

Research Article

Association between iron deficiency anemia and various red cell parameters with febrile convulsions in children of age group 3 to 60 months

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ABSTRACT

Background: Febrile seizures are the most common seizures in children. Incidence is around 2-5% among children of age group 3-60 months. There is variable association between febrile convulsions and hematological parameters associated with iron deficiency anemia in children. Iron deficiency is also associated with many of the behavioural disorders in children. Our study compares the various blood indices and their associations with febrile convulsions in children.

Methods: This is a prospective case control study conducted over a period of one year in a tertiary care hospital. Consecutive fifty children with first episode of febrile seizure in the age group of 3 months-60 months admitted in the institution were taken as cases and fifty children with fever due to other causes without seizures were taken as controls. Various blood parameters were compared among these two groups and statistically analyzed for the outcome.

Results: Our study clearly shows that the Hemoglobin level, MCH, MCHC, Serum Ferritin levels does not show any significant differences between the two groups disapproving the theory that iron deficiency anemia is a trigger for febrile seizures.

Conclusions: We concluded that a strong association between iron deficiency anemia and febrile seizures cannot be proven with these results. A study with a larger population is suggested.

Keywords: Febrile convulsion, Iron deficiency anemia, Serum ferritin, MCV, MCHC

INTRODUCTION

Febrile seizures are the most common seizures in children.¹ Their incidence is 2-5% in children.² It is peculiar to note the results of various studies conducted on the prevalence of anemia among children with seizure. While most studies have suggested iron insufficiency as a predisposing factor for febrile seizures, some have even described less frequency of iron deficiency anemia in children with febrile seizures.³ Pisacane and colleagues⁴ supported an association between iron deficiency anemia

and febrile seizures whereas, Kobrinsky, et al reported that iron deficiency raises the threshold for seizures and Momen and Hakimzadeh reported that there was no relation between iron deficiency anemia and first febrile convulsions in children.^{5,6}

Behavioural disturbances have been observed in iron-deficient children such as irritability and disruptive behaviour, short attention spans, poor scholastic performance and lack of interest in their surroundings. An attention deficit was apparently the fundamental

abnormality in most.⁴ Madan, et al reported recently that children aged 6-23 months with moderate to severe iron deficiency anemia had lower mental and psychomotor scores that persisted to as long as 19 years of age.⁷ These children also had lower scholastic achievement and needed more special education assistance than iron sufficient children. These impairments may be related to several effects of iron deficiency auditory evoked potentials.⁸

Kumari, et al provides evidence that iron deficiency is also in the developing brain including altered development of neurons in the hippocampus that encodes memories, impaired energy metabolism, delayed maturation of myelin, and slowed visual and a risk factor for febrile seizures in children 6 months to three years of age.⁹ This carefully done case-control study with a large sample size showed a highly significant association between iron deficiency and febrile seizures.

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

The maximum age of febrile convulsions occurrence is 14-18 months, which overlaps with the maximum prevalence of Iron Deficiency Anemia which is 1-2 years old.¹¹ In developing countries the prevalence of anemia is little lower than 50%.¹² Among children in Tamilnadu, a recent study conducted in 2011 by scholars from SRM University revealed that prevalence of iron deficiency anemia in preschool children was 58.1%.¹³

Considering the high prevalence of the two conditions in similar age group, this study was conducted to find a relationship between the two conditions and also substantiate the causative relationship with the evidence of alteration in other red cell parameters.

METHODS

This is a prospective case control Study was carried out from October 2014 to October 2015 in a tertiary care teaching and referral hospital catering mainly to rural population. Consecutively selected 50 children with first episode of febrile seizure in the age group of 6 months-60 months admitted in the institution were taken as cases and 50 children with fever due to other causes such as upper and lower respiratory tract infections and gastroenteritis but without seizures were taken as controls. Children with a history of seizures, central nervous system infections, neurologic deficit and head injury were excluded from the study. Controls were group-matched to cases for age and sex. Febrile seizure was defined as an event occurring between ages 3 months and 5 years, associated with fever but without any intracranial infection or other defined causes of seizures.

Blood samples were collected from all participants, after getting informed consent from the care takers for measurement of Hemoglobin (Hb), Haematocrit (Hct) Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), and Serum Ferritin, Serum Iron, $P < 0.05$ being considered significant. Iron deficiency anemia was defined as hemoglobin $< 11 \text{ g/dL}$, MCV $< 73 \text{ fl}$, MCHC $< 24 \text{ pg/dl}$. For all children diagnosed with Iron Deficiency anemia Serum Ferritin and Serum Iron was done irrespective of them falling under case or control group.

Statistical analysis

Data was analysed using the Statistical Package for Social Science (SPSS). The independent t-test was used for comparison of data between two groups. Chi square test was used to compare type of anemia.

RESULTS

Of the 100 children studied, 50 with febrile seizures were enrolled in the case group, and 50 with fever but no seizures were considered as controls. The controls and cases were age and sex matched. Mean age of the study group was $25.28 \text{ months} \pm 13.23$. There were 24 males in the case group where as the number of males in the control group was 26.

Of the 50 patients with seizure 48% had anemia and 20 % had anemia in the non-seizure group. Among the cases 26 out of total 50 cases had Microcytic Hypochromic anemia. 24 among the control group had microcytic hypochromic anemia. None among the cases or controls had megaloblastic anemia or hemolytic anemia. When analysed with Chi square test there was no significant difference in the two groups regarding type of anemia.

