

Iron Deficiency Anemia in Children with Febrile Seizures: A Retrospective Cross-Sectional Study

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ABSTRACT

Febrile seizures (FS) are common in children aged 6 months to 6 years, with potential links to iron deficiency. This study aimed to assess the prevalence of iron deficiency anemia (IDA) among children with FS at Alkadra Hospital. A retrospective descriptive cross-sectional study was conducted from November 2021 to April 2022. Children (6 months–6 years) diagnosed with FS per American Academy of Pediatrics guidelines were included, excluding those with neurological/metabolic disorders or developmental delays. Data on demographics, seizure characteristics, and hematological parameters (Hb, MCV, MCH, serum ferritin) were collected via questionnaire and laboratory analysis. Statistical analysis was performed using SPSS, with $p^* \leq 0.05$ considered significant. Among 39 FS cases (mean age 27.11 months), 77% were aged 12–36 months, with a male predominance (62%). Generalized tonic-clonic seizures (87%) were most common, primarily triggered by urinary tract infections (43.6%). Mean Hb was 11.09 g/dl (50% <11 g/dl), MCV 74.08 fl (18% <70 fl), and serum ferritin 69.75 ng/ml (36.8% <30 ng/ml). Low Hb, MCV, and ferritin levels were statistically significant ($p^* = 0.001$). Iron deficiency was prevalent in children with FS, suggesting a potential association. Further studies are needed to explore this relationship and the role of iron supplementation in FS prevention.

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INTRODUCTION

Febrile seizure (FS) is one of the most common neurological conditions of childhood, with an incidence of about 2-14% in different societies [1]. Several theories, such as genetic factors, have been proposed as the pathogenesis of this condition. Although the role of micronutrients such as zinc and iron has been largely studied as predisposing factors, there is still a need to explore their relation to febrile seizures [1,2].

Febrile seizures (FS) are the commonest cause of seizures in children, with 2-5% of neurologically healthy children experiencing at least episode, Febrile seizure episodes are agonizing to the parents and child and can cause psychological trauma to both and Seizure is one of the most common neurological symptoms in children accounting for 1% of visits to the emergency department [3]. Iron deficiency is reported to be one of the most prevalent nutritional problems in the world today, especially in developing countries, with an estimated 46%-66% of people affected [3,4]. American Academy of Pediatrics (AAP), defined FS as sudden, abnormal, excessive electrical discharges of nerve cells (gray matter) that spread along nerve processes (white matter) to affect the end organ in a clinically measurable manner, occurring during infancy or childhood., usually between 3 months and 5 years of age, accompanied by fever, but

without signs of intracranial infection or an identified cause. Most recently, the AAP (2008) defined FS as a seizure occurring in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizure [5]. FS is considered a “syndrome” because it fulfils several characteristics that are similar among affected children. FS generally occurs within a restricted age range; the majority of children with FS show normal neurological and structural development after the episode; and FS is not associated with structural or developmental anomalies in the brain, although the existence of such pathology may enhance susceptibility to FS. Genetics, comorbidities (premature birth, fetal growth retardation), and environmental risk factors (exposure to nicotine in utero, or antihistamine use) may increase risk of FS in addition to the age factor [6].

A study was done in Iraq, which found that 57(20%) patients had a positive family history of FS, and 32 (11%) patients had a positive family history of epilepsy. FS was the first episode in 110 (71%) patients, and 45 (29%) patients had recurrent FS. Simple FS was seen in 142 (90%) patients, while 15 (9.5%) patients' kernel with complex FS [2]. Another study conducted in Tripoli reported that the sample population was generally a mix of urban and rural civilians with average levels of education and

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employment. The majority of febrile seizure cases admitted to our hospital in 2007 and 2008 involved people of the same sex. The maximum age of patients with febrile seizures in this study was from 6 to 12 months, i.e., 44% in 2007 and 29% in 2008. Mothers' attitudes before and after the introduction of the information on the leaflet have not changed significantly [7]. The study aims to evaluate the iron status in children with febrile seizures admitted to Alkhadra Hospital, Tripoli, Libya

Methods

Study Design

This study was a retrospective descriptive cross-sectional study that was carried out between the 1st of November 2021 and the 31st of April 2022

Study Setting

The Study was carried out at Alkadra hospital at both the emergency department and the pediatric ward.

