

Original Research Article

Study the iron status in children with febrile seizures: a hospital based cross sectional study

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ABSTRACT

Background: Febrile seizures are most common among childhood seizures, accounts to 2% to 5% in children below 5 years of age. Iron deficiency can cause many neurological deficits and may lower the seizure threshold. The present study was conducted to determine the iron status in children with febrile seizures.

Methods: The present cross-sectional study was conducted in the Department of Pediatrics, HIMS, Dehradun, over a period of 12 month from January 2018 to December 2018. A total of 105 children of age group 6 month to 5 years, coming to pediatrics department were included in the study. Total study subjects were divided into two groups, Group I (febrile seizure) and Group II (other than febrile seizure). A consecutive sampling method was done for selection of study subjects.

Results: In Group I (febrile seizure), the number of males were 71.7% while females were 28.3% with male: female ratio of 2.5:1. In Group I (febrile seizure), 61.7% of subjects had deficient iron level while 38.3% of subjects had normal serum iron level. Our study shows significantly low mean serum ferritin and mean serum iron level in subjects with febrile seizures.

Conclusions: We concluded that iron deficiency is more common in febrile seizures and there is a positive association between serum iron level and febrile seizures.

Keywords: Febrile seizures, Iron status, Neurotransmitters, Serum ferritin, Serum iron

INTRODUCTION

Febrile seizures are most common form of childhood seizures. These accounts to 2% to 5% in children below 5 years of age.¹ Febrile seizures are seizures that occur in the age group of 6 months to 5 years with the temperature of 38°C (100.4°F) or higher, that are not caused due to the result of central nervous system infection or any metabolic cause and without any history of prior afebrile seizures.²

Febrile seizures are mostly benign and seldom leads to brain damage, but it causes more of emotional, physical,

psychological and mental stress to parents and hamper family's quality of life.³ The recurrence rate after first episode of febrile seizure in children under 1 year of age is 50% and 28% in children older than 1 year of age.⁴

Febrile seizures can be simple or complex. Around 80% of febrile seizures are mostly simple febrile seizures. 78% of these simple febrile seizures lasts for less than 6 minutes.⁵

In India 70% of children between 6 to 59 months have anemia among which the cause in >50% is iron deficiency anemia (IDA) which also coincides with the

peak incidence of febrile seizure, i.e., 14 to 18 months of age.⁶ The fall in the serum ferritin levels is an indicator of iron deficiency and can be seen prior to the appearance of anemia. The serum ferritin level acts as an indicator of iron stores in the human body.⁷

Iron is an important micronutrient required for the production of neurotransmitters (serotonin, dopamine, gamma amino butyric acid), enzymes (monoamine and aldehyde oxidase) and for myelination. Hence the deficiency of iron in children may lower the seizure threshold.⁸

As the age prevalence of iron deficiency anemia in children and febrile seizures are the same and it is also known that fever can aggravate symptoms that results from anemia, therefore relationship between iron deficiency anemia and febrile convulsions is probable.⁹ Thus, the present study was conducted to determine the iron profile in children with febrile seizures and also to find out the association between iron levels and febrile seizures.

METHODS

The present study was observational cross-sectional study conducted in the Department of Paediatrics, Himalayan Institute of Medical Sciences (HIMS), Dehradun, over a period of 12 month from January 2018 to December 2018.

A total of 105 children, coming to paediatrics outpatient department and admitted in pediatric ward were enrolled in the study. A consecutive sampling method was done for selection of study subjects.

All children of age between 6 months to 5 years having history of seizures with fever were included in the study. Children who were already on Iron therapy, having known hematological problems other than iron deficiency and whose guardians refused to give consent were excluded from the study.

Ethical clearance for the study was obtained from the ethics committee of the institute. Written informed consent from the guardians was obtained for enrolling the subjects in the study. Data was collected on predesigned proforma having demographic profile, details of seizure episode and complete clinical evaluation of the subjects including history and examination was noted. All children enrolled in the study were grouped into two groups, namely, Group I comprising of subjects with 'Febrile seizure' and Group II comprising of subjects 'other than febrile seizure' on the basis of clinical scenario.

Under full aseptic precautions, blood sample was taken for hematological parameters namely hemoglobin (Hb) and analysis of serum iron, serum ferritin was done to assess the iron status of study subjects. Serum iron

estimation in blood was done by Ferrozine-no depolarization method on Unicel Dx C 800, serum ferritin by enzyme linked fluorescence assay on Vidas PC and hemoglobin (Hb) estimation by Beckmann coulter apparatus and Roller-20 LC apparatus.

