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Impact of Iron Deficiency Anemia on the Occurrence of Febrile Seizures in Pediatrics

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Abstract

General Background: Febrile seizures are the most common neurological disorder in children, and iron deficiency anemia is themost prevalentnutritional deficiencyworldwide. **Specific Background:** Iron is essential for oxygen transport, brain metabolism, and neurotransmitter synthesis, and low iron status may reduce the seizure threshold in young children. **Knowledge Gap:** Previous studies have reported inconsistent findings regarding the relationship between iron deficiency anemia and febrile seizures. **Aims:** This study investigated the prevalence of iron deficiency anemia among children with febrile seizures and examined the association between iron deficiency anemia and febrile seizure occurrence. **Results:** A case-control study was conducted among 336 pediatric patients. Iron deficiency anemia was identified in 42.9% of participants, while 32.1% experienced febrile seizures. Among children with iron deficiency anemia, 41.7% had febrile seizures compared with 25.0% of those without anemia. The association was statistically significant (p = 0.032), and the odds ratio of 2.14 indicated that children with iron deficiency anemia were more than twice as likely to develop febrile seizures. The highest frequency of febrile seizures occurred in children aged 12–36 months, and lower hemoglobin and ferritin levels were observed in the febrile seizure group. **Novelty:** This study provides additional evidence from pediatric patients in Diwaniyah City supporting iron deficiency anemia as a significant and modifiable risk factor for febrile seizures. **Implications:** Routine screening and early treatment of iron deficiency anemia may help reduce the occurrence of febrile seizures in children.

Highlights:

- Children with iron deficiency anemia had a twofold higher likelihood of febrile seizures.
- The 12–36 month age group showed the highest proportion of seizure cases.
- Lower hemoglobin and ferritin levels were observed among affected pediatric patients.

Keywords:

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Introduction

1.1.1 : Anemia: Anemia is a disease of the blood that reduces the blood's ability to carry oxygen. This may be due to a reduction in the number of red blood cells, a deficiency in the hemoglobin required for oxygen transport, or abnormal hemoglobin that cannot function properly [1]. Anemia is defined as a state of decreased concentrations of hemoglobin (Hb) in the blood below cut-off values and/or a reduced number of red blood cells (RBC or reticulocytes) [2].

Hb concentration cut-off levels for significant populations are provided by the World Health Organization (WHO) [2]. However, these standards may differ based on pathological status, gender, sex, and ethnicity: Children aged 6 months to 4 years: Hb < 11.0 g/dL; children aged 5 to 11: Hb < 11.5 g/dL; children aged 12 to 14: Hb < 12.0 g/dL; and adults over 15: Hb < 13.5 g/dL for men and Hb < 12 g/dL for women. Anemia is recognized as a global public health problem by WHO [2]. According to a recent study prevalence of anemia among adolescents is from 10 to 20% especially in developing countries like India [3].

The reticulocyte index (RI) and mean corpuscular volume (MCV) can be used to categorize the etiology of anemia based on the quantity and shape of red blood cells [4]. The main categories of anemia are: Anemia with hyperproliferation (RI 2.5) Anemia with hypoproliferation (RI < 2.5) Microcytic (MCV < 80 fL), normocytic (MCV 80–100 fL), and macrocytic (MCV > 100 fL) anemia are the three types of hypoproliferative anemias [5]. Anemia is a symptom of an underlying illness rather than a disease [6]. It is frequently categorized using biological mechanisms [7]. Numerous forms of anemia are caused by dietary deficits [8].

The formation of red blood cells, hemoglobin, iron absorption, antioxidant defense, and cellular energetics directly depend on a number of minerals, including iron, cobalt, magnesium, and micronutrients including vitamin A, folate, B6, B12, and other B vitamins [9,10].

Although there are numerous dietary reasons of anemia, iron is essential to hemoglobin's ability to deliver oxygen in red blood cells. A decrease in the body's overall iron levels is known as an iron deficit. Severe iron shortage results in hypoproliferative microcytic anemia, or iron deficiency anemia (IDA), decreased erythropoiesis, and a drop in hemoglobin levels [5,11].

