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IRON DEFICIENCY ANEMIA IN PEDIATRIC PATIENTS WITH FEBRILE SEIZURES: A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: Febrile seizures are a common neurological concern in children. Their recurrent nature highlights the importance of identifying predisposing factors and addressing them appropriately.
Objective: Evaluate the frequency and correlates IDA in pediatric patients with febrile seizures.
Methodology: This study employed a cross-sectional design and was conducted at the pediatric unit MMC from July 2019 to Jan 2020. The study population consisted of 135 patients diagnosed with febrile seizures, aged between 6 months to 5 years. Patients with underlying medical conditions such as meningitis, past history of febrile fits, patients with delayed milestones and past history of blood transfusion were not included in the study. The data was collected from the guardians and laboratory investigation sent from all patients that include CBC, Serum ferritin, Serum TIBC. The independent t Test was applied to compare the blood indices of patients with and with iron deficiency anemia. Chi square test was used to assess the association between categorical variables.
Results: The mean age of the patients was 30± 16.05(months). The gender distribution was 103(54.5%) males, and 86(45.5%) females. The mean value for Hemoglobin was 10.49 ±1.95. Mean MCV was 67.9±7.1, Mean MCHC 30.6±1.9, Mean serum Iron was 37.97± 29.1, Mean TIBC was 351±47.0, mean serum ferritin was 67± 41.2. Iron deficiency anemia was found in 43.9% of patients with febrile seizures.
Conclusion: The current study revealed a significant prevalence of iron deficiency anemia in children with febrile seizures. This finding highlights the importance of considering iron deficiency anemia as a potential comorbidity in pediatric patients with febrile seizures.

Key Words: Iron deficiency anemia, Febrile seizures, pediatric patients.

INTRODUCTION

Febrile seizures are a common concern among pediatric patients presenting to the emergency department [1]. They are the most frequent type of seizures in children, affecting approximately 2–5% of the pediatric population [2]. Febrile seizures are defined as convulsions occurring in children aged 6 months to 5 years, associated with a fever exceeding 38°C, in the absence of central nervous

system (CNS) infection, metabolic disturbances, or a prior history of afebrile seizures [3]. These seizures are categorized into two types: simple febrile seizures, characterized by generalized tonic-clonic activity lasting less than 15 minutes and not recurring within 24 hours, and complex febrile seizures, which involve focal features, exceed 15 minutes in duration, or recur within 24 hours [4].

Although febrile seizures are generally not linked to long-term adverse outcomes, the risk of recurrence is notable. Approximately 30% of children experience a recurrence following the first episode, while the risk increases to 50% after two or more episodes. The likelihood of recurrence is also higher in children who experience their first febrile seizure before the age of one. Additional risk factors include younger age at onset, fever lasting more than 24 hours, and a family history of febrile seizures or epilepsy [5].

The precise etiology of febrile seizures remains unclear; however, certain risk factors have been identified. These include a rapid rise in body temperature (exceeding 102°F), genetic predisposition (evidenced by a positive family history), and environmental triggers such as viral infections and vaccinations [6]. Iron deficiency, in particular, has been implicated in lowering the seizure threshold through mechanisms such as disrupting neurotransmitter metabolism (e.g., monoamine oxidase), reducing brain neurotransmitter concentrations, and impairing neuronal myelination and growth. Notably, the peak ages for iron deficiency anemia (IDA) and febrile seizures overlap, suggesting a possible link [7]. Iron deficiency anemia is one of the most prevalent nutritional deficiencies in children, particularly in infants. It is primarily caused by inadequate dietary iron intake but may also result from blood loss or malabsorption syndromes [8]. While its prevalence has significantly declined in developed countries, it remains high in underdeveloped regions, where 46–66% of children under four years old are anemic, with iron deficiency accounting for nearly 50% of cases. Children with IDA are at risk of central nervous system dysfunction, manifesting as behavioral, attentional, and auditory impairments [9].

Several studies have explored the association between IDA and febrile seizures, with most reporting a significant correlation. For instance, Chaudhary BR et al. (2021) identified a strong association, reporting IDA in 59.5% of cases, with an odds ratio of 2.5 and a p-value of <0.05 [2]. Similarly, Potros Wasfy Gaballah et al. (2022) found a significant association, noting IDA in 70% of cases compared to 30% of controls (p-value <0.001) [10]. In contrast, Awais M et al. (2022) reported no significant association, with IDA observed in 18.9% of cases, an odds ratio of 1.25, and a p-value of 0.326 [11]. Despite extensive research, findings on the relationship between IDA and febrile seizures remain inconsistent. Some studies suggest an increased frequency of IDA among children with febrile seizures, while others find no significant association. Given these conflicting results, this study aims to address this gap by examining the relationship between IDA and febrile seizures. The findings will contribute to evidence-based guidelines for the rational use of iron supplementation in children with febrile seizures and provide a foundation for future research and preventive strategies.

