

THE RELATIONSHIP BETWEEN IRON DEFICIENCY ANEMIA AND SIMPLE
FEBRILE SEIZURE

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ABSTRACT

Background: Simple febrile seizure is the most common neurologic disease in pediatrics. There are hypotheses suppose that iron deficiency may affect febrile convulsion and the threshold of neuron excitation. **Objective:** The aim of the study was to understand the relationship between iron deficiency anemia (IDA) and simple febrile seizure (SFS) in children aged between 6 months to 5 years. **Patients and Methods:** This analytic, case-control study was conducted on 100 children aged from 6 months to 5 years who attended the Emergency Department of Tishreen University Hospital during the period from Mai 2023 to Mai 2024. The children were categorized into two groups: case and control groups. Each group contains 50 patients. Hemoglobin (Hb), mean corpuscular volume(MCV), mean corpuscular Hb(MCH), mean corpuscular Hb concentration(MCHC), Red cell distribution width (RDW), serum iron(SI), serum ferritin(SF), were assessed for the two groups. **Results:** A total of (64%) children in the case group had IDA compared with (28%) in the control group, which was statistically significant (P:0.0001). **Conclusions:** Iron deficiency anemia is an important risk factor which predispose children to develop simple febrile seizure. Evaluation of iron status is encouraged to be performed in children with SFS.

KEYWORDS: anemia, simple febrile, iron, seizures.

INTRODUCTION

Febrile Seizure (FS) is the most common disorder in the nervous system of children and 2-5% children become affected every year.^[1] Febrile seizure is defined as convulsion resulting from fever. It occurs in children aged between 6 months to 5 years of, it is accompanied by fever higher than 38°C, and does not involve symptoms of central nervous system infections or any other background causes.^[1] Risk factors of this disorder include history of convulsion or FS in the family, head injuries, mothers who smoke or consume alcoholic beverages, and high fevers.^[2,3,4,5,6] Since FS has the probability to develop into epilepsy, various studies have been carried out with the purpose of identifying correctable risk factors in order to reduce the prevalence of FS.

^[2,3,7,8,9]Iron deficiency is the most common micronutrient deficiency and can decrease the production of hemoglobin and this cause iron deficiency anemia (which is a correctable and remediable condition).^[10] Iron is essential for the metabolism of brain and neurotransmitters, and in the production of myelin which is required for nerve cells and can change the amplitude and the threshold of neurons excitation.

The relationship between iron deficiency anemia (IDA) and (FS) has been evaluated in several studies with conflicting results.^[11]

MATERIALS AND METHODS

This analytic case-control study was conducted on 100 children aged 6 months to 5 years who attended the Emergency Department of Tishreen University Hospital during the period from Mai 2023 to Mai 2024

The children were categorized into two groups:

1. The case group: included 50 children with SFS.
2. The control group: included 50 children but without SFS.

After admission, all children were thoroughly examined to exclude children with a complex febrile seizure, previous history of epilepsy, developmental delay, neurological deficit, and CNS infection. Detail Information was investigated included: ((age, sex, body temperature upon admission, cause of fever, duration between initiation of fever and convulsion, family history of febrile convulsion, and details of the seizure history including duration, frequency, and type of seizure were recorded for all children)). Tonic clonic or tonic seizures lasting for less than 15 min without focal signs with a short postictal period were defined as simple, whereas seizures of more than 15 min duration occurring

more than once in 24 hr, focal features were considered complex.

Inclusion criteria: simple febrile seizures associated with fever which are generalized, with short duration (<15 min), and no recurrence of seizures within 24 h, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizures.

Exclusion criteria

Following were the exclusion criteria: atypical FS, (complex febrile seizures), any signs of CNS infection, any chronic neuro development problems, previous diagnosis of other hematological problems, on iron supplementation, chronic digestive diseases such as celiac disease.

Blood investigations carried out to diagnose iron deficiency included: hemoglobin (Hb) level, mean corpuscular volume (MCV), (mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), Red cell distribution width (RDW), serum ferritin level, serum iron level (SI).

Iron deficiency was diagnosed by hematological investigations of: Hb less than 11 g/dl, MCV less than 70 fl, MCH less than 24 pg, MCHC less than 32%, RDW more than 15%, SI less than 50 µg/dl, SF less than 12 µg/dl.

Statistical analysis

The chi-square or Fisher exact test was used to study the relationships between categorical variables. The Independent T student test was employed to compare the mean differences between the two groups. All variables

were tested using univariate regression, and the statistically significant variables were then entered into a multivariate analysis equation. Results were considered significant if the p-value was less than 5%. IBM SPSS Statistics software was used to compute the statistical parameters and analyze the results.