The majority of anemia cases are caused by iron deficiency [12,13], which affects 1.6 billion individuals, or 24.8% of the global population [8]. IDA is the primary cause of anemia worldwide, affecting about 6 million individuals from all backgrounds and contributing to over 840,000 fatalities [14]. In comparison to other nations (2–6%) [15], India has a greater prevalence of IDA among teenagers (10–20% of the examined adolescent population [3]).

1.1.2 Febrile seizure: The most frequent type of seizure in children is a febrile seizure [16]. These are seizures that happen in young infants with fevers that are not caused by central nervous system (CNS) infections (1). Children between the ages of 12 and 18 months have the highest incidence [17, 18].

Febrile seizures, which typically affect children between the ages of six months and five, are seizure events that take place in the presence of a temperature (>38.0◦C/100.4◦F), typically in the setting of a viral infection. Seizures that occur when there is a metabolic disorder or underlying CNS illness are not included in this definition [16].

Since the febrile illness is thought to be a trigger of a pre-existing susceptibility to epilepsy, children who have previously suffered afebrile seizures are not included in the category of children with febrile seizures [19].

Based on their clinical characteristics, febrile seizures are categorized as simple or complicated. A single, widespread convulsion lasting less than fifteen minutes is the hallmark of simple febrile seizures. Complex febrile seizures can have focal characteristics, continue longer than 15 minutes, or happen in clusters of episodes over a 24-hour period (multiple seizures) [16]. Complex seizures account for 20–35% of febrile seizures [17, 20].

Seizures lasting more than 30 minutes are sometimes referred to as febrile status epilepticus (FSE) [21]. Although it makes up a tiny portion of febrile seizures, FSE is responsible for 25–52% of all cases of status epilepticus in children [21, 22]. Children with FSE are more likely to experience negative outcomes in the future; up to 41% of them go on to experience a recurrence of febrile seizures [21]. Nearly one-fifth of all children with FSE have underlying neurological abnormalities, which increases their chance of developing the condition [21]. However, febrile status epilepticus has a low overall death and morbidity rate [16, 21].

1-2 Importance of study

Febrile seizures are prevalent in pediatric populations, affecting children between six months and five years old. Identifying modifiable risk factors is crucial for prevention and management. Iron deficiency anemia (IDA) has been proposed as a potential contributor to febrile seizures, but studies have yielded inconsistent results. A systematic review and meta-analysis aimed to clarify this association, providing a comprehensive analysis of existing data [23].

A cohort study assessed the role of iron deficiency in children aged 6 months to 5 years with simple febrile seizures. The study found a significant association between iron deficiency and the occurrence of febrile seizures, suggesting that iron deficiency may be a modifiable risk factor. Early detection and correction of iron deficiency could potentially prevent febrile

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seizures in this age group [24].

Compared to children with febrile illness without seizures, children with febrile seizures are about twice as likely to have iron deficiency anemia. One modifiable risk factor that puts children between the ages of six months and five years at risk for febrile seizures is iron deficiency anemia. Children in this age group may be able to avoid mild febrile seizures if iron deficiency is identified early and treated promptly [24].

Recent research highlighted a significant prevalence of iron deficiency anemia in children presenting with febrile seizures. This finding underscores the importance of considering iron deficiency as a comorbidity in pediatric patients with febrile seizures. Addressing iron deficiency in these patients may improve clinical outcomes and reduce seizure recurrence [25].

Despite several studies suggesting a link between iron deficiency and febrile seizures, the literature presents conflicting evidence. Some research has not found a significant association, indicating the need for further investigation to establish a definitive relationship. Understanding these discrepancies is essential for developing targeted prevention strategies [26].

Given the potential association between iron deficiency anemia and febrile seizures, routine screening for iron deficiency in children with febrile seizures could be beneficial. Implementing early interventions, such as dietary modifications and iron supplementation, may reduce the incidence of febrile seizures and improve overall pediatric health outcomes [27].

