

Original Research Article

Association between iron deficiency anaemia and simple febrile seizure in South Indian rural population

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ABSTRACT

Background: Simple febrile seizure is a common problem worldwide, 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. Hence, we aimed to determine the association between iron deficiency anaemia and simple febrile seizures in south Indian rural population.

Methods: It is an observational study done in paediatrics department at Sri Venkateshwaraa medical college hospital and research centre. A total 120 (60 cases and 60 control) were included in the study. Children with febrile seizures and controls were included fever without seizures. Informed consent was taken from parents of each child. Children were divided into two groups, cases and controls. Serum ferritin level, Hb, HCT and MCV levels were assessed.

Results: Mean Hb level in cases and controls were 9.1 ± 1.2 and 12.7 ± 1.7 mg/dl respectively. Mean MCV value in cases and controls was 78.1 ± 6.2 and 81.4 ± 6.9 respectively. Mean serum iron level in cases was 29.9 ± 4.9 and in controls mean serum iron level was 42.8 ± 7.4 .

Conclusions: Iron deficiency anaemia is considered as a risk factor for febrile seizures in children.

Keywords: Iron deficiency anemia, Simple febrile seizures, Rural population

INTRODUCTION

Febrile seizure is a seizure associated with a high fever of any underlying clinical condition without serious systemic/neurological illness. Though it's not a serious condition still a much-worried problem among the parents. Febrile seizure most commonly occurs in children between the ages of 6 months and 5 years.¹ The diagnosis of febrile seizure often involves verifying that there is no evidence of neuro-infection/neurological illness and metabolic problems which might cause seizure. There are two types of febrile seizures; simple febrile seizures and complex febrile seizures. Simple febrile seizures are defined as seizures of generalized

tonic-clonic type lasting less than 15 minutes in a 24-hour period. The incidence of febrile seizure is about 2-5% in neurologically healthy child.^{2,3} The exact cause and mechanism of febrile seizure is not clearly understood but genetic and environmental factors have a predisposition.

Anaemia and predominantly iron deficiency anaemia are the most common nutritional deficiency in the children in India and various developing countries. Iron is a vital micronutrient which used by almost all the cells in human body and also an important cofactor for the several enzymatic functions. Iron also places vital roles in production of neurotransmitters and their functions, DNA duplication and several hormonal functions.⁴ 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).⁵ Serum ferritin level is also affected by fever severity, inflammation and by male gender.⁶

Iron is a nutritional micro element not only needed for the synthesis of haemoglobin, but also essential for enzymes involved in neurochemical reactions, such as myelin formation, brain energy metabolism, some neurotransmitters and enzymes metabolism such as monoaminoxidase and aldehyde oxidase, are reduced in iron deficiency anemia.⁷⁻¹² Many studies and research have been done on febrile seizures and iron deficiency to postulate as important risk factors but still we do not have promising results. It's more noted various studies done to prove the relationship between iron deficiency anaemia and febrile convulsions have been negatively proven.¹³⁻¹⁶ Few studies have proven that iron deprivation plays a role in the pathogenesis of febrile seizures.^{13,15,17,18} As we observed controversy in the association of iron deficiency anaemia and febrile seizures, we conducted a study to evaluate the association between iron deficiency anaemia and febrile seizures.

METHODS

Presented study was an observational study conducted at the department of pediatrics, in Sri Venkateshwarraa medical college hospital and research centre at South India serving the rural population. The sample size was calculated as 120 (60 cases and 60 controls) based on consecutive cases and concurrent controls selected using 95% confidence level 7% margin of errors 69% of population proportions and population size was 440. The study group consisted of 120 children of age 6 months to 5 years admitted during April 2018 to March 2019. All children admitted with simple febrile seizure were included for the study with both the gender.

Table 1: Normal range and criteria taken for defining anemia.

