Research Article

Association between iron deficiency anemia and febrile seizures

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Abstract

Background: Febrile seizure is a common cause of seizure in young children, with an excellent prognosis. There is high prevalence of febrile seizure and iron deficiency anemia in preschool children, the aim of this study was to investigate the role of iron deficiency anemia in simple febrile seizure patients. **Methods:** This prospective case-control study was performed in 50 children with simple febrile seizures (cases) and 50 febrile children without seizures (control), referred to Tata Motors Hospital, Jamshedpur. All children were aged between 6 months-5year. The groups were matched in age, gender, height and weight. Laboratory investigations performed were complete blood count, serum electrolytes, liver function test and renal functions test. Specific test advised were hemoglobin (Hb), (MCH), Mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and plasma ferritin (PF). **Results:** There is lower value of hematological indices like mean Hemoglobin, Mean corpuscular hemoglobin, Mean corpuscular volume, Mean corpuscular hemoglobin concentration and Serum Ferritin in the cases group compared to the control group but no statistically significant difference. **Conclusion:** This study did not establish any association between iron deficiency anemia and febrile seizures.

Keywords: Febrile Seizure, Iron Deficiency Anemia, Plasma Ferritin.

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Introduction

Febrile seizure is defined as a seizure occurring with febrile illnesses with no previous history of a febrile seizure or without acute systemic metabolic abnormality that may produce convulsions or nervous system infection in a neurologically normal 6 months to 5years old child [1-4]. The incidence of febrile convulsion is about 2-5% in neurologically healthy child [5]. The exact cause of febrile convulsion is unknown, but genetic and environmental factors have influence on its occurrence [6]. Factors responsible the febrile seizures include abnormality in cerebro spinal fluid (CSF) neurotransmitters, CSF neoptrin concentration and family history of febrile convulsions. [7-9]. Age for peak incidence of febrile seizure is 14 to 18 months, which overlaps with that of iron deficiency anemia which is more pronounced from 6 to 24 months of age [10]. Iron is an essential element for metabolism, with many enzymes depending on iron for its function [11].Iron deficiency anemia is the most common nutritional deficiency in the children. It is an important micronutrient which used by almost all the cells in human body. It is also important cofactors for the several enzymes for their proper functions. Iron also has roles in production of neurotransmitters and their functions, DNA duplication and several hormonal functions. [11].

Iron deficiency leads to improper myelination and synthesis of tyrosine and tryptophan hydroxylase which are necessary for synthesis and release of neurotransmitters like serotonin, dopamine and gamma amino butyric acid (GABA) [7,12]. Serum ferritin level is also affected by fever severity, inflammation and by male gender [13]. Iron is a nutritional micro element not only needed for the synthesis of hemoglobin, but also essential for enzymes involved in neurochemical reactions [14,15], such as myelin formation [16], brain

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energy metabolism [17], some neuro-transmitters and enzymes metabolism such as monoaminoxidase and aldehyde oxidase, are reduced in iron deficiency anemia [10,18-19]. Neurological symptoms like poor attention span, learning deficits, weak memory, delayed motor development and behavioral disturbance caused by iron deficiency are well-known [10].

Despite these facts, some studies show that antipyretics do not affect prevention of seizures caused by fever [20-21], so other variables that affect this process have special circumstances and considering that fever can intensify the anemia symptoms by increasing body metabolism [19], there is a need to explore relation between febrile seizures and iron deficiency anemia. Many studies have investigated the etiology and natural history of febrile seizures and evaluated various management strategies, but very little information is available about iron deficiency as a risk factor. Previous studies examining the relationship between iron deficiency anemia and febrile convulsions have been conflicting [19,22-24]. Some of them concluded that iron deprivation plays a role in the pathogenesis of febrile seizures [19,23, 25-26].

In contrast, there are some studies that reported that iron deficiency raises the threshold for seizures [22]. Also, recently some reports have shown that although iron deficiency anemia is less frequent among the cases with febrile seizures, but there is no protective effect of iron deficiency against febrile convulsion [27]. Keeping in mind the prevalence of these two clinical entities, we conducted a case-control study to evaluate the association between iron deficiency anemia and febrile seizures.

Material and Methods

This was an observational case-control study conducted at the department of pediatrics, Tata Motors Hospital, Jamshedpur, Jharkhand. The study group consisted of 100 children of age 6 months to 5 years admitted during August 2008 to July 2010. 50 consecutive children admitted with febrile convulsions were the considered as cases, and 50 children treated for febrile illness (gastrointestinal or respiratory cause) without convulsion or previous history of convulsion was taken as controls. Controls were matched to the cases by gender and age, weight, height, head circumference and the history of using any supplemental iron. Exclusion criteria for all subjects included co-morbidity conditions like epilepsy, patients already on iron therapy, patients with delayed development and patients known for other causes of anemia. Children with history of perinatal asphyxia and born with low birth weight babies were also excluded from study. The Ethics Committee at Tata Motors Hospital, Jamshedpur approved the study. Written informed consent was taken from parents or guardian of all the subjects.

Demographic information collected for cases and controls included age, sex, height, weight, and head circumference. In all patients who did not have a history of any iron supplement therapies for previous 30 days were included in the study. 5 mL of 8 hour fasting blood sample was collected at 8:00 AM, from all the individuals and subjected to routine investigations such as complete blood count (CBC), blood sugar, serum sodium, serum calcium serum potassium, liver function test (LFT), renal function test(RFT). Hematological investigations performed were hemoglobin (Hb), (MCH), Mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and plasma ferritin (PF).

Anemia was defined as the Hb concentration less than 2 standard deviation (SD), below the mean for that age and sex as per WHO guidelines. (Table 1). After data collection, statistical analysis was performed by SPSS-18 and independent t-test used to compare the groups. P value of <0.05 was considered as significant.