RESULTS

Form the 100 children studied, 50 with SFS were enrolled in the case group and 50 were considered as controls. IDA was more frequent in children with SFS and this difference was statistically significant (P :0.0001, Table 1).

In our study 48% were female and 52% were male child, Majority of the children 46% belongs to 1-2yrs of age group followed by 30% of the children belongs to 2-3yrs age group, there were no differences in gender and age between the two groups.

A comparison between laboratory characteristics of complete blood count in the two groups indicated, there was a significant difference between the studied groups regarding (Hb, MCV, MCH, MCHC) which were lower in the case group than in the control group (P < 0.05%), and also there was significant difference between the studied groups regarding RDW, which was higher in the case group than in the control group (P : 0.001%;) (Table 2).

A comparison between laboratory characteristics of iron profile in both groups indicated that there was a significant difference between the studied groups regarding the level of (SI, SF) which were lower in the case group than in the control group (P < 0.05% Table 2).

Table 1: The Relationship between Iron deficiency anemia and Simple febrile Seizure.			
	Case	Control	p-value
Iron deficiency anemia	64%	28%	0.0001
No iron deficiency anemia	36%	72%	

Table 2: Mean levels of (HB,MCV,RDW,MCH,MCHC) concentration among cases with simple febrile seizures and controls.			
	Case	Control	p-value
HB	10.48 ± 1.4	11.66 ± 1.6	0.0001
MCV	69.72 ± 10.2	81.23 ± 14.06	0.0001
MCH	25.76 ± 2.6	28.60 ± 2.5	0.03
MCHC	30.40 ± 3.2	35.40 ± 2.5	0.01
RDW	17.41 ± 1.49	13.65 ± 1.97	0.001

Table 3: Serum iron, serum ferritin among cases with simple febrile seizures and controls.			
	Case	Control	p-value
Serum iron	50.16 ± 29.6	70.20 ± 35.3	0.003
Serum ferritin	51.76 ± 73.8	108.44 ± 72.9	0.0001

DISCUSSION

FS occurs in 2–5% of all children with a recurrence rate of 30–40%. Age for peak incidence of FS is 14–18 months, which overlaps with that of IDA, which is from

6 to 24 months.^[13,14] iron deficiency may alter the seizure threshold of a child.^[15,16] Iron deficiency is postulated as a risk factor for FS in children and is an easily correctable condition.^[17,18]

Iron is important for catecholamine metabolism and for the various enzymes and neurotransmitters present in the central nervous system. Iron deficiency increases extracellular dopamine and norepinephrine levels in the caudate-putamen and decreases the levels of dopamine D1 and D2 receptors and monoamine transmitters.^[19] Furthermore, iron deficiency in early life alters metabolism and neurotransmission in major brain structures, such as the basal ganglia and hippocampus, and disrupts myelination.^[20]

In our study we found that IDA was more frequent in the case group than in the control group, and the difference was a statistically significant ($P :0.0001$).

In our study, we measured iron status components (SI, SF, Hb, MCV, MCH, MCHC, RDW) among cases and controls. In the present study there was a significant difference between the studied groups regarding (Hb, MCV, MCH, MCHC, SI, SF), and also there was significant difference between the studied groups regarding (RDW), which were higher in the case group than in the control group.

This was in agreement with *Shafie et al.*^[21], who compared the levels of (Hb, MCV, MCH, MCHC, HCT, SI, FI, Transferrin saturation) among controls and patients with SFS, and reported that iron deficiency anemia was significantly more frequent among cases than controls.

Mallikarjun et al.^[22] performed a study on 100 children and found that the mean values of serum iron were 44.46 ± 2.6 in the case group versus 120.54 ± 29.08 in the control group. They concluded that iron deficiency was an important risk factor in simple febrile seizure.

Jang et al.^[23] showed that SF levels were significantly lower in children with FS compared with controls ($P:0.0001$), and suggested that iron deficiency increases the risk of developing FS.

In 2017, *Byung et al.*^[24], reported in a meta-analysis study that children with iron deficiency anemia were twice as likely to have SFS.

Limitations

The study duration was short, and the sample size was relatively small.

This is a single-center study, so the results may have limited generalizability to other hospitals with different diagnosis protocols.

CONCLUSIONS

- The frequency of iron deficiency anemia was higher and statistically significant in patients with simple febrile seizure.
- Iron deficiency anemia is a risk factor for the development of simple febrile seizure.

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