

## IRON STATUS IN FEBRILE SEIZURE: A CASE-CONTROL STUDY

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### Abstract

#### Objective

Data on the relationship between iron deficiency anemia and febrile convulsions are controversial. The aim of this study was to determine the association between iron deficiency anemia and febrile convulsions among children

#### Materials & Methods

This case-control study was conducted during 2006-2007, on 90 children with febrile seizures (case) and 90 febrile children without seizures (control) referred to the Amirkola children hospital (a referral hospital in the north of Iran). Two groups were matched for age and sex. In all children hemoglobin (Hb) level, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and plasma ferritin (PF) were determined and the data collected were analyzed statistically using the t-test.

#### Results

The mean PF and TIBC levels were not significantly different in the febrile seizure compared to the reference group; neither were differences in Hb levels statistically significant between two groups. However MCV and MCH were significantly higher in the febrile seizure group ( $p < 0.05$ ) compared to reference group.

#### Conclusion

Plasma ferritin levels were not significantly lower in children with febrile seizures in comparison with the children in control group. It seems that iron insufficiency does not play a role in pediatric febrile seizures.

**Keywords:** Febrile seizure, Iron deficiency anemia, Children

### Introduction

Febrile seizures are the most common seizures in children (1). Their incidence is 2-5% or 4.8/1000 person-years (2). A family history of Febrile Convulsions (FC) or epilepsy, head injury, maternal smoking and alcohol consumption during pregnancy, features of the acute underlying illnesses accompanying the FC, and the temperature peak have been associated with febrile seizures (3-6) To date, the pathophysiology of febrile seizures is unknown (1). Pisacane and colleagues (7) report that an association between iron deficiency anaemia and febrile seizures in Neapolitan children, whereas, in contrast, Kobrinsky et al (8) reported that iron deficiency raises the threshold for seizures and Momen and Hakimzadeh (9) reported that there was no relation between iron deficiency anemia and first febrile convulsions in children younger than 5 years. Iron is involved in the metabolism of several neurotransmitters,

and in iron-deficiency anemia, monoamine and aldehyde oxidases are reduced; this is common during the second and third years of life, and has variably been associated with behavioral and developmental disturbances (10). Considering the above mentioned, we investigated the iron level in patients with febrile seizures compared to a control group.

### Materials & Methods

In this case-control study, 90 children, aged between 9 months and 5 years, with first febrile seizure admitted to the Amirkola children Hospital, between April 2006 and April 2007, were enrolled in the study. A febrile convulsion was defined as a seizure that occurred while the child had a rectal temperature of at least 38.3°C or an axillary temperature of at least 37.8°C documented either in the emergency department or in the history. A single generalized seizure in 24-hour of fever period with the duration of less than 15 min without focal features is defined as a simple FC, whereas seizures are defined as complex if they are lasted more than 15 min, had focal features, or occurred more than once in 24 hours (10). Children with a history of seizures, thalassemia, central nervous system (CNS) infections, developmental delay, and/or neurologic deficit were excluded from the study. A reference group (90 children) was selected from among children hospitalized for a febrile illness (such as upper and lower respiratory tract infections and gastroenteritis) but without seizures. Controls were group-matched to cases on age and sex. An informed consent was obtained from parents or the legal guardian. Age, sex and family history of febrile seizure or epilepsy were recorded for all cases and controls, as well as details of the seizure history, duration and frequency for all cases with febrile seizure. Blood samples were collected from all participants for measurement of hemoglobin (Hb), Hematocrit (Hct) mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and plasma ferritin (PF). PF level was measured using the IMx Ferritin assay in a microparticle enzyme immunoassay (MEIA) for quantitative determination of human PF (10). The Ethics Committee at Babol University of medical Sciences approved the study. The independent t-test was used for comparison of data between two groups,  $P < 0.05$  being considered significant.

### Results

We studied 90 children (43 male, 47 female), with febrile seizure and a reference group of 90 patients (47 male, 43 female). The mean ages of patients in the febrile seizure and control groups were  $1.6 \pm 1.2$  and  $2 \pm 1.7$  year respectively. Type of seizure was generalized in 85(94.4%) patients and focal in 5 (5.6%) patients. Table 1 shows that mean PF and TIBC levels were not significantly different in the febrile seizure group compared with the reference group; nor was the difference in Hb level statistically significant between the two groups. However MCV and MCH levels were significantly higher in the febrile seizure group ( $p < 0.05$ ).

**Table 1.** Mean levels of Hb, TIBC, MCV, MCH, and PF among cases with febrile seizure and controls

	GROUP	Mean	Std. Deviation	p-value
<b>Hb</b>	febrile seizure	11.75	1.15	0.327
	Control	11.99	1.94	
<b>Hct</b>	febrile seizure	35.2	3.14	0.053
	Control	36.4	5	
<b>MCV</b>	febrile seizure	76.69	7.4	0.018
	Control	80.5	13.19	
<b>MCH</b>	febrile seizure	25.51	3.46	0.001
	Control	28.29	7.15	
<b>FERRITIN</b>	febrile seizure	73.59	67.15	0.474
	Control	82.16	91.33	
<b>TIBC</b>	febrile seizure	336.02	67.11	0.176
	Control	349.83	65.67	

### Discussion

Result show that the mean PF and TIBC levels were not significantly different in the febrile seizure group compared to the control group. In the Mansouri et al study, mean Fe and Ferritin were higher in the convulsive group with no statistically significant differences (11), results

similar to those of the present study but in contrast with others; Pisacane (7) reported a significantly higher rate of iron-deficiency anemia among children with first febrile seizure than in their controls; Kobrinsky (8) suggested that anemia raises the threshold for first febrile seizure. In the Rehman and Billoo study (12), Plasma ferritin level was significantly lower in cases as compared to controls and suggested that iron deficient children are more prone to febrile seizures. Hartfield et al, in a case control study, reported that children with febrile seizures were almost twice as likely to be iron deficient as those with febrile illness per se and suggested that screening for iron deficiency should be considered in children presenting with febrile seizure (13). Idjradinata reported that iron-deficiency anemia can cause developmental delay and behavioral disturbances early in life and that early correction of anemia may reverse this (14). Ferritin is an iron-containing protein that functions in the body as an iron-storage compound. Plasma ferritin provides a sensitive, specific, and reliable measurement for determining iron deficiency at an early stage, and it may be the best indicator of total body iron status (15). It is known that ferritin is an acute-phase reactant that increases nonspecifically in response to any febrile illness (8). In our study, since fever was present in all patients in the two groups, the differences in ferritin concentration between the two groups cannot be explained by fever. It was not possible to control other potential confounders such as maternal anemia and child's developmental delay because of lack of information on these variables in the present study. Low level of PF may lower the seizure threshold, as iron is important for the function of various enzymes and neurotransmitters present in the central nervous system (16). Fever may worsen the negative effects of low PF level on the brain, and therefore seizures can be triggered (7).

In conclusions, PF level was not significantly lower in children with febrile seizure in comparison with the children in control group and a possible role for iron insufficiency in febrile seizure is not considered. As Contradictory results have been reported regarding the role of iron insufficiency in febrile seizures further studies are highly recommended.

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