Table 1: Normal range and criteria taken for defining anemia [28]

Age (6months-5 Years)	**Normal Range**	**Criteria taken for Anemia**
Hb (Hemoglobin g/dl)	11-13.6	<11
MCV(Mean corpuscular volume fl)	75-87	<75
MCH(Mean corpuscular hemoglobin pg)	25.4-29.6	<25.4
MCHC (mean corpuscular hemoglobin concentration –g/dl)	32.9-35.7	<32.9
S. Ferritin (ng /mL)	10-300	<10

Results

We studied 100 children with fever, out which 50 children were having simple febrile convulsion and comprises of cases while 50 children with fever of respiratory or gastrointestinal cause without convulsion or history of convulsions were studied as controls.

In our study, out of 50 children from cases, 35 were boys and 15 were girls. Among the controls, 39 were male and 11 were female children. Mean age for the case group was 18.16 ± 8.09 months while among the control group mean age was 20.64 ± 5.16 months. There was no significant difference in height, weight and head circumference among the both groups. (TABLE-2). Among the cases, 54% children were anemic and among the control group, 27% were anemic according to the criteria taken for anemia in the study .There was no statistical significant difference in routine blood examination finding including CBC, serum electrolytes, LFT and RFT value of both groups. of iron deficiency anemia among two groups in comparison to hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and serum ferritin (TABLE-3).

Table 2: Demographic profile

	Cases	Control	t value/p
AGE(Mean ± SD) in Months	18.16 ± 8.09	20.64 ± 5.16	t=1.80/p=NS*
SEX(MALE:FEMALE)	35:15	39:11	t=0.83/p=NS
HEIGHT (Mean ± SD) in cm	80.29 ± 7.45	85.27 ± 5.68	t=3.47/p=NS
WEIGHT(Mean ± SD) in kg	11.08 ± 1.43	11.80 ± 1.20	t=0.137/p=NS
HEAD CIRCUMFERENCE (Mean ± SD) in cm	46.79 ± 1.91	46.73 ± 4.50	t=0.07/p=NS

*NS=NOT SIGNIFICANT

There was no significant difference was noted between two groups in demographic characteristics, clinical presentation except for convulsions and routine blood and electrolytes examination. Hematological profile of both groups is described in table 3 and not showing any significant difference.

Table 3: Hematological profile

	Cases	Control	t value/ p value
Hemoglobin (gm/dl)	10.86 ±1.23	12.72 ±1.33	t=0.97/p=NS
MCV(fl) (MEAN ± SD)	72.37±5.77	74.07±5.34	t=1.52/p=NS
MCH (pg) (MEAN ± SD)	23.02±2.88	23.72±3.85	t=1.03/p=NS
MCHC(gm/dl) (MEAN ± SD)	31.76 ±1.79	32.09 ±1.94	t=0.89/p=NS
S.FERRITIN(ng/ml) (MEAN ± SD)	42.17 ±17.15	50.40 ±30.12	t=1.66/p=NS

Discussion

Febrile seizures are most common convulsions of early childhood and incidence reported are varies from 2-5% to 14% at different part of world [5], In India and other countries several studies were conducted to address association between iron deficiency anemia and febrile seizures, but fail to provide unequivocal results.

In this study basic demographic characteristics, anthropometry value and routine investigations values were comparable in two groups with no significant difference.

In our study, the result shows that the mean Hemoglobin, Mean corpuscular hemoglobin, Mean corpuscular volume, Mean corpuscular hemoglobin concentration and Serum Ferritin were comparatively less in case group compared with control group, but the difference was not statistically significant.

Pisacane [19], reported a significantly higher rate of iron-deficiency anemia among children with first febrile seizure than in their controls. In the study of Naveed-ur-Rehman [23], plasma ferritin level was significantly lower in cases as compared to controls and suggested that iron deficient children are more prone to febrile seizures. Hartfield DS. et al [25], reported that children with febrile seizures were almost twice as likely to be iron deficient as those with febrile illness per se and

suggested that screening for iron deficiency should be considered in children presenting with febrile seizure. Daoud AS.et al [26] found serum ferritin level was significantly lower in children with first febrile seizure than in the reference group, suggesting a possible role for iron insufficiency in first febrile seizure. Vaswani et al [29], had concluded that iron deficiency could be a potential risk factor for febrile seizure in children, and in study of Jun Y S [30], results were that the iron deficiency anemia is associated with febrile convulsion, and screening for iron deficiency anemia should be considered in children with febrile convulsions.

In contrast, Bidabadi et al [27] found that mean iron level and serum ferritin were higher in the convulsive group with no statistically significant differences, and Kobrinsky et al [22] suggested that anemia raises the threshold for first febrile and in study of Im S et al [31], shown that iron deficiency may thereby raise the febrile seizure threshold like previous studies.

Febrile convulsion is a multi factorial disease. Independent risk factors for febrile convulsions are height of temperature, family history of febrile convulsions, fever episodes per year, history of maternal smoking or alcoholism during pregnancy. It is also found that children with iron deficiency anemia are mostly from low socio economic status and may have deficiency of other micronutrients like zinc, magnesium, selenium and copper which may act as important confounding factors [32]. The problem with cases- control study was that the subjects we include are from hospital admission which is influenced by so many factors like availability of health services, severity of diseases, social class and certain unidentified variables and not the true representative of the population.

Conclusion

On the basis of this study, we can arrive to conclusion that although lower mean values of hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin and serum ferritin were found in cases group compared with control group but no statistically significant difference were observed in both group. One of the limitations of our study was the small sample size. Finally, a community based case control study or Meta-analysis should be carried out to find out the association between febrile seizure and iron deficiency anemia.

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