Table 1: Comparison of laboratory data between cases and controls.

	Seizure group (mean \pm standard deviation)	Non seizure group (mean \pm standard deviation)	P value
Hemoglobin	11.04 \pm 1.03	11.38 \pm 0.87	0.2134
MCV	68.84 \pm 12.68	76.76 \pm 5.64	0.007*
MCH	24.63 \pm 3.62	25.88 \pm 2.83	0.18
MCHC	32.74 \pm 2.96	33.64 \pm 1.78	0.19
Serum ferritin	17 \pm 5.115	25.34 \pm 10.33	0.11
Serum Iron	61.42 \pm 20.61	119.40 \pm 35.87	<0.001*

Unpaired t test was used to check for statistical significance; *Statistically highly significant

There were no significant differences between the cases and controls in the parameters like Hemoglobin, MCH, MCHC, Serum Ferritin levels. MCV and Serum Iron were significantly low in the febrile seizure group as

compared to control group (Table 1). In terms of Serum Iron and MCV this difference was statistically highly significant.

DISCUSSION

This study was conducted in a tertiary care hospital in South India where the incidence of iron deficiency anemia is very high when compared to the developed world. It was conducted to reach a conclusion regarding the possibility of iron deficiency anemia being one of the triggering factors for febrile seizures and if so, it is preventable by nutritional management by giving iron supplements and iron rich foods.

Our study clearly shows that the hemoglobin level, MCH, MCHC, Serum ferritin levels does not show any significant differences between the two groups disapproving the theory that iron deficiency anemia is a trigger for febrile seizures. MCV was significantly low with a p-value of 0.007. Serum Ferritin showed low value among the seizure group but it was not significant. Serum iron showed significantly low value in the seizure group. Many of previous studies also show this type of varied results for various parameters.

A study done in Iran had similar results as the mean ferritin and hemoglobin was not significantly different in the febrile seizure compared to the reference group; However MCV, MCH was significantly higher in the febrile seizure group ($p < 0.05$) compared to reference group in contrast with our study were MCV was the only red cell parameter which showed some difference.¹⁰ In the Mansouri, et al study, mean Fe and Ferritin were higher in the convulsive group but with no statistically significant differences.¹⁴ Again, in the study of Kobrinsky, et al the febrile convulsion group suffered less from iron deficiency.⁵ Patients with febrile seizures were less frequently iron deficient as defined by a free erythrocyte protoporphyrin level, hemoglobin concentration, hematocrit. They concluded that iron deficiency could have a protective effect against febrile convulsions. In a paper by Bidabadi, iron deficiency in the febrile convulsion group (44%) was less than in the control group (48%), Serum iron, and plasma ferritin were significantly higher among the cases with first febrile convulsions than in the controls.³ The amount of Hb, MCV, MCH, and MCHC were also higher among cases than controls, but differences were not statistically significant. The protective effect of iron deficiency against febrile convulsions was not confirmed. The study by Derakhshanfar, et al the amount of Hb, Hct, MCV, MCH, MCHC, RBC count, serum iron and plasma ferritin were significantly higher and TIBC was significantly lower among the cases with febrile convulsion than the controls.¹⁵ The incidence of iron deficiency anemia was significantly higher in controls compared with the cases (p less than 0.016).

Results of another study showed 22.5% of the children in the febrile convulsion group suffered from anemia, while 34.0% of the children in the control group were afflicted with it ($P < 0.001$).¹⁶ There were significant differences between the febrile convulsion group and the control group regarding blood indices such as Hb, MCV, MCH, and MCHC, so that all these indices were higher in the febrile convulsion group as compared to the control group. Even though the mean serum iron and serum ferritin in the cases were higher than the means of the control group, these differences were not significant. A cross sectional studies done by Waheed, et al Talebian, et al, also confirmed this.^{17,18}

There are many studies which contradict our results. In the study of Hartfield, et al iron deficiency was found to be 9% and 5% in the children of two groups of febrile convulsion and febrile without convulsion, respectively; and iron-deficiency anemia was found to be 6% and 4% in the former and latter groups, respectively.¹¹ The one done by Modaresi M which proves that Hb, S iron, S. Ferritin were lower in Febrile seizure group and also MCV which does not show a significant difference in contrast with our result in which MCV showed significantly low level in febrile seizures.¹⁹ Similar results were observed by Pisacane, et al Daoud, et al showed mean serum ferritin was significantly low in children with first febrile seizure and also proportion of children with low ferritin was significantly higher in febrile seizure group than in controls.^{4,20} Some studies done in India also agrees with these findings.^{9,21}

One finding which stands unique in our study Serum Iron which is less in case group which shows that iron deficiency can have positive association with febrile seizures. This finding is seen in other studies like but there are studies disapproving this.^{9,10,22} The importance for this finding is debatable as Serum Iron has got a wide range for the normal values and it is age dependent and our population was very small. These factors would have altered our result.

The limitations of our study was that the study involved only a small sample size, controls were from those attending the hospital not from general population and the cases and controls were not matched for temperature.

CONCLUSION

Our results showed varied results for different parameters but majority of the parameters Hemoglobin, MCH, MCHC, Serum Ferritin showed no significant difference between the children with febrile convulsions and those having fever without convulsions. MCV, Serum Iron was less in the case group than in the control group. It is concluded that a strong association between iron deficiency anemia and febrile seizures cannot be proven with these results. A study with a large population is suggested.

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