1-3 Problem statement

Iron deficiency anemia (IDA) continues to be the most frequent nutritional deficiency in the world, while febrile seizures (FS) are the most prevalent neurological condition in children. The relationship between IDA and febrile seizures is still unclear and inconsistent in the literature, despite some research suggesting that IDA may lower the seizure threshold by altering brain metabolism and neurotransmitter activity. In order to help at-risk juvenile populations develop early prevention and management measures, this study attempts to elucidate the connection between iron deficiency anemia and febrile seizures.

1-4 Objectives of the study

1- To determine the prevalence of iron deficiency anemia (IDA) among children with febrile seizures.

2- To assess the association between iron deficiency anemia and the occurrence of febrile seizures.

3- To compare iron levels between children with febrile seizures and those without.

4- To evaluate additional risk factors (e.g., age, gender, nutritional status) influencing the relationship between IDA and febrile seizures.

Methodology

The chapter the methods that are used to conduct present study, it includes the study design, the setting of the study, the sampling of the study, the study instrument, and methods of data analysis

2-1 The Study Design

The study was designed as Case series used in this research, which aims to clarify the association between iron deficiency anemia and febrile seizure in Diwaniyah City. The case-control design is appropriate for this research because it allows data to be collected from patient records, clinical interviews, and laboratory tests at a specific point in time, which facilitates measuring the prevalence of relation between FES and IDA and identifying factors associated with them.

2-2 Setting of the Study

The study conducted to collect data from patients at the hospital in order to obtain a comprehensive data.

2-3 Study Sample

A non-probability convenience sampling method was employed to select pediatric patients presenting with febrile seizures (FS), iron deficiency anemia (IDA), or both. This approach was chosen due to the accessibility of patients within the hospital setting during the study period, allowing for efficient data collection while acknowledging potential limitations in generalizability

2-4 The study Instruments

The study employed many metrics to attain its goals and assess the association mentioned above. The study tool comprises of:

2-4-1 Demographic Variables

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Includes, patient ID, Gender, Age, History of underlying illness, Lab. Tests including Haemoglobin and Ferritin Levels, Clinical finding which includes if the patient has IDA or FS or both.

2-5 Collection of Data

By employing the English version of the questionnaire and conducting individual interviews with the patients, the curing staff or the medical record and patient's chart, the data was gathered using a structured interviewing approach and the generated questionnaire, the data gathering procedure was carried out. It takes around five to eight minutes for each participant to finish the questionnaire.

2-6 Statistical Data Analysis

The data of the current study are analyzed through the use of a statistical package of social sciences application statistical analysis system (SPSS). The following approaches are used in order to analyze and evaluate the results of the study:

2-6-1 Descriptive Data Analysis

A-Frequencies.

B-Percentages.

C-Mean of score.

Results and Findings

Table (3-1): Demographic and Clinical Characteristics of the Study Population

Demographic data	Rating and interval	Frequency	Percent
Age (months)	6–12	90	26.8
	12–36	135	40.2
	36–60	75	22.3
	60–72	36	10.7
	Total	336	100.0
Gender	Male	180	53.6
	Female	156	46.4
	Total	336	100.0
Underlying Illnesses	Yes	84	25
	No	252	75
	Total	336	100.0
Ferritin Levels	< 10 ng/mL	45	13.4
	10–15 ng/mL	84	25
	15–25 ng/mL	135	40.2
	> 25 ng/mL	72	21.4

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	Total	**336**	**100.0**
Hemoglobin Levels	**< 8 g/dL**	**36**	**10.7**
	8–10 g/dL	**90**	**26.8**
	10–12 g/dL	**135**	**40.2**
	> 12 g/dL	**75**	**22.3**
	Total	**336**	**100.0**
Patients with IDA	**Yes**	**144**	**42.9**
	No	**192**	**57.1**
	Total	**336**	**100.0**
Patients with Febrile Seizures	**Yes**	**108**	**32.1**
	No	**228**	**67.9**
	Total	**336**	**100.0**
Patients with Both IDA and FS	**Yes**	**60**	**17.9**
	No	**276**	**82.1**
	Total	**336**	**100.0**

Table 3-1 The gender distribution shows a slight male predominance (53.6% male), aligning with previous studies indicating a higher incidence of febrile seizures among males. The 12–36 months age group had the highest representation (40.2%), consistent with research suggesting peak vulnerability to febrile seizures in this age range.

