ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF IRON AND ITS INDICES IN CHILDREN WITH FEBRILE SEIZURES – A MULTIVARIATE STUDY

Paediatrics

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ABSTRACT

OBJECTIVE: To study relationship between iron and its indices [haemoglobin , S. Iron, S.ferritin and Total Iron Binding Capacity (TIBC)] with febrile seizures in children.

MATERIAL AND METHODS: 37 children with febrile seizures and equal no of age and sex matched febrile children (controls) were included. After obtaining history and clinical examination, blood samples were obtained and sent for haemoglobin,S.iron,S.ferritin and TIBC. A stepwise approach was used to enter terms into the model with a limit of p<0.10,in univariate analysis. Multivariate logistic regression model was then used to identify independent risk factors for febrile seizures.

RESULTS : Mean haemoglobin (10.81 ± 1.27vs 11.50 + 0.76g%), Serum iron (65.16 ± 36.36 vs 90.72 + 31.1 ug/dl) and serum ferritin (44.59 ± 28.52 vs 83.60 + 37.87ug/l) were significantly lower in febrile seizure cases as compared to controls .The number of children with abnormal Iron indices were also significantly higher in febrile seizure group. However, TIBC levels were comparable in cases and contol. On multivariate analysis S. Ferritin was identified as an independent risk factor for febrile seizures with an odds ratio of 0.673 (95% CI 0.460-0.984).

CONCLUSION: It was concluded that there exist a positive association between Iron deficiency anemia and febrile seizures.Moreover, S. Ferritin was identified as an independent risk factor for febrile seizure.

KEYWORDS

Febrile seizures , Ferritin , Haemoglobin , Serum Iron ,TIBC.

INTRODUCTION

Febrile seizures are seizures occurring during a febrile illness in infancy or childhood usually between 6 months to 5 years of age but without evidence of intracranial infection or well defined cause for the seizure [1]. Febrile seizures the most common seizures in children [2].Many factors have been identified as risk factors for febrile seizures [3].

Prevalence of iron deficiency anemia has been reported to be in between 70-80 % in Indian children with peak age between 1-2 years which coincides with peak age of febrile seizures (NFHS -3) [4].As iron is considered as an important micronutrient for neurological functioning .Studies were done to evaluate its role in etiopathogenesis of febrile seizures.These studies have however yielded conflicting results. In some studies iron deficiency has been identified as a risk factor while others iron deficiency has been postulated as neuroprotective factor.

There is lack of such studies from India. This study was therefore e aimed to evaluate any relation of iron and its indices in febrile seizure patients.

MATERIALS AND METHODS

The case control study was conducted in Department of Pediatrics of SM HOSPITAL ,New Delhi after obtaining due clearances from the institutional ethical committee. Thirty seven children between 6 months to 5 years of age presenting with first episode of simplefebrile seizures were included as Cases. Children with developmental delay, CNS infections, past history of non febrileseizures, multisystem chronic diseases or those presenting with complex febrile seizures were excluded. Thirty seven age and sex matched febrile children without seizures were taken as Controls.

After obtaining informed consent from caregiver,history was taken from the parent and clinical examination was done.Blood samples were collected from cases as well as controls using standard aseptic precautions.Samples were sent for measurement of Hemoglobin (HB), Serum iron, Serum ferritin and Total iron binding capacity (TIBC).Iron deficiency anemia was defined as Haemoglobin < 11 gm/dl as per standard WHO guidelines.

Statistical analysis was performed by the SPSS program for windows. Continuous variables were presented as mean +/- SD, and categorical variables were presented as absolute numbers and percentage A t- test was used for comparison of data between 2 the groups.Data were checked for normality before statistical analysis. Categorical variables were analyzed using either the chi square test orFisher's exact test. Multivariate logistic regression model was used to identifyindependent risk factors for febrile seizures. For all statistical tests, a p≤0.05 was taken to indicate a significant difference.

RESULTS

Thirty seven consecutively selected children presenting with febrile seizures in age group of 8 months to 60 months (22.4 +/- 13.4),weight mean SD (11.2 +/- 2.1 Kg) and male to female ratio of 1 .17 were included in the study. Thirty seven age and sex matched febrile children (without seizures) were also taken as controls. The comparison of various parameters between cases and controls is given in table 1.

Table 1 .The comparison of various parameters

	Cases (n=37)		Controls (n=37)		P-value
	Min-Max	Mean ± SD	Min-Max	Mean ± SD	
HB (mg/dl)	7.8 - 12.8	10.81 ± 1.27	9.5 - 12.8	11.50 ± 0.76	0.006
S.Iron (ug/dl)	13 – 140	65.16 ± 36.36	34 - 143	90.72 ± 31.14	0.002
S.Ferritin (ug/L)	8.40 - 110.60	44.59 ± 28.52	14 - 140.30	82.60 ± 37.87	<0.001
TIBC (ug/dl)	250 - 494	339.49 ± 71.17	232 - 450	301.22 ± 54.23	0.051

Mean Hb, mean S.ironand S.ferritinlevels were noticed to be significantly lower in the febrile convulsion as compared to controls .Mean TIBC values although higher in febrile seizure group as compared to control no statistically significant difference was ascertained on comparison.