Study Population

After receiving ethical approval from the hospital ethics committee, we also obtained verbal informed consent from the parents after explaining the benefits of this study. Children aged 6 months to 6 years with a diagnosis of febrile seizures were included according to the American Academy of Pediatrics guidelines (3,6).

Inclusion and exclusion criteria

Children from 6 months to 6 years, with any type of febrile convulsion, were included in this study. While we didn't include children with any neurological and metabolic diseases, patients on iron therapy, and patients with developmental delay or asphyxia

Data collection

Data collected using a questionnaire, including age, sex, family history of febrile seizure to education level of the mother, detailed information about the febrile seizure. A full systemic examination was performed by a paediatrician, and axillary temperature was taken for the study group. Venous blood samples were collected from FS children. The child's haemoglobin (Hb), haematocrit (Hct), and mean corpuscular volume (MCV) were measured at the Alkadra Hospital laboratory. The most commonly used definitions of anemia come from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). Newborn to 4.9 years Hemoglobin level < 11 g/dl and children from 5 to 11.9 years old Hb level < 11.5 g/dl (27,28).

Statistical Analysis

Collected data were coded and analyzed using SPSS software. Means and standard deviations were reported according to age, hemoglobin, and ferritin levels, and evaluated by chi-square test, and p-values ≤ 0.05 were considered significant.

Results

Out of 378 hospitalized children, 39 children with FS were included. The mean age was 27.11 months. Table 1 shows the age distribution of patients admitted with FS. The maximum number of children (77%) belonged to the age group of 12 to 36 months. The least number of children is under the age of one year. Table 2 shows the sex distribution of patients admitted with FS; the male/female ratio is 1.27:1.

Table 1. Age distribution of patients admitted with FS.

Age (months)	Case no.=39	%
6-12 months	2	6.1%
12-36 months	30	77%
36-60 months	7	21.2%

Table 2. Sex distribution of patients admitted with FS.

Sex	Case no.=39	%
Male	24	62%
Female	15	45%

Table 3 shows the socioeconomic status, mother's education, and f/HO of FS; the majority of children belonged to the middle socioeconomic group (69%). Regarding the mother's education level, most of them have a university degree (56.4%). In H/O, febrile seizures were found in 64% of families.

Table 3. Distribution of socioeconomic status, marital status, and family history among Libyan children admitted with febrile seizures.

Variables	Case no (n=39)	%
Socioeconomic status		
High income	6	15.4%
Medium income	27	69.23%
Low income	6	15.4%
mother's Education		
Secondary school	6	18.2%
High school	7	21.2%
University/college	22	56.4%
Institute/ Academy	4	12.1%
Family H/O Febrile seizure		
Yes	25	64.1%
No	14	42.4%

According to data analysis, 87% of cases had generalized tonic-clonic seizures (Table 4). The temperature distribution showed that 20 cases (51.3%) developed seizures at 40°C. The average temperature is 39.5 °C with a minimum temperature of 38°C Table 5. In Figure 4, the most common cause of FS was due to Urinary tract infection 17 (43.58%), followed by respiratory tract infection 13 (23.07%) and Gastrointestinal tract infections 9 (23.07%). The majority of cases had a fever of 40°C in the study subjects (42.2%) (Table 6, Figure 4).