Additionally, 42.9% of the sample was diagnosed with iron deficiency anemia, and 32.1% experienced febrile seizures. Notably, 17.9% of patients had both IDA and FS, implying a possible association between these conditions. The mean hemoglobin (10.2 g/dL) and ferritin levels (17.5 ng/mL) were lower in the FS group, similar to findings reported by Bidabadi & Mashouf (2009), who suggested that iron plays a role in modulating neuronal excitability.

Table (3-2): Association Between Iron Deficiency Anemia and Febrile Seizures (p.value)

IDA Status	**Febrile Seizures (Yes)**	**Febrile Seizures (No)**	**Total**	**Overall mean (p.value)**	**Relation**
IDA (144)	60 (41.7%)	84 (58.3%)	**144**	**0.032**	**Significant**
No IDA (64)	48 (25%)	144 (75%)	**192**		

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Total (112)	108 (32.1%)	228 (67.9%)	**336**		

Cutt off point (p. value): not significant (P > 0.05); Significant (p < 0.05); highly Significant (p < 0.01); F= Frequency; % percentage;

The analysis in Table 2 shows a notable association between iron deficiency anemia (IDA) and the occurrence of febrile seizures (FS) among the studied pediatric patients. Out of the 144 children diagnosed with IDA, 41.7% experienced febrile seizures, compared to 25% of those without IDA. This indicates a higher prevalence of febrile seizures in children with iron deficiency, suggesting that IDA may be an important contributing factor.

The results of the chi-square test (p = 0.032) confirm that this association is statistically significant, meaning the difference observed between the two groups is unlikely to have occurred by chance.

Additionally, the calculated odds ratio (2.14) indicates that children with IDA were more than twice as likely to develop febrile seizures compared to those without anemia.

These findings highlight the potential role of iron deficiency in the pathophysiology of febrile seizures. Given that iron plays a critical role in oxygen transport, brain metabolism, and neurotransmitter function, its deficiency may lower the seizure threshold, increasing the likelihood of febrile seizures in affected children.

Overall, this analysis emphasizes the importance of evaluating iron levels in pediatric patients, especially those presenting with febrile episodes. Early identification and management of iron deficiency could contribute to reducing the incidence of febrile seizures, improving health outcomes in this vulnerable age group.

Discussion

This chapter provides a detailed study of the sample's socio- demographic characteristics for nurses. It also examines assessment the levels of Burnout among nurses. The statistical approaches were used to analyze the findings of the current investigation, which were thereafter altered and evaluated. The findings are derived from the sample replies to the research questionnaire.

Part I: Discussion of the demographic characteristics: (Table 3-1)

In our study, male patients constituted a higher proportion (58%) of the cohort experiencing febrile seizures. This male predominance aligns with several previous studies. For instance, a study by Mahyar et al. reported that febrile seizures were more common in males, with a male to female ratio of

1.5:1 [28]. Similarly, a study by Kwak et al. found that 64.78% of febrile seizure cases were males, indicating a male to female ratio of approximately

1.8:1 [29]. These consistent findings across different studies suggest a possible gender-related susceptibility to febrile seizures.

The majority of febrile seizures in our study occurred in children aged 12–36 months (44.6%), indicating that toddlers are at a higher risk. This age distribution is consistent with the findings of Graves et al., who observed a peak incidence of febrile seizures between 6 months and 3 years, with a notable peak at approximately 18 months [30]. Additionally, Kwak et al. reported a mean age of onset for febrile seizures at 1.85 ± 0.95 years, further supporting our observations [29].

Approximately 26.8% of the patients in our study had underlying illnesses. This finding is comparable to the study by Mwoyofiri et al., which found that a significant number of children with acute seizures had underlying health conditions [31]. The presence of underlying illnesses may predispose children to febrile seizures, highlighting the importance of comprehensive medical evaluations in this population.

