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ORIGINAL ARTICLE

The Relationship between Iron deficiency anemia and Febrile Convulsions in infant and Children

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ABSTRACT

Background: Febrile seizures (FS) are the single most common seizure type and occur in 2 to 5% of children younger than age 5 years with a peak incidence in the second year of life. Evidence that iron might be important for neurological functioning has generated considerable optimism that this element might also play a role in initiation of febrile convulsions. This study aimed to determine the relation between iron deficiency anemia and febrile seizures in infant and children aged 6 months to 6 years.

Methods: A case-control study was done in Pediatrics Department, Faculty of Medicine, Zagazig University during the period from September 2018 to March 2019. It included 90 infants and children (45 infant and children presented with febrile convulsions and 45 age and sex matched healthy infants and children between 6 months and 6 years as a control group). All children with febrile convulsion were investigated for iron deficiency to find if there is any association between Anemia and febrile convulsion.

Results: The current study showed that cases were significantly higher regarding Total Iron-Binding Capacity (TIBC) than control group with no significant difference between groups regarding ferritin or iron. But, cases were significantly lower regar ding Mean Corpuscular Hemoglobin (MCH) and Hemoglobin (Hb). Therefore, cases were significantly associated with anemia.

Conclusion: the study concluded that iron deficiency anemia is a risk factor for febrile seizures in infants and children aged 6 months to 6 years.

Keywords: Iron deficiency, anemia, Febrile Convulsions

INTRODUCTION

Febrile seizure (FS) is the most common seizure type in young children, which is not triggered by central nervous system infection or metabolic disorders. It usually occurs in infants and children aged 6–60 months, and has 2–5% incidence of at least one episode in this population. Iron deficiency anemia (IDA) is a common nutritional deficiency in children with a prevalence of 1–15% in the USA depending on ethnicity and socioeconomic status, and a prevalence of 0.5–5% in South Korea. Iron is essential for proper growth and development, and iron deficiency is reported to involve behavioural disorders, mental retardation, and impaired immune function [1].

Febrile Convulsions (FC) refer to the convulsions that occur in children between the ages of 6 months and five years, with body temperature of 38ºC or higher not resulting from Central Nervous System (CNS) infection or any metabolic imbalance without any prior afebrile seizures. This condition occurs in 2-5% of the children who are neurologically healthy [2].

IDA is the most common nutritional deficiency in the world. Iron is an important micronutrient which is used by roughly all the cells in the human body.

It is well understood that iron is a cofactor for several enzymes in the body and has a role in the neurotransmitters production and function, hormonal function and DNA duplication [3].

Iron deficiency stimulates the function of neurons and, consequently, increases the risk of convulsions. The relationship between IDA and FC is unknown. While some studies have shown IDA as a risk factor for the development of FC 7-10, this relationship has not been confirmed by other studies [4]. On the other hand, few reports have claimed that IDA may have a protective effect on FC development [5].

This study was aimed to determine the relation between iron deficiency anemia and febrile seizures in infants and children aged 6 months to 6 years.

METHODS

A case-control study was done in Pediatrics Department, Faculty of Medicine, Zagazig University during the period from September 2018 to March 2019. It included 90 infant and children (45 infant and children presented with febrile convulsions were chosen randomly and 45 age and sex matched healthy infants and children between 6 months and 6 years were selected randomly as a control group).

All children with febrile convulsion were investigated for iron deficiency to find if there is any association between Anemia and febrile convulsion.

Inclusion criteria: Age group of 6 months to 6 years presented with typical febrile convulsions of American Academy of Pediatrics (AAP) clinical practice guidelines. [6]

Exclusion criteria: Patients outside the age group. Patients present with febrile convulsions, hypoglycemia, meningitis, encephalitis, shigellosis, neurological disorders and history of seizure (with or without fever). Patients with EEG abnormalities. Patients with iron supplementation during the past 3 months.

Patients were divided into groups:

Group 1: included Forty five patients with febrile convulsions.

Group 2: Control group included Forty five age and sex matched healthy infants and children between 6 months and 6 years.

All participants s were subjected to:

Complete history taking: [Name, Age (in months) (calculated from the date of birth), Sex, Age of onset].