METHODOLOGY

The current study employed a cross sectional designed was conducted at pediatric unit MMC Mardan between July 2020 to Jan 2021. The study protocol was approved by Ethical committee (No: 161/ BKMC, Date 02/07/2020. Using the WHO formula for sample size determination, taking 56.5% prevalence of IDA in children with febrile seizures with a desired confidence level of 95%, margin of error was 75, the estimated sample size was 189.[2]

The inclusion criteria were: children aged 6 months to 5 years, diagnosis of febrile seizures, both genders. The exclusion criteria were: previous underlying disorder such as meningitis, past history of febrile fits. Developmentally delayed patients, patients with a history of blood transfusions. Prior to enrollment into the study a written consent was formally obtained from parents or guardians. The demographic data was collected from the parents and laboratory investigation sent to laboratory that included CBC, serum ferritin, serum TIBC, Serum Iron

Iron deficiency anemia was diagnosed when a child had a hemoglobin level <11g/dl, with microcytic and hypochromic picture, and a serum ferritin less than 15ng/ml.

Febrile seizures were diagnosed when a child presented with seizures and a fever> 38c in the absence of CNC infection or other identifiable cause.
Statistical analysis was performed using SPSS 22. Descriptive statistics was used for demographic and laboratory data. An independent sample t test was applied to compare the hematological profile of patient with and without iron deficiency anemia. Categorical values were presented in the form of frequencies and percentages. The study population was stratified by age, gender, type of seizures, socioeconomic status and vaccination status, and A chi square test was used to measure association between categorical variables, in which p value <0.05 was taken as significant.

RESULTS

The current study comprises 189 patients divided into male and female groups comprising 103(54%) males, females were 86(45.5%). The age range of the patients was 6 months to 5 years, with the majority belonging to age group 2 (25-42 months) with a frequency of 53(28%)**.** The mean age of the patients was 30± 16.05 (months). Patients with simple febrile seizure comprises 113(59.7%) of the total whereas**.** 79(41.7%) of the total subjects were fully vaccinated, 65(34.3%) were incompletely immunized whereas 45(23.8) have unknown status.
Regarding the immunization status, 75(55.6%) were completely immunized, 36(26.7%) have incomplete immunization while in the remaining 24(17.8%) the immunization status was unknown. The most common underlying illnesses were URTI, AGE and LRTI affecting 49(25.9%), 38(20.1%), 31(16.45%) respectively. The socioeconomic profile of the patients was predominantly satisfactory comprising 109(57.6%), whereas 80(42.3%) belongs to poor socioeconomic status.

TABLE 1: BASELINE ATTRIBUTES

INDICATORS	VLAUES(FREQUENCY/PERCENTAGE)
AGE BASED GROUP(MONTHS)	
60- 24	53(28%)
25- 42	79(41.7%)
43-60	57(30.1%)
GENDER	
MALE	103(54%)
FEMALE	86(45.5)
UNDERLYING DISEASES	
AGE	38(20.1%)
URTI	49(25.9%)
AOM (Otitis Media)	28(14.8)
LRTI (pneumonia)	31(16.45)
UTI	19(10%)
AEFI	07(3.7%)
UNKNOWN	17(8.9)
FEBRILE SEIZURES TYPE	
SIMPLE FEBRILE SEIZURES	113(59.7%)
COMPLEX FEBRILE SEIZURES	76(40.2)
VACCINATION PROFILE	
FULLY VACCINATED	79(41.7)
PARTIALLY VACCINATED	65(34.3)
UNKNOWN	45(23.8)
SOCIAL ECONOMIC PROFILE	
SATISFACTORY	109(57.6)
POOR	80(42.3)

