Original Research Article

Study of role of iron deficiency anaemia in childhood febrile seizures in a tertiary care centre

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Abstract

Background: Febrile convulsion (FC) is the most common disorder in the nervous system of children and 2‑5% children affected every year. Studies conducted on the role of iron deficiency in febrile convulsion have yielded completely conflicting results. In some of these studies, iron deficiency has been identified as a risk factor, while in others it has been stated that iron deficiency increases the threshold of neuron excitation and thus can play a protective role against febrile convulsion. Present study was aimed to study the relationship between iron deficiency anaemia and febrile convulsion in children hospitalized at our tertiary care centre. **Material and Methods:** This prospective, case–control study was conducted in children aged 6 months to 5 years were categorized into two groups: 1. The case group with 30 children with first attack of FS. 2. The control group with 30 febrile children but without seizures at the same age. **Results:** After applying inclusion and exclusion criteria, total of 60 children were included in present study with 30 cases in each group. Maximum children belonged to the age group of 6 months to 1 year in both the groups 25 (41.67%), followed by age group of 1-2 year in both the groups were 24 (40 %). Iron deficiency anaemia was more prevalent in cases (56.67 %) as compared to controls (26.67%). Low haemoglobin with p value of 0.006 which is highly significant. RDW >15 % was noticed in 5 (16.67%) cases and 4 (13.33%) controls with p value of 0.63 which is insignificant. Serum Ferritin <12 ng/ml was noticed in 16 (53.33%) cases and 11 (36.67%) controls with p value of 0.01 which is highly significant. Peripheral smear showing Microcytic Hypochromic (PS MCHC) anemia was noticed in 14 (66.7%) cases and 7 (40%) controls with p value of 0.016 which is a significant value. **Conclusion:** From the results of our study, it seems that iron deficiency anemia is strongly correlated with febrile convulsion probably through increasing the threshold of convulsion in patients with iron deficiency.

Key Words: anemia, febrile seizures, iron.

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INTRODUCTION

Febrile convulsion (FC) is the most common disorder in the nervous system of children and 2‑5% children affected every year. Febrile convulsion is defined as convulsion resulting from fever. It occurs in children of 6 months to 6 (full six) years of age, is accompanied by fever higher than 38°C, and does not involve symptoms of central nervous system infections or any other background causes[1]. Studies identified various risk factors for febrile seizures, including developmental delay, discharge from a neonatal unit after 28 days, day-care attendance, viral infections, family history of febrile seizures, certain vaccinations, and nutritional deficiencies, including iron and zinc, mothers who smoke or consume alcoholic beverages[2,3]. Children with FC are susceptible to subsequent development of convulsion and epilepsy, various studies have been carried out with the purpose of identifying correctable risk factors to reduce the prevalence of FC[4,5]. Iron deficiency is the most

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common micronutrient deficiency which is a correctable and remediable condition[6]. Iron is an important nutrient that acts as a cofactor for several enzymes in the body, as well as playing roles in the production and function of neurotransmitters, hormones, and DNA (deoxyribonucleic acid) duplication. Iron is also essential for enzymes involved in neurochemical reactions, such as myelin formation, metabolism of some neurotransmitters, and brain energy metabolism[7]. Studies conducted on the role of iron deficiency in febrile convulsion have yielded completely conflicting results. In some of these studies, iron deficiency has been identified as a risk factor[8], while in others it has been stated that iron deficiency increases the threshold of neuron excitation and thus can play a protective role against febrile convulsion9. Present study was aimed to study the relationship between iron deficiency anaemia and febrile convulsion in children hospitalized at our tertiary care centre.

MATERIAL AND METHODS

This prospective, case–control study was conducted in department of Paediatrics, XXX medical college, XXX. Study duration was of 6 months from January 2019 to July 2019. Institutional ethical committee approval was taken.

The children aged 6 months to 5 years were categorized into two groups:

1. The case group: It included 30 children with first attack of FS
2. The control group: It included 30 febrile children but without seizures at the same age.

