

Study of Role of Iron Deficiency Anaemia in Febrile Seizures in Children in a Tertiary Care Centre

Sreenivasa B¹, Kumar GV², Manjunatha B³

Abstract

Introduction: The world health organization estimates that anaemia largely caused by iron deficiency, affecting between 500 million and two billion people worldwide. Considering the age prevalence of iron deficiency anaemia and febrile convulsion which are the same, the role of iron in the metabolism of neurotransmitter and some enzymes, 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. Some studies have suggested iron deficiency as a predisposing factor for febrile seizures. We designed this case control study to evaluate the relationship between iron deficiency anaemia and febrile convulsions. The objective of this study was to study the role of iron deficiency as a risk factor for febrile seizures.

Materials and Methods: Hundred cases and 100 controls were included in the study. Cases were children of age group six months to six years presenting with febrile seizures. Controls were children of same age group presenting with febrile illness but without any seizures. After informed consent, detailed history was taken and clinical examination done in both cases and controls and blood investigations were done to diagnose iron deficiency anemia. Two groups were matched for age and sex. In all children hemoglobin (Hb) level, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW) and plasma ferritin (PF) were determined and the data collected were analyzed statistically.

Results: The mean PF was significantly lower in cases compared to controls ($p=0.000$) and RDW was significantly higher in cases compared to controls ($p=0.00$). The mean Hb%, MCV, MCH are lower in cases compared to controls but it was statistically not significant. **Conclusion:** Iron deficiency is a significant risk factor for febrile seizures in children of age group six months to six years. Early detection and timely correction of iron deficiency may be helpful for prevention of febrile seizures in children

Key words: Febrile seizures, iron deficiency anemia, serum ferritin

Introduction

The world health organization estimates that anaemia largely caused by iron deficiency, affecting between 500 million and

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two billion people world wide^{1,2}. It is the most common nutritional deficiency and haematological disease of infancy and childhood³. Iron is a nutritional element not only needed for the synthesis of haemoglobin, but it is also essential for enzymes involved in neurochemical reactions⁴. To date, the pathophysiology

of febrile seizure is unknown⁵. 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 months^{6,7}. 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 aldehydoxidase), 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^{8,9,10}.

Some studies have suggested iron deficiency as a predisposing factor for febrile seizures, some described iron deficiency anaemia is less frequent in children with febrile seizures¹¹. Considering the conflicting results of the previous studies, we designed this case control study to evaluate the relationship between iron deficiency anaemia and febrile convulsions.

Material and Methods

A case control study was conducted from July 2010 to October 2014 in Basaveshwara Medical college hospital Chitradurga. One hundred children aged between 6 months to 6 years with febrile seizures were enrolled as cases. Sample size was based on Z formula and confidence interval of 95% with 80% power, type one error of 5% to detect any significant difference between the two groups with a level of 0.05. Febrile seizures were defined as a seizure occurring in association with a febrile illness, in the absence of CNS infection or any other defined causes of seizures¹². Children with a history of seizures, thalassaemia, central nervous system (CNS) infections, developmental delay and neurological deficits, on iron therapy were excluded from the study. A control group of 100 children was selected from among children hospitalized for a febrile illness (such as upper and lower respiratory tract infections and gastroenteritis) but without seizures. Controls were group matched to cases on age and sex. An informed consent was obtained from parents or the guardian. Demographic data, seizure details, nature of febrile illness, the family history of epilepsy/febrile seizures, temperature at admission, and nutritional status were recorded. Blood samples were collected from all participants for measurement of haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), red cell distribution width (RDW) and serum ferritin was done. Ethical committee clearance was sorted out.

Iron deficiency anaemia was defined as Hb <11g/dl, MCV <70 fl, MCH <27 pg, RDW >15%, serum ferritin <12 ng/ml (WHO)¹³. In presence of fever, a higher cut-off value of serum ferritin (25-50ng/ml) was considered¹⁴. Cases and controls were compared with respect to blood indices and serum ferritin. Chi-square and ANOVA tests for discontinuous variable and unpaired t-test for continuous variable at 5% significance ($p < 0.05$) level were used for statistical analysis.

Results

100 cases (56 male, 44 female) and 100 controls (52 male, 48 female) were enrolled. The mean ages of patients in the febrile seizure and control groups were 1.5 ± 1.2 and 1.9 ± 1.5 year respectively.

Table 1: Peak temperature on admission, underlying causes of fever among cases and controls

Characteristic	Febrile seizure cases (n=100)	Controls (n=100)	p-value
Temperature peak at admission in $^{\circ}\text{C}$ (mean)	39	38.8	0.61 (N.S)
Respiratory tract infections	60	59	N.S
Gastroenteritis	15	14	N.S
Dengue fever	10	10	N.S
Enteric fever	10	9	N.S
Viral fever	5	8	N.S

N.S = Not significant statistically

Respiratory tract infections were the most common cause of fever in our study followed by gastroenteritis.

Table 2: Haematological parameters of cases and controls

Parameters	Cases n=100 (Mean \pm SD)	Controls n=100 (Mean \pm SD)	p-value
Hb %	9.4 \pm 1.2	9.5 \pm 1.0	0.70
MCV (fl)	73.3 \pm 5.1	74.0 \pm 4.9	0.36
MCH (pg)	25.1 \pm 3.6	25.7 \pm 3.1	0.26
RDW %	16.8 \pm 1.3	12.7 \pm 1.1	0.00
Serum ferritin (ng/ml)	29.5 \pm 21.3	53.3 \pm 37.6	0.000

In this study we observed significantly low serum ferritin and significantly higher RDW in febrile seizure cases compared to controls

Discussion

Numerous studies have addressed the association between iron deficiency anemia and febrile seizure in children. The results, however, have been controversial and even primary researches with high number of cases have failed to provide unequivocal results. We observed significantly low serum ferritin levels in children with febrile seizures than in controls. Similar results were observed by Pisacame, et al¹⁵. But in contrast with these studies Mansourietal reported mean ferritin was higher in the convulsive group with no statistically significant difference¹⁶. Kobrinsky et al deduced that iron deficiency might have a protective effect on febrile convulsion¹⁷.

Iron has been found to act as a cofactor in a number of enzymatic reactions at the cellular level and effects neurotransmitter production and function, hormone function and DNA replication. Deficiency of iron, therefore, results in disruption of normal cell and organ function.

Iron deficiency is associated with neurological problems in young children, including developmental delay, stroke, and breath-holding spells. Screening for IDA should be considered in children with febrile seizures. Fever can worsen the negative effect of anaemia or for iron deficiency on the brain and a seizure can occur as a consequence. Alternatively, anaemia can be associated with the severity of a febrile illness, and more severe cases could be more likely to get seizures¹⁷.

Iron deficiency anaemia may reduce the seizure threshold in the infancy and childhood. Low PF level is associated with and may play a role in febrile seizures.¹⁷

The study has some limitations. 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.

Although serum ferritin levels rise in inflammatory conditions, MCV and RDW are not affected by acute infection¹⁸. RDW has been shown to distinguish between patients with lead poisoning and iron deficiency in children with microcytic anaemia. Specifically the RDW is elevated in iron deficient patients with lead poisoning and normal in children with lead poisoning alone¹⁹.

Conclusions

Iron deficiency anaemia is a modifiable risk factor for febrile seizure in children. Early detection and timely correction of iron deficiency may be helpful for prevention of febrile seizures in children.

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