Age (6 months to 5 years)	Normal range	Criteria taken for anemia
Hb (g/dl)	11-13.6	<11
MCV(fl)	75-87	<75
MCH(pg)	25.4-29.6	<25.4
MCHC (g/dl)	32.9-35.7	<32.9
S. ferritin (ng/ml)	10-300	<10

Exclusion criteria for all subjects included co-morbidity conditions like epilepsy, patients already on iron therapy, patients with developmental delay and patients known for other causes of anaemia. Children with history of perinatal asphyxia and born with low birth weight babies were also excluded from study. Written informed consent was taken from parents or guardians of all the subjects.

Demographic information collected for cases 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 haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), TIBC, serum iron and serum ferritin level. Anaemia 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<0.05 was considered as significant.

RESULTS

Simple febrile seizures in our study were more common in the age group between 1-3 years with 62 patients (51.66%). In our study we noted a statically significant difference in the mean haemoglobin level, MCV, MCH, MCHC in case group when compared to the control group. In our study we also observed mean serum iron which was statically significant low when compared with the control group. In this study we observed significantly low serum ferritin, haemoglobin and mean serum iron in febrile seizure cases compared to controls.

Table 2: Demographical data.

Age (years) (n=60)	Case group	Control group	No. of patients
6 month-1 year	09	10	19
1-2	20	14	34
2-3	12	16	28
3-4	10	10	20
4-5	09	10	19
Total	60	60	120

Table 3: Comparison of serum makers.

Serum makers (n=60)	Case group	Control group	P value
Mean HGB (g%)	9.1±1.2	12.7±1.7	<0.0001
MCV (fl)	78.1±6.2	81.4±6.9	<0.0001
MCH (pg)	27.5±1.9	29.4±2.8	<0.0001
MCHC (g%)	33.4±2.7	35.2±1.9	<0.0001
Mean serum iron(mcg/dl)	29.9±4.9	42.8±7.4	<0.0001
TIBC (mcg/dl) >400	407±7.2	439±5.7	>0.07
MPF (ng/ml) mean plasma ferritin	16.4±4.7	21±6.7	<0.00001

DISCUSSION

Iron deficiency was found as a significant risk factor for simple febrile seizures in children of age group 6 months to 5 years in our study. The level of the haemoglobin was seen lower in the febrile seizures' patients compared to the control study group patients. Level of the mean corpuscular volume is observed on lower level in febrile seizures. The mean corpuscular haemoglobin concentration is seen slightly on lower side in normal patients as compared to the enrolled study patients. Iron has been found to act as a cofactor in a number of enzymatic reactions at the cellular level and effects neurotransmitter produce on 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 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 seizures.¹⁷ Iron deficiency anaemia may reduce the seizure threshold in the infancy and childhood. Low plasma ferritin level is associated with and may play a role in febrile seizures.¹⁷ The level of the serum iron is seen as decreased in the study group when compared to normal patients. There is no significant change in the total iron binding capacity in both the study group. Mean plasma ferritin is also seen on lower in study group.

Piscane et al studied children's less than 2 years of age and reported that anaemia was significantly more common in cases than controls.¹² Cut off value for MCV <70 fl in their study but did not analyze other blood indices. Rehman and Billoo in 2001 studied in 6 month to 5 year age on 60 patients (30 cases and 30 controls) and reported that iron deficiency anemia was significantly more frequent among the case as compared to the controls as evident from parameters studied i.e. haemoglobin <10 gm/dl (p<0.000), hematocrit <30% (p<0.01), MCV <70 fl (p<0.002), MCH <24 pg (p<0.001), and serum ferritin <110 ng/dl (p<0.000).¹⁵ In their study they did not rule out effect of febrile illness on ferritin. Reverse observation had reported by Korbrinsky et al study to determine the effect of iron status on seizure threshold and documented that Iron deficiency may protect against the development of febrile seizures.¹⁴ Our observation support the hypothesis provided by previous worker about role of iron deficiency as a risk factor for febrile seizures. Hence, it's more important to identify and treat iron deficiency in children's.

Limitations

Limitations of current study were study population was low with a rural serving centre which could add to the cause and unicentre.

CONCLUSION

Hence, we concluded that plasma ferritin level and other parameters was significantly lower in cases as compared to controls suggesting that children with iron deficiency anaemia were more associated with febrile seizure.

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