Exclusion criteria -

Children with atypical FS, afebrile seizures, any signs of CNS infection, any chronic neurodevelopment problems, previous diagnosis of other hematological problems, bleeding or coagulation disorders, hematological malignancy, on iron supplementation, and any serious illness. A written informed consent was taken from parents, prior to participation in present study. After admission, all children were thoroughly examined to exclude children with a previous history of epilepsy, developmental delay, neurological deficit, and CNS infection. Demographic details, clinical details such as body temperature upon admission, cause of fever, duration between initiation of fever and convulsion, family history of febrile convulsion, and details of the seizure history including duration, frequency, and type of seizure (simple or complex) were recorded for all children. Diagnostic criteria for simple FS included seizures associated with fever and the seizures were generalized, short duration (<15 min), no recurrence of seizures within 24 h, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizures. Blood investigations carried out to diagnose iron deficiency included hemoglobin (Hb) level, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), serum ferritin level (SF), serum iron level (SI), total iron‑binding capacity (TIBC), and transferring saturation of children. Other explanatory variables such as urine routine, stool routine and chest x-ray which can be the potential confounders were also included in the study and considered for analysis. Data were entered and analysed using SPSS software. Nominal data were expressed as frequency and percentage. Numerical data were expressed as mean, SD and were compared using Student's t‑test. P values of less than 0.05% were considered significant, and P values of less than 0.01% were considered highly significant.

RESULTS

After applying inclusion and exclusion criteria, total of 60 children were included in present study with 30 cases in each group. The mean age in the case group was 1.29 (0.74) years and in the control, group was 1.42 (0.89) years. Distribution of children in the different age groups amongst the cases and controls is shown in table 1. Maximum children belonged to the age group of 6 months to 1 year in both the groups 25 (41.67%), followed by age group of 1-2 year in both the groups were 24 (40 %). Children above 3 years in both groups were 6.67%. Male children were common in both groups (cases 70%, control 66.67%) as compared to female children.

Table 1: Age distribution among case and control in the study population

Age in years	Number of Children (%)	
	Febrile Seizures (Cases)	Febrile Illness without seizures (Controls)
6 months to 1 year	13 (43.33%)	12 (40 %)
1 to 2 years	11 (36.67%)	13 (43.33%)
2 to 3 years	3 (10.00%)	4 (13.33%)
3 to 4 years	2 (6.67%)	0
4 to 5 years	1 (3.33%)	1 (3.33%)
Total	**30 (100.00%)**	**30 (100.00%)**

Table 2: Prevalence of iron deficiency anaemia

Group	Number of Children (%)	
	Febrile Seizures (Cases)	Febrile Illness without seizures (Controls)
Iron deficiency anaemia	17(56.67%)	8(26.67%)
No iron deficiency anaemia	13(43.33%)	22(73.33%)

Iron deficiency anaemia was more prevalent in cases (56.67 %) as compared to controls (26.67%). Iron deficiency was diagnosed by hematological investigations of Hb less than 11 g/dl, HCT less than 33%, MCV less than 74 fl, MCH less than 24 pg, MCHC less than 32%, SI less than 50 µg/dl, SF less than 12 µg/dl, TIBC more than 400 µg/dl, and transferring saturation less than 15%10. We compared various hematological indices among cases and controls. Low haemoglobin value (<11 g/dl) was noticed in 17 (56.67%) cases and 8 (26.67%) controls with p value of 0.006 which is highly significant. Red cell distribution width (RDW), is also good indicator of anaemia. RDW >15 % was noticed in 5 (16.67%) cases and 4 (13.33%) controls with p value of 0.63 which is insignificant. Serum Ferritin <12 ng/ml was noticed in 16 (53.33%) cases and 11 (36.67%) controls with p value of 0.01 which is highly significant. We also find significant p value for MCV and MCHC among cases and controls. Peripheral smear showing Microcytic Hypochromic (PS MCHC) anemia was noticed in 14 (66.7%) cases and 7 (40%) controls with p value of 0.016 which is a significant value.