Table 4. Types of convulsion distribution in the study group

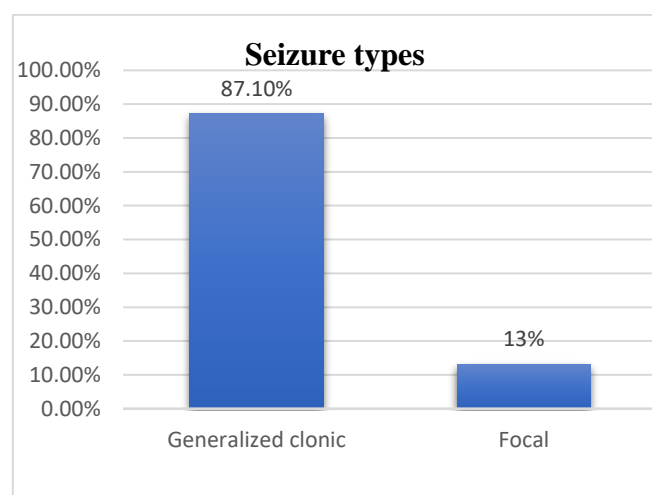
Type of convulsion	Case no.=39	%
Generalized tonic-clonic	34	87.17%
Focal	5	13%

Table 5. Body temperature distribution among children with fever.

Body temperature (°C)	Case no.=39	%
38-39(°C)	9	23.1%
38-39(°C)	10	25.6%
40(°C)	20	51.3%

Table 6. Distribution of Causes of fever in the study group

Infectious diseases cause fever	Case no.=39	%
Respiratory	13	33.33%
Gastrointestinal tract infection	9	23.07%
Urinary tract infection	17	43.58%

**Figure 6. Distribution of seizure types among study subjects**

According to laboratory analysis, all red blood cell parameters [Hb, MCV, MCH, MCHC and RDW] were significantly affected in the group of causes related to iron content, Hb (15% recorded received in 11 cases (28%) and SF <30 ng/ml was observed in 14 cases (37%). 7 cases (18%) may have mean MCV platelet count <70 fl and 36 cases (92%) had MCHC serum ferritin <30 % SF above 14.(36.8%) <30 ng/ml Children with Hb <11 g/dl or HCT <33 % and serum ferritin <33% and serum ferritin <30%.30 ng/ml is considered anemia (Table 7).

Table 7. Prevalence of haematological parameters in the study group.

Parameter N(%)	Rate
Hb (<11g/dl)	19 (50%)
RDW (>15%)	11 (28.9%)
SF (<30ng/ml)	14 (36.8%)
MCV (<70 fl)	7 (18%)
MCHC (<30%)	36 (92%)

In Table 8 Mean Hb level among cases was 11.09

and the minimum range was 7.93g/dl which was statistically significant (p-value=0.001), which referred to high prevalence of iron deficiency Mean MCV and MCH levels in the cases were 74.0875, 26.6375 respectively which was statistically significant (p-value=0.001) and the mean RDW among cases was 14.7406%, which was not statistically significant.

Table 8: Red blood cell index and iron content in the study group

Parameters	Cases		Minimum	Maximum	P Value
	Mean	SD			
Haemoglobin (gm/dl)	11.09	1.17	7.93	13.30	0.01
HCT (mcg/dl)	33.22	3.37	26.40	41.10	0.01
RBCs (mcg/dl)	4.43	.45	3.21	5.32	0.001*
MCV (pg)	74.08	5.70	59.50	86.00	0.001
MCH (mcg/dl)	26.63	9.24	17.90	75.00	0.001
RDW%	14.74	2.19	10.40	19.50	0.291
Serum ferritin (mcg/dl)	69.75	48.82	8.20	152.00	0.001*
MPV	8.84	.46	8.10	9.60	0.001

*Significant result $p < 0.05$

Discussion

The average age of onset of febrile seizures in this study was 27.11 months, similar to that in India, where the average age of onset of febrile seizures was 32 months, which was higher than our results [8]. The average age of first detection of febrile seizures was 20.76 ± 11 months. Compared with the national study conducted in Benghazi, patients under 12 months had 36 (29.8%) patients in the relapse group, while in the non-relapse group, there were 85 (72.2%) patients. In the group without recurrence and age over 12 months, there were 55 (20%) patients. In the recurrence group, while 220 (80%) patients were in the non-recurrence group, age was considered a risk factor for FS recurrence, $p = 0.038$ [9].

