile seizure children. Iron deficiency in this setting may contribute to neuroexcitability and thus predispose children to seizure. This is to underscore the need to discover iron deficiency not just for medical reasons, but also to prevent, and as a result the incidence and severity of febrile seizures from occurring, in pediatric populations. [19]

The case control study by Mahmoud et.al from The Egyptian Journal of Hospital Medicine demonstrated that in children between 6 months to 6 years of age with Febrile convulsions, the association between iron deficiency and seizure susceptibility was quite significant with an occurrence of 56%.According to this study, children with febrile seizures had significantly lower ferritin and hemoglobin levels than healthy controls, supporting the idea that iron plays a crucial role in maintaining neuronal neuroregulation and thermoregulation. These results are consistent with previous research that identifies IDA as a factor which lowers seizure threshold and puts a patient at risk for and the severity of, febrile convulsions. This association is a compelling reason to screen early for iron and implement nutritional interventions as potential means of limiting seizures and reducing their severity in at risk pediatric population. [20]

Although this study had several strengths, including a well-defined population and standardized measurement of iron levels, certain limitations must be acknowledged. Similar to most small-scale studies, it is limited by a relatively small sample size and single-center design. Additionally, other potential contributing factors were not assessed, such as inflammatory markers, genetic predisposition, and deficiencies of other micronutrients that may be associated with febrile seizures.

Future research should involve larger, multicenter studies incorporating genetic, nutritional, and inflammatory parameters to provide a more comprehensive understanding of the relationship between iron deficiency anemia and febrile seizures. Furthermore, interventional trials evaluating whether iron supplementation can prevent febrile seizures are warranted to inform clinical guidelines and recommendations.

Conclusion

This study supports the necessity for early detection and treatment of iron deficiency anemia (IDA) in the pediatric population by confirming a high correlation between IDA and febrile seizures (FS). The majority of the evidence suggests that IDA increases the risk of seizures, while some researches have produced contradictory findings. Iron supplementation and frequent screening can help lower the risk of FS and improve neurological outcomes. More research will be needed to establish causality and prevention measures.

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