Statistical analysis

Interpretation and analysis of obtained data were done by using Microsoft Excel and statistical package for social sciences version 20. Independent student T-test was used for comparison of quantitative data. Chi-square test/Fisher's exact test was used for comparison of qualitative data and for association between different variables. P value less than 0.05 was taken significant.

RESULTS

Total of 105 subjects were grouped into Group I (febrile seizure) and Group II (other than febrile seizure). Group I had 60 subjects and Group II had 45 subjects.

Table 1: Distribution of subjects according to age (n=105).

Age interval (months)	Group I (%) (n=60)	Group II (%) (n=45)
6-24	43 (71.7)	20 (44.4)
25-42	8 (13.3)	9 (20)
43-60	9 (15)	16 (35.6)

P value = 0.015

Table 1 shows that among all the subjects, the maximum number of children having seizures, i.e., 63 out of 105 (60%) belong to age group of 6-24 month. The difference in the distribution of subjects according to the age in the two group was statistically significant (p value=0.015). The mean age in Group I was 25.18±15.26 months while in Group II was 33.42±19.19 months, which was found to be statistically significant (p value=0.016).

Table 2: Distribution of subjects according to gender (n=105)

Gender	Group I (%) (n=60)	Group II (%) (n=45)
Male	43 (71.7)	23 (51.1)
Female	17 (28.3)	22 (48.9)

P-value = 0.543

Table 2 shows that in Group I (febrile seizure) the number of males were 71.7% while females were 28.3% with male: female ratio of 2.5:1. In Group II (other than febrile seizure) there were less number of females i.e. 48.9% in comparison to males i.e. 51.1%. The male: female in Group II was 1:1. The male: female ratio of both the groups was not found to be statistically significant (p value=0.543).

Table 3 shows that in Group I (febrile seizure) 40% subjects had anemia while 60% subjects had no anemia. In Group II (other than febrile seizure), only 33.3% subjects had anemia. The difference in the distribution of subjects according to anemia status in the two group was not statistically significant (P-value 0.48).

Table 3: Distribution of subjects according to haemoglobin (n=105).

Haemoglobin	Group I (%) (n=60)	Group II (%) (n=45)	P value
≤10.5 gm/dl*	24 (40)	15 (33.3)	0.48
>10.5 gm/dl	36 (60)	30 (66.7)	

*Hb level ≤10.5 gm/dl was considered as anemia¹⁰

Table 4: Distribution of subjects according to hematological parameters (n=105).

Hemato-logical parameters	Group I (mean ±SD) (n=60)	Group II (mean ±SD) (n=45)	P value
Haemoglobin (mg/dl)	10.70±1.55	10.58±1.70	0.697
Serum iron (µg/dl)	23.7±19.2	43.02±41.62	0.002
Serum ferritin (ng/ml)	58.31±116.68	180.47±325.09	0.008

Table 4 depicts that the difference in the mean Hb in the two groups was not statistically significant (P value =0.697). The difference in the mean serum Iron and mean serum ferritin level in the two groups was found to be statistically significant.

Table 5: Distribution of group I (febrile seizure) according to the serum iron and serum ferritin level (n=60).

	Number of Subjects	Percentage
S. iron level (µg/dl)		
<22	37	61.7
22-184	23	38.3
Serum ferritin level (ng/ml)		
<10	14	23.3
10-60	26	43.3
>60	20	33.4

Ref. values of serum iron and serum ferritin were taken as 22-184 µg/dl and 10-60 ng/ml respectively

Table 5 shows that in Group I (febrile seizure), 61.7% of subjects had deficient iron level while 38.3% of subjects had normal serum iron level.

While 23.3% subjects in Group I (febrile seizure) had low serum ferritin level, 43.3% had normal levels while 33.4% had high serum ferritin level.