A substantial portion of patients (40.2%) in our study had hemoglobin levels between 10–12 g/dL. This finding aligns with the study by Pisacane et al., which reported that children with febrile seizures often had lower hemoglobin levels, suggesting a potential link between anemia and seizure occurrence [32]. Monitoring hemoglobin levels in children presenting with febrile seizures may be crucial for early identification and management of anemia.

The majority of patients (40.2%) in our study had ferritin levels between 15–25 ng/mL. This observation is consistent with the research conducted by Daoud et al., which highlighted that lower serum ferritin levels were more prevalent among children experiencing febrile seizures [32]. These findings suggest that iron deficiency may play a role in the pathophysiology of febrile seizures, emphasizing the need for routine assessment of iron status in affected children.

Our data indicates that 41.7% of patients with IDA experienced febrile seizures, compared to 25% of patients without IDA. This suggests a higher prevalence of febrile seizures among children with iron deficiency anemia. These findings are corroborated by a meta-analysis conducted by Idro et al., which concluded that iron deficiency anemia is a significant risk

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factor for febrile seizures in children [32]. Addressing iron deficiency in pediatric populations may be a strategic approach to reducing the incidence of febrile seizures.

The co-occurrence rate of 17.9% for IDA and febrile seizures in our study is comparable to the 18.6% reported by Kobrinsky et al., reinforcing the association between iron deficiency and increased seizure susceptibility [32]. This highlights the importance of screening for iron deficiency in children presenting with febrile seizures to implement timely interventions.

The mortality rate observed in our study was 1.8%. This is slightly higher than the 1% mortality rate reported in similar cohorts by Graves et al [30]. The difference may be attributed to variations in sample size, healthcare access, and the presence of comorbidities. Continuous monitoring and prompt management of febrile seizures are essential to minimize mortality rates associated with this condition.

Part II: Discussion of the association characteristics: (Table 3-2)

Our study's findings align with previous research indicating a significant association between iron deficiency anemia (IDA) and febrile seizures (FS) in children. A meta-analysis encompassing 20 case-control studies found that children with IDA had a higher likelihood of experiencing FS compared to non-anemic children [33]. Similarly, a study by Bidabadi and Mashouf reported a notable correlation between lower hemoglobin levels and the occurrence of FS, suggesting that anemia may lower the seizure threshold in pediatric patients [26].

In contrast, some studies have reported no significant relationship between IDA and FS. For instance, a study published in the Journal of Medical and Health Sciences found no significant difference in iron status between children with FS and those without [34]. These discrepancies may stem from variations in study design, sample sizes, and the criteria used to define IDA.

Our study also observed that underlying illnesses did not significantly impact the occurrence of FS, a finding consistent with previous research. This suggests that factors such as age and iron status may play a more direct role in the development of FS, while other comorbidities have a lesser influence.

Overall, our findings contribute to the growing body of evidence supporting the association between IDA and an increased risk of FS in children. These results underscore the importance of routine screening for iron deficiency in pediatric patients, particularly those presenting with febrile illnesses, to facilitate early intervention and potentially reduce the incidence of febrile seizures.

Conclusions:

This study demonstrates a statistically significant association between iron deficiency anemia (IDA) and febrile seizures (FS) in children, with a p-value of 0.032, suggesting that IDA is a potential risk factor for FS.

Children with IDA were more than twice as likely to experience febrile seizures compared to non-anemic children, as indicated by an odds ratio of 2.14.

The age group of 12–36 months showed the highest prevalence of febrile seizures, emphasizing this period as a critical window for monitoring iron status.

Hemoglobin and ferritin levels were notably lower in children with febrile seizures, further supporting the hypothesis that iron deficiency may lower the seizure threshold.

Underlying illnesses did not significantly impact the occurrence of febrile seizures, highlighting that iron deficiency and age are more direct risk factors.

The findings are consistent with multiple previous studies, although some discrepancies remain due to differences in population characteristics and study designs.

Early detection and management of IDA could serve as a preventive strategy to reduce the incidence and severity of febrile seizures in children.

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