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STATUS OF SERUM IRON IN CHILDREN WITH FEBRILE SEIZURES

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ABSTRACT: INTRODUCTION: Febrile convulsions are most common seizures of developing brain. Results of data on the relationship between iron deficiency anemia and febrile convulsions are controversial. We hereby studied effect of iron deficiency as a cause of febrile seizure. **AIM OF STUDY:** The aim of this study is to find the association between iron deficiency anemia and febrile convulsion among children. **SETTING AND DESIGN:** Case control study. **MATERIAL AND METHODS:** Study include 80 children with febrile seizure (Cases) and age and sex matched 80 children without febrile seizure (Controls) during a period of 1 year. Hemoglobin level, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and plasma ferritin level were determined in all cases and compared with that of controls. **RESULTS:** Mean plasma ferritin level ($29.5 \pm 21.3 \mu\text{g/l}$) was significantly lower in febrile seizure group than control group ($55.3 \pm 37.6 \mu\text{g/l}$) ($p < 0.0001$). Proportion of cases with a plasma ferritin level $< 30 \mu\text{g/l}$ were significantly higher ($p = 0.001$) than controls. **CONCLUSION:** Plasma Ferritin levels were significantly lower in children with febrile seizures than reference group suggesting a possible role of iron insufficiency in febrile seizures.

KEYWORDS: Febrile seizures; Plasma Ferritin; Children.

INTRODUCTION: Febrile Seizure (FS) is most common type of seizure of developing brain.⁽¹⁾ with incidence of 2.5% or 4.8/1000 person years.⁽²⁾ A febrile convulsion is defined as a seizure in neurologically healthy infants and children between 6 months to 6 years of age with an axillary temperature of at least 37.8°C (Rectal temperature 38.3°C) but without evidence of intracranial infection as a cause or other defined causes of seizures in 24 hours. A single generalized seizure in 24 hours lasting less than 15 minutes without focal feature is categorized as simple febrile seizure and contribute to 80-85% of febrile seizure patients; while complex febrile seizure constitute 15-20% and characterized by focal seizure lasting more than 15 min, with recurrence within 24 hrs., and associated with postictal findings.⁽³⁾

There are flurry of studies recently relating to iron deficiency in variety of neurological problems. Iron deficiency has been implicated in developmental abnormalities, breath holding episode, attention deficit hyperactivity disorder (ADHD), ischemic strokes, but relation between iron deficiency and febrile seizure in children is unclear. To date, the pathophysiology of febrile seizure is unknown.⁽¹⁾ Decrease in plasma ferritin levels may lower seizure threshold. Iron is important for function of various enzymes and neurotransmitters in central nervous system.^(4,5) In view of the above, this study was under taken to evaluate the serum iron (Fe) status in febrile seizure and to find a possible association between serum iron and febrile seizure if any.

MATERIALS & METHODS: A case control study was conducted in Pediatric Department of the MLB Medical College and Hospital Jhansi, Uttar Pradesh, India during 2013-2014. All hospitalized children between ages of 6 months to 6 years who fulfill criteria of febrile seizures were included in the study.

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Central nervous system (CNS) infections like meningitis and encephalitis, serum electrolyte imbalance and other acute neurological illness, or history of iron therapy for more than one week or other conditions known to alter serum iron level, were excluded. Age, sex and socioeconomic status matched children, hospitalized for a febrile illness without seizure such as respiratory and gastrointestinal infections were selected as control group.

After taking consent from parents, detailed history regarding age, sex, developmental mile stone, family history of febrile seizure or epilepsy, mean of temperature peak at admission and underlying illness were recorded for all cases and controls as well as details of seizure, history, duration, frequency and locality for all cases with febrile seizure. Detailed clinical examination including anthropometry and systemic examination were done to find out cause of fever. Detailed CNS (Central nervous system) examination was also done to rule out other causes of seizure in the cases.

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) level. Plasma ferritin level was measured using enzyme immunoassay method. 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 including brain. Cases and controls were compared with regards to Hb, MCV, MCH and PF as continuous and as dichotomous variables.

The chi- square (χ^2) test was used to assess the statistical significance of the differences in proportions, whereas the sample t-test was used when data was tested as continuous. P-value <0.05 being considered significant.

RESULTS: We studied 80 children (49 male and 31 female) with febrile seizures and age & sex matched reference group of 80 patients with febrile illness without seizures.

Among patients of febrile seizures; 52 (62%) were of simple febrile seizures and rest 28(35%) were of complex febrile seizures. Seizures were found to be more prevalent in 1-3 years of age group with no sex predilection in type of febrile seizure. PF level ($29.5\mu\text{g/l} \pm 21.3$) was significantly lower in febrile seizure group than with reference group which was statistically significant ($P=0.001$).

Mean level of Hb, MCV, MCH and Plasma ferritin were lower in children with complex febrile seizures than simple febrile seizure but differences were statistically significant in Hb and MCH only.

DISCUSSION: Results show that the mean PF level was significantly lower in children with febrile seizure group than control group. Similar to our study Pisacane et al.⁽⁶⁾ reported a significantly higher rate of iron deficiency anemia among children with first febrile seizure than in their controls; Korbinsky et al.⁽⁴⁾ suggested that anaemia decreases the threshold for first febrile seizure. Idjradinata et al.⁽⁷⁾ reported that iron deficiency can cause developmental delay and behavioral disturbances early in life. In contrast to our study Salehi Omran et al.⁽⁸⁾ shows no significant correlation of plasma ferritin with febrile seizure. In the Rehman and Billoo study,⁽⁹⁾ plasma ferritin level was significantly lower in cases as compared to controls and suggested that iron deficient children are more prone to febrile seizure.

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,⁽¹⁰⁾ our finding suggests that the mild reduction in plasma ferritin ($\leq 30\mu\text{g/l}$) is associated with febrile seizures. Selection of this cut-off point is arbitrary, because the commonly used cut-off point for iron deficiency

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anaemia is between 10 and 20µg/l. However only few patients had levels of plasma ferritin <20µg/l, and therefore we selected a higher cut-off point of 30µg/l. It is known that ferritin is an acute-phase reactant that increases nonspecifically in response to any febrile illness.⁽³⁾ However, fever was present in all patients in our two study groups. Therefore differences in ferritin concentration between the two groups cannot be explained by fever.

The lack of significant differences in Hb, MCV and MCH between the two study groups may be explained by the small sample size. Selection bias as an explanation for the differences in iron status between the two groups is unlikely. Eligible children with and without FS were matched on age and sex and socioeconomic status. 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.

The exact explanation for the significant differences in the level of plasma ferritin among children with FS compared with the reference group is unknown.

In conclusions, plasma ferritin level was significantly lower in children with febrile seizure than control in our study. Considering small sample size in this study; further studies on the subject will be worthwhile to be undertaken.

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