Table 3: Incidence of IDA in cases and controls

Parameter	Cases (%)	Controls (%)	P value	Significance
Hb (<11 g/dl)	17 (56.67%)	8(26.67%)	0.006	highly significant
HCT (< 33%)	5(16.67%)	4(13.33%)	0.63	insignificant
SF (< 12 µg/dl)	16(53.33%)	11(36.67%)	0.01	highly significant
MCV (< 74 fl)	11(36.67%)	7(23.33%)	0.14	significant
MCHC (<32 %)	5(16.67%)	3(10.00%)	0.33	significant
PS MCHC	14(46.67%)	7(23.33%)	0.016	significant

DISCUSSION

Iron deficiency anaemia is one of the most prevalent micronutrient deficiencies in young children in India and other parts of the world, and it is strongly associated with persistent cognitive and motor delays even after the anaemia and iron deficit have been corrected[11]. Age for peak incidence of febrile seizure is 14 to 18 months, which overlaps with that of iron deficiency anaemia which is from 6 to 24 months1. Considering the age prevalence of iron deficiency anaemia and febrile convulsion which are the same, the role of iron in the metabolism of neurotransmitter (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehidoxidase), the function of hemoglobin in conveying oxygen to the brain and since fever can exacerbate symptoms that result from anaemia, a relationship between iron deficiency anaemia and febrile convulsions is probable[12,13]. The mean age in the case group was 1.29 (0.74) years and in the control, group was 1.42 (0.89) years. Findings were similar to that by Pisacane A *et al*[14] [15 (5.6) months], Ali A *et al*[15] had a mean age of 18.8 months and Kumari PL *et al*[8] [17.5 (8.81) months]. Kumari *et al*.[8] performed a study on 308 children aged 6 months to 3 years old and found 63.6% of the case group suffered from iron deficiency in comparison with 24.7% of the control group. They concluded that iron deficiency was an important risk factor in simple febrile convulsion. In a study by Vaswani *et al*.16 had 68% of the cases were iron deficient compared with 30% of the controls. In 2009, Hartfield *et al*. 17 from the University of Alberta, Canada, reported in a retrospective study that children with FS were twice as likely to have iron deficiency as those with febrile illness alone. Our study had an mean Hb of 9.4 (1.35) g/dl and 10.7 (1.42) g/dl in case and control respectively with a p value of 0.006 which is similar to study conducted by Pisacane A *et al*[14], with a mean Hb of 10 g/dl and 12.5 g/dl in case and control respectively (p value of 0.0001).We observed significantly low serum ferritin levels in children with febrile seizures than in controls. Similar results were observed by Pisacame, *et al*[14]. But in contrast with these studies Mansouri *et al* reported mean ferritin was higher in the convulsive group with no statistically significant diff erence18. Kobrinsky *et al* deduced that iron deficiency might have a protective effect on febrile convulsion[19]. S. ferritin being an acute phase reactant, low levels in the setting of fever makes it a more reliable indicator. Although RDW is an indicator of iron status our study did not have significant difference in RDW in cases and controls. Derakhshanfar *et al*.[20] found that the level of iron deficiency and iron deficiency anemia in the control group were significantly higher than those in the case group, and concluded that the risk of febrile convulsion in children suffering from iron deficiency was less than the risk in other children. Probable reason for the protective role of iron deficiency,

was the role iron plays in the activity of exciting neurotransmitters such as monoamine oxidase and aldehyde oxidase. They added that the lack of iron leads to a reduction in the excitation power of the neurons and to a decline in the probability of excitation and convulsion in iron deficiency anemia, although their results contradict those obtained in other studies. Pisacane *et al*.[14] conducted a case‑control study on 156 children who were from six to 24 months of age in and found that 30% of the patients in the febrile convulsion group and 14% in the control group exhibited anemia. They concluded that fever can deteriorate the negative effect of anemia on the brain and, hence, can cause convulsion.

CONCLUSION

From the results of our study, it seems that iron deficiency anemia is strongly correlated with febrile convulsion probably through increasing the threshold of convulsion in patients with iron deficiency. Iron deficiency anaemia is easily correctable and preventable, most common micronutrient deficiency. Early detection and prompt correction may help in reducing febrile seizures incidence in children below 5 years of age.

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