DISCUSSION

The present study was hospital based cross sectional study and total of 105 children were enrolled in the study. In Group I (febrile seizure), maximum number of subjects were in age group 6 to 24 month followed by 43 to 60 months and 25 to 42 months, i.e., 71.7%, 15% and 13.3% respectively (Table 1). Kumawat et al in their study stated that majority of cases of febrile seizures occur in age group of 6 to 24 months, i.e., 83.3%. They also stated that febrile seizures are age dependent and this age group should be considered critical for developing febrile seizure.¹¹

In present study, mean age of subjects in Group I (febrile seizure) was 25.18±15.26 months while in Group II (other than febrile seizure) was 33.42±19.19 months. The difference of the mean age in the two groups was found to statistically significant with P value = 0.016. In a study done by Gupta et al reported that the mean age of children with febrile seizure were 28.41 months. The higher incidence of febrile seizure in early childhood is due to rapid brain maturation and maximal hippocampal growth occurring in the at age group of 15-36 months. Hence, this is the period of enhanced neurological excitability.³

In present study, in Group I (febrile seizure) the number of males were 71.7% while females were 28.3% with male: female ratio of 2.5:1 (Table 2). In a case control study done by Nigade et al, reported preponderance of male gender in febrile seizure group with male:female ratio of 2.5:1 which was similar to the present study.¹² Male preponderance in febrile seizure was also reported in the study conducted by Kumawat R et al.¹¹

In present study, it was found that in Group I (febrile seizure) 40% of subjects had hemoglobin level ≤10.5 gm/dl, i.e., they had anemia with the mean hemoglobin level of 10.70±1.55 mg/dl while in Group II (other than febrile seizure) only 33.3% subjects had anemia and had mean hemoglobin level of 10.58±1.70 mg/dl. This difference of the mean Hb in the two group was not found to be statistically significant (P value =0.697) (Table 4). In a case control study conducted by Sit et al, reported that mean haemoglobin in febrile seizure cases were 10.42±0.83 gm/dl as compared to controls, i.e., 11.27±0.94 gm/dl.⁶ Ghasemi et al in the study reported that anemia can be associated with the severity of febrile illness and patient may have convulsions. Febrile convulsions occur after onset of febrile illness but before developing anaemia in the patient due to infectious disease.¹³

In present study in Group I (febrile seizure), 61.7% subjects had serum iron <22 µg/dl i.e., had iron deficiency while 38.3% subjects had normal serum iron level (22-184 µg/dl) with mean serum iron of 23.7±19.2 µg/dl (Table 4, 5). In Group II (other than febrile seizure), mean serum iron was 43.02±21.62 µg/dl (Table 4). The

difference between the mean serum iron between both the groups was found to be statistically significant (P value =0.0002) suggesting that subjects with febrile seizure had significantly lower serum iron in comparison to the subjects having fever with seizure. Fallah et al in a case control study reported that 48% of subjects of febrile seizure had iron deficiency with mean serum iron level of 48.91 ± 22.96 $\mu\text{g/dl}$. They reported significantly low mean serum iron level in febrile seizure group as compared to control group. They also reported that iron deficiency can alter brain synaptic neurotransmitter activity (increase in glutamate excitatory neurotransmitter activity and decrease in GABA inhibitory transmitter) which may be responsible for induction of seizure due to iron deficiency.¹⁴

The mean serum ferritin level in Group I was 58.31 ± 116.68 ng/ml while in Group II (other than febrile seizure) was 180 ± 325.09 ng/ml. This difference of mean serum ferritin was found to be statistically significant (p value 0.008) (Table 4). This suggests that subject with febrile seizure (Group I) had significantly lower serum ferritin in comparison to the subjects having fever with seizure (Group II). In a study conducted by Gowda and Samuel in 2018, reported that mean serum ferritin level was significantly low in febrile seizure cases as compared to control with mean serum ferritin level of 34.73 ± 3.4 ng/l among cases and concluded that iron deficiency was a possible risk for febrile seizure in children.⁹ Similar findings were reported by study conducted by Singh P and Mehta, where serum ferritin level in study group was 57.10 ± 42.8 ng/l as compared to control group 135.42 ± 15 ng/l.¹ In present study, 33% subjects with febrile seizure had higher serum ferritin levels. This may be because serum ferritin also acts as acute phase reactant (non-specific) and may be raised in any of the inflammatory condition.¹⁵

In the present study, the results shows that significantly low mean serum ferritin and mean serum iron level in subjects with febrile seizures. Thus, the present study suggests that iron deficiency is more common in febrile seizures. It has been also reported in the literature that fever may worsen the negative effects of low plasma ferritin levels on the brain and therefore seizures may be triggered.

Limitation of our study was that the limited numbers of subjects were included and the effect of iron therapy were not taken into consideration.

CONCLUSION

The present study shows that iron deficiency is more common in febrile seizures and there is a positive association between serum iron level and febrile seizures. It is, therefore, suggested that early detection and replenishment of iron stores in children by timely iron therapy may be helpful in prevention or decrease in frequency of febrile seizures.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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