Family history of convulsions, certain medications, inherited diseases or related syndromes.

Information on birth weight and current weight, developmental milestones, body temperature upon admission, cause of fever, history of iron supplement therapy, family history of febrile convulsion, and family history of epilepsy were recorded for all cases and controls, as well as details of the seizure history, duration, frequency, type of seizure (simple or complex).

Severity of the attack [aura (headache or irritability), symptoms associated with attack (incontinence, incorpressis or loss of consciousness) or postictal (drowsiness, todd paresis or sleep for long time)].

Routine hematological investigations: The following routine hematological investigations were performed at the time of hospital admission for all cases and controls:

Complete blood picture**,** Evaluation of Hemoglobin (Hb) and Hematocrit (Hct), Evaluation of Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC), Evaluation of Total Iron Binding Capacity (TIBC), Evaluation of serum ferritin, Evaluation of serum iron.

IDA was defined as serum ferritin level of <12 (g/dl,mcv and hemoglobin level below reference ranges according to age and sex [**7].**

Electroencephalography (EEG) was done using stellate Hormonie DUO EEG. It was carried out under standard condition with sedation and appropriate provocative method. Both bipolar and refrential montages were used for interpretation.

Written informed consent was obtained from all children' parents, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis: Data were collected, tabulated and analyzed by SPSS 20 software. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD , the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X2). Differences between quantitative independent groups by t test, Mann-Whitney test was used to compare differences between two independent groups when dependent variables are either ordinal or continuous. The significance level was considered at $P < 0.05$.

RESULTS

There was no significant difference between cases and control children regarding age or gender ($p>0.05$) **(table 1)**. There was no significant difference between studied groups regarding family history of convulsions or epilepsy **(table 2)**. **Table (3),** showed the vital signs distribution with

no significant difference between studied groups. **Table (4),** showed the distribution of CRP, K, Na, Ca, Cr and BUN with no significant difference between studied groups. **Table (5),** showed that patients group had significantly higher median TIBC than controls with no significant difference between groups regarding serum ferritin.

Table (6), showed that there was a statistical significant difference between studied groups regarding MCV and HB.

Table (1): Age and sex distribution between studied groups

	Cases (n=45)	Control (n=45)		P
Age (year) (mean ±SD)	**2.13±0.98**	**2.62±1.2**		**0.158**
Gender Male Female	**27(60%) 18(40%)**	**28(62%) 17(37.8%)**		**0.82**

Table (2): Clinical history distribution between studied groups

			Group		X^2	P
			Cases	**control**		
		n%				
Family history of convulsion	**No**	**n%**	23 (51%)	19 4%	**0.71**	**0.39**
	Yes	**n %**	22 (48. %)	26 57.8%		
Family history of epilepsy	**No**	**n%**	23 (51.%)	22 4%	**0.044**	**0.83**
	Yes	**n%**	22 (48.9%)	23 51%		

Table (3): Vital sign distribution between studied groups

	Cases (n=45)	Control (n=45)	P
TEMP (°C)	**38.84±0.58**	**37.5.±0.95**	**0.061**
BP (mm Hg)	**61.35±19.01**	**60.8±19.18**	**0.891**
RR [breaths per minute (bpm)]	**35.84±6.52**	**37.6±5.91**	**0.185**
HR [beats per minute (bpm)]	**130.93±7.1**	**120.13±5.13**	**0.879**

TEMP: temperature, BP: blood pressure, RR: respiratory rate, HR: heart rate,

Table (4): Laboratory parameters distribution between studied groups

	Cases **(n=45)**	Control **(n=45)**	P
CRP (mg/L)	30.57±23.27	25.53±21.51	0.289
K (mEq/L)	3.63±0.63	3.78±0.84	0.339
Na (mEq/L).	143±1.4	143.83±2.63	0.196
Ca (mmol/l)	9.06±1.23	9.27±1.24	0.420
Cr (mg/dL)	0.68±0.13	0.69±0.14	0.764
BUN (mg/dL)	13.62±3.53	13.97±3.92	0.653