Table 2 shows the comparison of number of children with abnormal iron and its indices between cases and controls.

	Cases (37)	Controls (37)	P-value
	n (%)	n (%)	
Hb<11g /dl	15 (40.5 %)	7 (18.9%)	0.021
SF<30 ug/L	15 (40.5%)	7 (18.9%)	0.002
S.Iron<50 ug /dl	15 (40.5%)	4 (10.8%)	0.007
TIBC>360 ug /dl	14 (37.8%)	7 (18.9%)	0.071

Of the 37 febrile seizure patients 15 (40.5 %) had anemia whereas in control group only 7 (18.9%) had anemia on hemoglobin estimation. There are significant differences seen in the number of anemic febrile seizure children and anemic controls on basis of all hematological parameters except TIBC.

Table 3 Multivariate logistic regression table

	Sig.	OR	95% C.I.	
			Lower	Upper
HB (g/dl)	0.176	2.234	0.697	7.163
S.Iron (ug/dl)	0.635	0.995	0.976	1.015
S.Ferritin (ug/L)	0.041	0.673	0.460	0.984
TIBC (ug/dl)	0.078	0.986	0.972	1.002

While applying Forward Stepwise Logistic Regression (Table 3), we found Serum ferritin as an independent risk factor for simple febrile seizure with odds ratio of 0.673

DISCUSSION

In various studies low levels of Hemoglobin, serum iron, serum ferritin and increased levels TIBC have been significantly related with the incidence of febrile seizures.In our study it was found that mean haemoglobin, S.iron and S,ferritin levels were significantly lower in children with febrile convulsions as compared to controls.On comparing the anemic children (Hb< 11 gm %) in the groups a simple trend was noticed and it was seen that the no of anemic children with abnormal indices (S.iron,S.ferritin) were significantly more in febrile seizure group.However, TIBC levels as well as the number of children with abnormal TIBC were comparable between the groups. S Ferritin also came out as an independent risk factor in multivariate analysis.It was determined that with a unit decrease in S.Feritin there is (1/0.673) times chance that it will be a case.

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).Kobrinsky [5] suggested that anemia raises the threshold for first febrile seizure. They studied the level of HB, and serum iron and found that in children younger than 2 years from Naples, 30% of Febrile Seizure children had anemia compared with 14% in the controls. However PF level was not measured in his study. Differences in Hb reflect differences in chronic iron status which are not affected by acute stress reactions.

Iron is an essential element in neurotransmitters and its association with febrile seizures was first observed and published in mid 90's in an Italian study [6]. This was followed by few more international studies [2],[5],[8],[10],[11].

Ferritin is an iron-containing protein that functions in the body as an iron-storage compound. Serum 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 [9]. It is known that ferritin is an acute-phase reactant that increases nonspecifically in response to any febrile illness [8] In the studies done by Daoud, *et al*. [7] and Vaswani, *et al.* [8] from Mumbai it was found that the mean serum ferritin level was significantly low in children with first febrile seizures (31.9±31.0 mcg/L) as compared to controls (53.9±56.5 mcg/L) (*P*=0.003). However, nosignificant difference was noted in the mean hemoglobin value of cases (9.4±1.2 g/dL) and controls (9.5±1.0 g/dL) (*P*=0.7), or in the mean value of blood indices.

Also in consonance with studies by the Rehman and Billoo et al , Hartfield et al and Idjradinataet al our findings suggest that mild reduction in Serum Ferritin (SF) level (<=30 ug/L) is associated with Febrile Seizure. As ferritin is an acute phase reactant and it levels are higher in febrile illnesses and a higher cut off was taken. In present 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.

The strength of present study included standardized criteria for diagnosing febrile seizures, and iron deficiency, elimination of incidence prevalence bias, concurrent enrollment of controls and cases, and no recall bias regarding exposure.The study does have some limitations. As it was 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. Iron deficiency and lead poisoning may be associated. Blood lead levels could not be determined in our subjects.

CONCLUSIONS :

It was concluded that there is a positive association between Iron deficiency anemia and febrile seizures. Moreover, S. Ferritin was identified as an independent risk factor for febrile seizure.

Future scope :

Iron deficiency is a modifiable risk factor for simple febrile seizures in Indian children of age group 6 months to 5 years. Early detection and timely correction of iron deficiency may be helpful for prevention of simple febrile seizures in children of this age group.

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