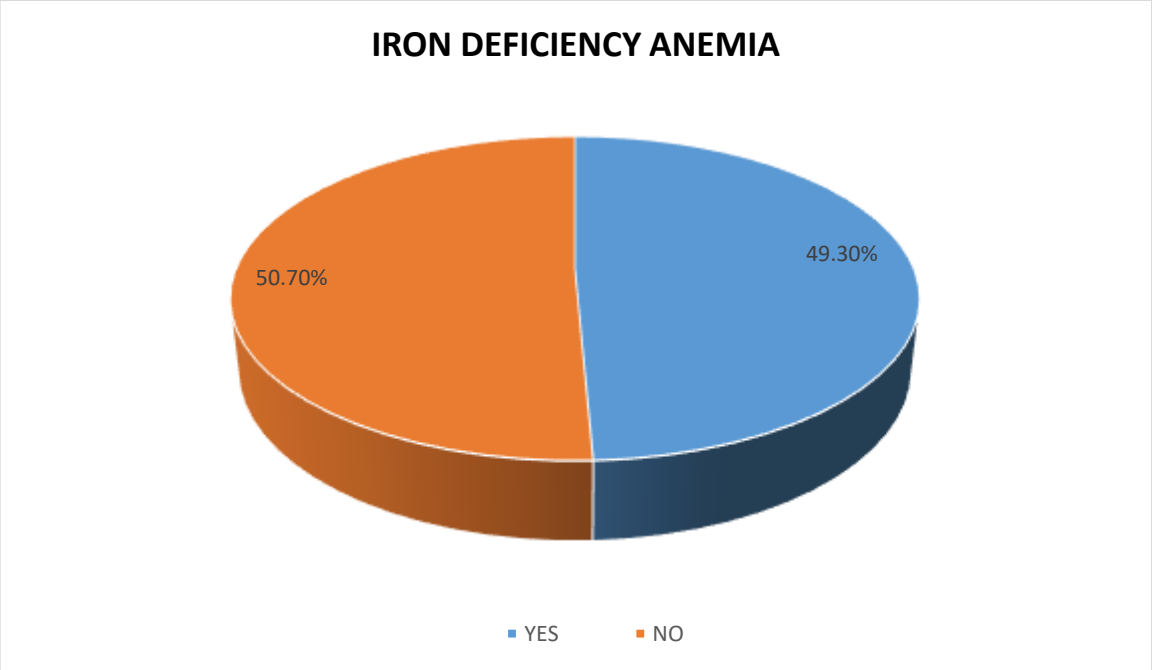
Mean hemoglobin was 10.49 ±1.95. Mean MCV was 67.9±7.1, Mean MCHC 30.6±1.9, Mean serum Iron was 37.97± 29.1, Mean TIBC was 351±47.0, mean serum ferritin was 67± 41.2. (Table2)

Table 2: Hematologic Parameters

VARIABLES	VALUES
Mean Hemoglobin(g%)	10.49± 1.95
Mean Hematocrit (%)	30.8±2.1
Red Blood cell count	4.32 $\times 10^6$
Mean Corpuscular volume	67.9 ±7.1
Mean Corpuscular hemoglobin concentration	30.6±1.9
Serum Iron level (µg/dl)	37.97± 29.1
Total iron binding capacity (µg/dl)	351±47.0
Serum ferritin µg/l	67± 41.2
Iron deficiency anemia	93(49.3%)

The prevalence of iron deficiency anemia was found in 49.3% of the patients with febrile seizures. (Figure1)

Figure 1: Iron deficiency anemia in patients with febrile seizures



The mean Hb, Hct, RBC count, Serum Iron and ferritin were significantly different among patient in relation to iron deficiency anemia. However no significant differences were found in terms of MCV, MCHC. (Table 3)

Table 3: Blood indices in relation to Iron deficiency anemia

Hematologic Parameter	IRON DEFICEINECY ANEMIA		P value
	Present	Absent	
Mean Hemoglobin(g%)	10.49± 1.95	11.7± 1.6	0.005
Mean Hematocrit (%)	30.8±2.1	33.2±2.7	0.01
Red Blood cell count (10^6)	4.32± 1.2	4.9±0.5	0.0001
Mean Corpuscular volume	67.9 ±7.1	72.3± 7.9	0.34
Mean Corpuscular hemoglobin concentration	30.6±1.9	33.1± 2.0	0.628
Serum Iron level (µg/dl)	37.97± 29.1	46± 33.4	0.036

Total iron binding capacity (µg/dl)	351±47.0	331 ±34	0.001
Serum ferritin µg/l	67± 41.2	89± 56	0.003

The data were stratified based on age, gender, type of fits, and immunization status. A post-stratification Chi-square test revealed significant association between iron deficiency anemia and age, gender, type of seizures. However, no significant association was observed with socioeconomic status (Table 4)