In this study, the socioeconomic status, mother's education, and f/HO of FS, the majority of children belonged to the middle socio-economic group (69%). Regarding the mother's education level, most of them have a university degree (56.4%). In H/O, febrile seizures were found in 64% of families. Similar observation was shown in a national study done by Amenh B. Yousif et. al (2017), 106 patients (93%) had a positive family history of FS, and 8(7%) patients had a positive family history of epilepsy out of 114 patients with a positive family history [3].

According to data analysis, 87% of cases had generalized clonic. The temperature distribution showed that 20 cases (51.3%) developed seizures at 40°C. The average temperature is 39.5 °C with a minimum temperature of 38°C, and the most common cause of FS was due to Urinary tract infection 17 (43.58%) followed by respiratory tract infection 13 (23.07%), and lower GIT infection 9 (23.07%). In this study, multivariable logistic regression analysis was performed to identify risk

factors. For recurrent febrile seizures. It was observed that a younger age of first seizure onset, lower temperature during seizures, seizure frequency, and family history of febrile seizures were significantly associated with febrile seizure recurrence in children, and there is a statistical relationship between low temperature at the time of the seizure.

The onset of the first crisis, febrile seizures, and disease relapse (p -value = 0.01). Similar observations were also observed in a study conducted by Elkafafy M et.al in Egypt, 2021, and a study in Saudi Arabia between 2010 and 2011, the maximum temperature increased significantly in the case group ($P=0.03$, 0.001) [10,11]. In this study, the average Hb level among cases was 7.5 g/dl, while in the control group it was 13,304 g/dl, which was statistically significant (p -value = 0.01). The average MCH level across cases was 26.6375, and the standard deviation was 9.2, and MCV was 74.0875, and the standard deviation was 5.70437, which were both statistically significant (p -value = 0.001). The average RDW among the cases was 14.7406%, which was not statistically significant. Similar observations by Kalmani M and Sanikam HB et al. (2021), India. All indicators of iron deficiency anemia, such as hemoglobin, MCV, MCH, serum iron, and serum ferritin, were low during febrile seizures, and the differences were found to be statistically significant (p -value = 0.001) [12].

In the present study, multivariable logistic regression analysis was performed to identify risk factors for recurrent febrile seizures. It was observed that a younger age of first seizure onset, lower temperature during seizures, seizure frequency, and family history of febrile seizures were significantly associated with febrile seizure recurrence in children, and there is a statistical relationship between low temperature at the time of the seizure. Onset of the first episode of febrile seizures and disease recurrence (p -value = 0.01). Similar observations in a study conducted by Elkafafy et al., in Egypt, 2021, and a study in Saudi Arabia between 2010 and 2011, the corresponding maximum temperatures increased significantly in the field group case [$P = 0.03$, 0.001] [10,11]. In our study, 39 children (50%) had iron deficiency anemia. Similar observations by El-Shafie AM et al. (2023) in Egypt, it was (52.5%) children in the case group had iron deficiency anemia (IDA), compared with 4 (20%) in the control group. The control group had statistical significance ($P < 0.05$) [13].

Conclusion

In conclusion, iron deficiency anemia (IDA) was more common in children with febrile seizures, and the median hemoglobin concentration among the cases was 7.5 g/dl, which was statistically significant. The results suggest that IDA may be a risk factor for febrile seizures. Early detection and rapid correction of iron deficiency can help prevent the recurrence of febrile seizures in children in this age group. Complex febrile seizures are more

frequent with Iron deficiency anemia than in those with simple febrile seizures. Guidelines and protocols in primary healthcare for the early diagnosis and treatment of children with ID anemia should be available.

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