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Original Research Article

Iron deficiency in febrile seizures: a prospective case control study

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ABSTRACT

Background: The objective of the study was to evaluate the role of iron deficiency in febrile seizures.
Methods: Case control study conducted at Pediatric department of Tertiary care hospital. A total 70 cases and 70 controls were included in the study. Consecutive cases and controls were selected. Cases were children of age group 6 months to 5 years with simple febrile seizures and controls were children of same age group with short febrile illness without any seizures. After consent, detailed history was taken and clinical examination were carried out for both groups. Blood investigations were done to diagnose iron deficiency in both cases and controls. Iron deficiency was diagnosed as per WHO criteria haemoglobin <11 g/dl in cases <5 years mean corpuscular volume<70 fl, mean corpuscular haemoglobin <27 pg and serum ferritin<30 microgram/dl.
Results: Mean corpuscular volume was less than 70 fl/ml in 51% cases and 31% controls and mean corpuscular hemoglobin was less than 27 pg/ml in 84% cases and 40% of controls indicating statistically significant association of MCV and MCH between cases and controls .Serum ferritin was less than 30 ng/ml in 44% in cases as compared to 26% of controls, there was statistically significant difference between serum ferritin levels in cases and controls. From the above findings, study showed statistically significant association between iron deficiency anaemia and febrile seizures (p value <0.01; OR- 8.05 (3.6-17.93) (df-1).
Conclusions: Iron deficiency is a major risk factor for simple febrile seizures in age group of 6 months to 60 months.

Keywords: Febrile seizures, Iron deficiency, Haemoglobin, Serum ferritin

INTRODUCTION

Febrile seizures are the most common cause of convulsions in children and a frequent cause of emergency hospital admissions.[1] Earlier in India febrile seizures were reported to be high as 10% but recent studies show that incidence has got down to match western world.[2] Factors found to be influencing febrile seizures have been explored in several studies. Iron plays a pivotal role in the metabolism of neurotransmitters and myelination. Any deficiency of iron will lead to alteration in seizure threshold in children. Iron deficiency is a treatable condition; therefore, the current study explores the role of iron deficiency in precipitating the febrile seizures.

METHODS

A prospective case control study was done in Paediatric ward of Bokaro General Hospital, Jharkhand, India. Study was conducted in between July 2014 to December 2015 All children aged 6 months to 5 years were admitted (in-patient) who had fever with seizures and fever without seizures. Children with central nervous infections, developmental delay and or neurologic deficit, protein energy malnutrition, who are on iron therapy were excluded from the study. Written informed consent were taken from the parents or caretakers of the subjects included in the study and the disease process and importance of treatment was explained to them. The study protocol was approved by the ethical committee of Bokaro General Hospital, Jharkhand. A study performa was designed and subject's history with detailed examination was carried out. Demographic data, seizure details, nature of febrile illness, family history of epilepsy/febrile seizures, temperature at admission and nutritional status was recorded. IAP weight for age classification was used to grade protein energy malnutrition. The group 1 comprises of children with febrile seizure and the group 2 comprises of children with febrile illness without seizure. Estimation of hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin done by auto analyzers and serum ferritin level by particle enhanced immunoturbidimetry. Iron deficiency considered as haemoglobin <11 g/dl in cases <5 years mean corpuscular volume <70 fl, mean corpuscular haemoglobin <27 pg and serum ferritin<12 microgram/dl. Serum ferritin is acute phase reactant, so its level is increased in fever, a higher cut-off value of serum ferritin <30 microgram/dl will be considered. Ethical approval was taken from ethical committee.

Data were analyzed using descriptive statistical methods using statistical package for the social science system version SPSS program for windows, version 17.0. Data will be tabulated in Microsoft excel sheet. Data were checked for normality before statistical analysis using Shaipro Wilk's test. Qualitative data was represented in form of frequency and percentage. Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Quantitative variables were compared between the study groups using Student t-test. Mann–whitney U test was used for non-normally distributed quantitative and ordinal data. For comparing categorical data, Chi square test was performed. Fisher's exact test was used instead in case of 2×2 tables and odds ratio were calculated wherever required. A probability value (p value) less than 0.05 was considered statistically significant.

RESULTS

In present study sample size was 140 which were divided into 2 groups, cases and controls of 70 each. Majority of patients were in age group between 12 and 23 months, comprising 39% among cases and 21% among controls. Among cases male:female ratio was 1.91:1 whereas in controls were 1.8:1. 41% of cases had single episode of convulsions and 51% had multiple episodes of convulsions before admission. Half of the cases were present with typical febrile seizures and remaining half with atypical febrile seizures. Bronchopneumonia accounted to 34 (48.6%) followed by WALRI 13 (18.6%) of total controls. 61.42% of total cases belonged to lower socioeconomic status.

Table 1: Comparison of mean corpuscular haemoglobin in cases and controls.

MCH	Group		Total
	Cases	Controls	
<27	59	28	87
	84%	40%	62.1%
>27	11	42	53
	16%	60%	37.9%
Total	70	70	140
	100%	100%	100%

p-value<0.01; OR-8.05(3.6-17.93) (df-1)

There were 67% cases with haemoglobin less than 11 gm% and 56% controls with haemoglobin less than 11 gm% in age group 6 months to 5 years. Mean corpuscular volume was less than 70 fl/ml in 51% cases and 31% controls, showing statically significant association of MCV between cases and controls.

