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IRON DEFICIENCY AS A RISK FACTOR FOR FEBRILE SEIZURES

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ABSTRACT

Febrile seizure (FS) is a common cause of seizure in young children and occurring in 3-4% children under 5 years of age. Iron deficiency is reported as commonest micro-nutritional deficiency worldwide and has been associated with febrile seizures. The aim is to evaluate role of Iron deficiency as a risk factor of febrile seizure. A total of 170 children (6m – 5 years) were included in the study. 70 cases had febrile seizure as defined by International League Against Epilepsy and rest 100 controls had short history of febrile illness (< 3 days) without seizures. Anemia was defined as decrease of the Hb <11gm%, and serum ferritin <12ng/ml. Discrete variables are expressed as counts (%) and compared using the Chi-square tests, Adjusted odds ratios and Statistical significance is set at $p < 0.05$. In the present study, 34.3% cases belong to 6-16 months age group and male to female ratio in cases was 1.69:1. 65.7% of cases and 45% of controls were iron deficient. On correlating iron deficiency with gender, male preponderance was observed in children with febrile seizure. The study observed 65.7% cases of FS had iron deficiency as compared to 45% of control group. (OR-2.34; $p<0.05$). Also, there was statistically significant association between recurrence of FS and iron deficiency. Early detection and timely correction of iron deficiency may be helpful for prevention of febrile seizures in children of this age group.

INTRODUCTION:

Febrile Seizures (FS) are most common cause of seizure in young children, and perhaps one of the commonest pediatric emergencies worldwide, occurring in 3-4% of children under the age of 5 years. Although FS is benign and rarely leads to brain damage, it causes emotional, physical, and mental damages, which are stressful for parents, and affects families' quality of life. Earlier Indian studies suggested that up to 10% of children experience a febrile seizure, though recent data indicate that the incidence rate in India is similar to western figures. Iron deficiency (ID) is reported as commonest micronutritional deficiency worldwide (30%) especially in developing countries and is a preventable and treatable condition. Iron deficiency reduces the metabolism of some neurotransmitters, such as monoamine and aldehyde oxidase and thus it may alter the seizure threshold of a child. Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition.

Hence, the current study is carried out to evaluate the relationship between iron status and febrile seizures, if any.

MATERIALS AND METHODS:

This is a descriptive-analytical case control study done in the Department of Pediatrics, Tripura Medical college, Hapania, Agartala during November 2021 to April 2023. Cases were children of age group 6 months to 5 years presenting with simple febrile seizures to the Pediatrics Emergency Department and wards of the hospital during the study period. Diagnostic criteria for simple febrile seizures according to the International League againstEpilepsy (1993) defines febrile seizure as a seizure occurring in childhood between 3 month and 5 years of age, associated with a febrile illness not caused by an infection of the CNS, without previous neonatal seizures or a previous unprovoked seizure and not meeting criteria for other acute symptomatic seizures.

Consecutive cases were selected for the study and concurrent controls were selected from the same setting and included febrile children of age group 6 months to 5 years who presented with short duration fever (<3 days) but without seizures.

Children presenting with afebrile seizures, history of seizure disorder, previous afebrile seizures, CNS infections, metabolic imbalance, developmental delay, neurological deficit, Iron supplementation for more than 3 days in last 6 months, previously diagnosed cases of other hematological problems like hemolytic anemia, bleeding or coagulation disorders, hematological malignancies were excluded from the study. After informed consent, detailed history was elicited and physical examination was done. Cases of anemia due to other causes were excluded on the basis of exclusion criteria mentioned earlier. At the time of enrollment - detailed history and physical examination were recorded on the performa. Blood samples for Hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), Red Cell Distribution Width (RDW) and plasma ferritin were collected for each patient. Blood investigations were done using an automated hematology analyzer (Mindray BC-3000Plus). Plasma Ferritin level was measured by using the ELISA method for quantitative determination of human Plasma Ferritin. Anemia was defined as decrease of the Hb <11gm%, and serum ferritin <12ng/ml (WHO).[6] Data were entered in MS Excel, cleaned and completeness checked. Analysis was done using SPSS Version 13. Discrete variables were expressed as counts (%) and compared using the Chi-square tests, Adjusted odds ratios and Statistical significance is set at $p< 0.05$.

RESULTS:

A total of 170 children (6m – 5 years) were included in the study. 70 cases had febrile seizure as defined by International League Against Epilepsy and rest 100 controls had short history of febrile illness (< 3 days) without seizures. In the present study, there were 44 males among cases and 60 males among controls.