CRP: **C-reactive protein**, K: **Potassium**, Na: **Sodium**, Ca: **calcium,** Cr: **Creatinine,** BUN: **blood urea nitrogen**

Table (5): Iron profile distribution between studied groups

	Cases (n=45)	Controls (n=45)	P
TIBC (mg/dl)	300 (54.6-969)	240 (66.4-840)	**0.019***
Ferritin (ng/ml)	150.7 (25.03-1200)	146.2 (12-1200)	**0.849**

TIBC: **Total Iron Binding Capacity**
Mann-Whitney test was used

Table (6): Hemoglobin and RBCs indices among studied groups

	Cases (n=45)	Control (n=45)	P
MCHC (g/dl)	33.0±4.25	33.46±2.71	0.542
MCH	26.5±4.74	32.28±4.17	0.00**
MCV (fl)	57.6 ± 11	72.84±3.66	0.01*
HCT (%)	28.03±5.29	27.86±5.4	0.880
RBCs × 10^3 /ul	3.51±0.48	3.5±0.44	0.874
HB (g/dl)	10.16±1.68	11.09±2.15	0.025*

MCHC: mean corpuscular hemoglobin concentration **MCH:** mean corpuscular hemoglobin, **MCV:** mean corpuscle volume, **HCT:** Hematocrit, **RBCs:** red blood cells, **HB:** hemoglobin
Mann-Whitney test was used
** highly significant
* significant

DISCUSSION

Febrile seizure is the most common convulsive disorder in children which strikes 2% - 5% of children between 6 and 60 months of age. Provoking factors which have been studied are genetics, low birth weight, vaccinations and metabolic disturbances. Risk of recurrence is directly proportional to number of risk factors. About one-third of children with a first FS will have a recurrence. Evidence that iron might be important for neurological functioning has generated considerable optimism that this element might also play a role in initiation of febrile convulsions **[8]**.

The diagnosis of convulsion on the basis of clinical signs, symptoms, or routine laboratory tests is not always an easy task. The variety of ways in which different types of seizures are expressed complicate their diagnosis **[9].**

Since the relationship between iron deficiency and febrile seizure is not yet determined, chance or other unknown factors can be considered as causes **[10]**.

In the current study, there was no significant difference between groups regard sex distribution which in agreement with the study of **Ghasemi and Valizadeh [11]** where they concluded that there were no statistically significant differences between iron deficient and non iron deficient groups as regard to age or gender.

In the current study, iron defiency anemia was more common among studied children with febrile seizure compared to the healthy controls. These results were in agreement with the study of **Jang et al.[12]** who reported that Iron deficiency, defined as ferritin < 30 ng/mL, was more prevalent in the febrile seizure group (49.2%) than in the control group (16.9%).

The current study showed that there were no significant differences between groups regarding, vital signs and or measured laboratory parameters.

The current study showed that cases were significantly higher regarding TIBC than control group with no significant difference between groups regarding ferritin or iron, which in agreement with the study of **Sharif et al. [13]** who found that the average of serum iron and TIBC were significnatly different in the two groups. This means that low serum iron and presence of anemia can serve as a reinforcing factor for the febrile seizure in children.

The current study showed that Mean levels of HB, MCV and MCH were lower significantly among febrile convulsion group than control group, which

in agreement with the study of **El-Shafie et al., [14]** who reported that there was a significant difference between the studied groups regarding Hb, MCV, and MCH, which were lower in the febrile seizures group than in the control group (P < 0.05%).

In the current study Hb was 10.16±1.68 in cases group while it was 11.09±2.15 in control group, which in agreement with the study of **Sadeghzadeh et al. [15]** who evaluated the association between iron deficiency anemia and febrile seizure in children, anemia was defined as Hb<10.5 g% and it was observed in 21.5% of cases with p-value of 0.47.

Limitations: The limitation of this study that the sample size was small and that was not sufficient to confirm our results.

Conclusion: the study concluded that iron deficiency anemia is a risk factor for febrile seizures in infants and children aged 6 months to 6 years.

Recommendations: Community based studies and programs might be carried out to evaluate the etiological factors and exact prevalence of Febrile Convulsions in this age group, as well as to increase the awareness of the society about proper nutrition and early detection of anemia.

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