Table 4: Categorical variables associated with Iron deficiency anemia

Attribute		**IDA**		**P VALUE**
		YES	**NO**	
GENDER	Male	43(41.7%)	60(58.2%)	0.021
	female	50(58.1%)	36(41.8)	
AGE BASED GROUP(MONTHS)	60- 24	19(35.8%)	34(64.1%)	0.038
	25- 42	46(58.2%)	33(41.7%)	
	43-60	28(49.1%)	29(50.8%)	
FEBRILE SEIZURES TYPE	Simple Febrile Seizures	40(35.3%)	73(64.6%)	0.009
	Complex Febrile Seizures	53(69.7%)	23(30.2%)	
VACCINATION PROFILE	Fully Vaccinated	42(53.1%)	37(46.8%)	0.039
	Partially Vaccinated	29(44.6%)	36(55.3%)	
	Unknown	25(55.5%)	11(44.44%)	
SOCIAL ECONOMIC PROFILE	Satisfactory	68(62.3%)	41(37.6%)	0.226
	Poor	25(31.25%)	55(68.75%)	

DISCUSSION

The present study aimed to investigate the frequency of iron deficiency anemia in children with febrile seizures. The mean age of the children in our study was 30± 16.05 months. In current study males were predominant 103(54%), In the present study, the mean age of participants was 28.3 ± 17.08 months, aligning with findings by Potros Wasfy Gaballah et al. (2022), who reported a mean age of 27.76 ± 14.67 months. [10] A similar observation was made by Khanna et al. (2020), where males predominated the study population. [13] Likewise, Tripathy et al. (2020) concluded that the majority of their study population was male. [14] In contrast, Surani et al. (2020) reported differing results, with females being predominant. [15]

The most common underlying illnesses were URTI, AGE and LRTI affecting 49(25.9%), 38(20.1%), 31(16.45%) respectively. The mean Hb, Hct, RBC count, Serum Iron and ferritin were significantly different among patient in relation to iron deficiency anemia. However no significant differences were found in terms of MCV, MCHC. The mean Hemoglobin concentration in the current study was 10.49 ± 1.95 g/dl that is consistent with the study done by Madavi D et al. where the mean HB was 10.05± 8.43 [16] Awais M et al. (2022) also reported similar findings.[11]

The mean MCV in the current study was 67.9 ± 7.1 Fl, similar results were reported by Sandip k Mandal et al. (2024).[17] the current study reported a mean serum iron level of 37.97± 29.1, Elkafafy M et al. (2021) also concluded a similar finding with mean serum iron level of 54.24±16.04 among patient with febrile fits.[18] The current study reported a mean serum ferritin level of 68± 40.93 µg/l, which is consistent with findings by Awais M et al. (2022), who documented a serum ferritin level of 51.80±209.04. [11]

The current study did not show any sigificant association between iron deficiency anemia and type of febrile fits, these results are consistent with a study conducted by jang HN et al. (2019) that concluded no significant difference between any hematologic variable with the type of febrile fits.[19]

There is long list of predisposing factors such as viral infections ,a positive family history of FS, zinc deficiency ,iron deficiency etc.iron plays a crucial role in miantaining optimal brain function and its deficiency may lead to an increased susceptibility to seizures.

Our analysis revealed a significant frequency of iron deficiency anemia in childrn with febrile seizures. This finding is consistent with previous researches suggesting an association between iron

deficiency anemia and febrile seizures. A study by Jang HN et al. (2019) reported that 49.2% of patients presenting with febrile seizures had iron deficiency anemia. [19] Similarly, Shaaib et al. (2020) identified a significant association between iron deficiency anemia and febrile seizures. [20] Mallela J et al. (2024) also concluded that 73.08% of children experiencing febrile seizures were diagnosed with iron deficiency anemia, highlighting a strong association. [21] Saleem MA et al. (2020) further supported this finding, reporting a significant link between iron deficiency anemia and febrile seizures. [22] Additionally, Awais M et al. (2022) found a notable association, with 18.9% of patients presenting with febrile seizures being diagnosed with iron deficiency anemia. [11]
In view of the studies, a strong correlation has been found between iron deficiency anemia and febrile fits ,as concluded from our study 31.9% of children with FS have iron deficiency anemia.

CONCLUSION

The results demonstrate a significantly higher frequency of iron deficiency anemia in children presenting with febrile seizures. This finding suggest that iron deficiency anemia is a significant risk factor, highlighting the importance of screening for iron deficiency anemia in children with febrile seizures and underscore the need for iron supplementation to prevent recurrences and improve overall health outcome.

Limitations:

The cross-sectional design limits to establish a causal relationship between iron deficiency anemia and febrile seizures. Secondly the use of ferritin in diagnostic criteria of iron deficiency anemia may be subject to bias, as it is an acute phase reactant which can be elevated in response to any infection.

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