26 females were present in case group as compared to 40 females in control group. This implies uniform distribution of children among the cases and controls according to gender. In age group distribution, 34.3% cases belong to 6-16 months age group and similarly control group has maximum number (35%) in this age group. The male to female ratio in cases was 1.69:1 and in control group was 1.5:1. On evaluation for Iron deficiency, 65.7% of cases and 45% of controls were iron deficient. On correlating iron deficiency with gender, male preponderance (72.7%) was observed in children with febrile seizure against 41.6% iron deficient males in control group. On correlating iron deficiency with prevalence of

febrile seizures, we observed that 65.7% cases of FS had iron deficiency as compared to 45% of control group. (OR-2.34; p<0.05) (Table 1). When correlating Iron deficiency with various demographic factors, a positive association has been found with male gender and lower socioeconomic status. There is statistically significant association between recurrence of FS and iron deficiency (Table 2). However, no statistical correlation was observed for type of febrile seizure and iron deficiency.

DISCUSSION:

In the present study, the mean age of children with febrile seizures in our study is 28.41 months. The incidence of febrile seizure in <3 years was higher (78.5%) as compared to >3years age groups (21.5%). Hartfield et al reported maximum cases in the age group less than 24 months and mean age of 17.9 months. Kumari et al reported 55.8% of cases and 56.5% of controls were in the age group less than 17 months. Higher prevalence of febrile seizure in younger age group could be because of immaturity of the brain as maximum hippocampal growth is noted to occur in the period 15-36 months, this is the period of normal brain maturation which is thought to have enhanced neuronal excitability.

In the present study there was male preponderance, which is similar to previous studies. Whether there is a biological basis for the gender specific differences in febrile seizure susceptibility, or whether boys just contract more fevers and therefore are at greater risk, is currently not established.

On correlating prevalence of FS with SES, present study shows majority of children of FS belong to lower SES (65.7%) in contrast to control group where maximum children belong to middle SES. This difference was statistically significant with Odds Ratio 3.16 (p=0.008). The plausible explanation could be that children belonging to LES are more prone to acute febrile illnesses, which predisposes them to higher chances of developing FS. Kumari et al [15] also found similar results where 115 of 154 cases belonged

Table 1: Iron Deficiency in Cases and Controls

	Cases(70)			Controls(100)				
	No	% of cases	% of iron deficient children	No	% of controls	% of iron deficient children	Odds ratio	p value
Iron deficient	46	65.7	50.5	45	45.0	49.5	2.3426	0.0082
Not deficient	24	34.3	30.3	55	55.0	69.6		

χ^2=7.103, p value = 0.008, , d.f. =1

Table 2: Correlation of iron deficiency with first and past history of febrile seizure

	Iron deficient (%)	Z Value	p value
First Seizure (48)	27(56.2)	2.45	0.0143
Seizures in Past (22)	19(86.3)		

χ^2= 6.570, p value = 0.037, d.f. =1 to lower socioeconomic status. This coincides with results of previous studies where lower socioeconomic status has been a risk factor for febrile seizures.

Iron deficiency was found as a significant risk factor for simple febrile seizures in children of age group 6 months to 5 years in our study. In the study done by Pisacane, et al among children of the same age group, similar results were noted and the odds ratio was 3.3 (95% CI of 1.7-6.5).

In present study iron deficiency was identified as a risk factor for febrile seizure with Odds ratio of 2.346 (p=0.0082). This has been very similar to prior studies relating iron deficiency with febrile seizure as a modifiable risk factor.

Daoud et al observed a significantly lower ferritin level in the first febrile seizures group than in the reference group proving that serum ferritin is 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. Vasvani et al observed significant low serum ferritin levels in children with FFS than in controls. On the contrary, few studies found no significant difference in serum ferritn level between the two groups.

On correlation of iron deficiency with number of FS, we observed that, there is statistically significant association between recurrence if FS and iron deficiency (z =2.45; p=0.0143) indicating iron deficiency as a risk factor of recurrence of febrile seizure. Though on correlation of iron deficiency with frequency of FS, no significant association was found The type of FS and iron deficiency were also correlated, where no statistically significant correlation was found. We found that, majority of cases were simple febrile seizures, out of which 64.5% were iron deficient and 75% of complex febrile seizures were iron deficient. In a similar study by Aliabad et al reported 86% cases to be of simple febrile seizures and 14% of complex FS.

The strength of current study included standardized criteria for diagnosing febrile seizures, and iron deficiency, concurrent enrollment of controls and cases, and no recall bias regarding exposure. The limitation of the study being a hospital-based study the prevalence of exposure and outcome variables may be different from a community setting. Serum ferritin, a nonspecific acute phase reactant can rise in any inflammatory conditions, although both cases and controls were having fever at the time of enrollment.

A strong correlation exists between iron deficiency and febrile seizure. Early detection and timely correction of iron deficiency may be helpful for prevention as well as recurrence of febrile seizures in children of this age group.