Table 2: Comparison of mean corpuscular volume in cases and controls.

MCV	Group		Total
	Cases	Controls	
<70	36	22	58
	51%	31%	41.4%
>70	34	48	82
	49%	69%	58.6%
Total	70	70	140
	100	100	100

P value -0.01; OR-2.45(1.22-4.92) (df-1)

Table 3: Serum ferritin level in cases and controls.

S.Ferritin	Group		Total
	Cases	Controls	
<30	31	18	49
	44%	26%	35%
>30	39	52	91
	56%	74%	65%
Total	70	70	140
	100%	100%	100%

P value-0.033; OR-2.3 (1.12-4.7) (df-1)

Mean corpuscular haemoglobin was less than 27 pg/ml in 84% cases and 40% of controls indicating statistically significant association of MCH between cases and

controls. Serum ferritin was less than 30ng/ml in 44% in cases as compared to 26% of controls; there was statistically significant difference between serum ferritin levels in cases and controls.

DISCUSSION

Febrile seizures are the foremost common seizure disorder in childhood, affecting 2% to five of youngsters between the ages of 6 and 60 months. It is generally believed that an FS is an age-dependent response of the immature brain to fever. This postulation is supported by the very fact that the majority (80-85%) febrile seizures occur between 6 months and three years aged, with the height incidence at 18 months.[3,5] The iron deficiency is identified as a risk factor for febrile seizure. The objective of the study is to determine whether any significant association exists between iron deficiency and simple febrile seizures. This prospective observational case control study has confirmed some well-known observations. In a similar study done by Sadeghzadeh et al noted 53% of cases were in 12-23 months age group.[4] In the study done by Kumari et al found that 55.8% of cases and 56.5% of control.[5] In present study, there is male predominance: 66% of cases and 64.28% in controls were males. This is similar to studies done by Gupta S et al (62.8%), Sadeghzadeh et al 4 (60%), Kumari et al (53.8%) and Hartfield et al (57.5%).[5-7] Controls were in the average age group 17.5±8.81 and 17.6±8.54 months, respectively. The incidence of iron deficiency anaemia among children 6 months to 59 months in India is 79%. This includes 26% who are mild anaemic, 40% who are moderately anaemic and 3% suffer from severe anaemia (NFHS 3 conducted in 2006-06). In the present study, haemoglobin was below the range of normal for the age in 47 (67.14%) among cases and 39 (55.72%) among controls. Mean Hb was 10.16 g% in cases and 10.56 g% in controls which were low for age according to WHO Standards. The mean Hb% in both cases and control groups was similar and not statistically significant (p=0.22). This is in accordance with the study by Sadeghzadeh et al, Bidabadi et al, Idro et al, Salehi omran MR et al as Hb differences were not statistically significant between cases and control groups (p value=0.47,0.11,0.71).[4,8-10] In the present study, 36 cases had MCV less than 70 and 22 (31.42%) in control group had MCV less than 70.There was a statistically significant assosciation between MCV and febrile seizures among cases with p value=0.039 odds ratio=2.18 ,95% CI=1.09-4.34. This is in accordance with study by Kumari et al, Yousefichaijan et al with statistically significant association between MCV and febrile seizures.[5,11] In the present study, MCH was below 27 in 59 with mean 23.74 of cases and 28 (37.14%) with mean 27.84 of controls which is statistically significant (p value<0.01; OR- 8.05 (3.6-17.93) (df-1). These results are similar to study by Kumari et al, Vaswani et al and Daoud et al.[5,12,13]

Comparison of serum ferritin with other studies

Serum ferritin may be an indicator of body stores of iron. Bone marrow aspiration procedure is considered to be the gold standard for determining iron stores in the body. However, this cannot be used in all patients as it is painfull. Serum ferritin is reliable indicator which can be used to determine body stores of iron can be repeated whenever required. A serum ferritin level below 30 ng/ml is indicator of iron deficiency status. In our study, 44% of cases (no=31) with mean ferritin level less than 30 mcg/l much lower than the values in the controls (62.99 mcg/l) which is statistically significant. (p=0.033, odds ratio=2.3 95%, CI=1.12-4.7). In the study by Daoud et al the significance of iron status as a possible risk factor was evaluated.[13] The mean serum ferritin level with in the cases was 29.5 mcg/l, much less than the values with in the controls (53.5 mcg/l).

Table 4: Comparison of variables in various previous studies.[4,5,12,14]

S. no.	Author	Parameters studied	Study sample size	Mean	P value
1	Sadeghzadeh et al[4]	Hb<10.5	100		0.47
		MCV<70			0.20
		Ferritin<30			0.65
		Fe/TIBC<12			0.00035
2	Kumari et al[5]	Hb<11	154	9.41±.2	0.7
		RDW>15 Ferritin<12		31.93±1.0	0.003
4	Vaswani et al[12]	Hb<11	50	9.4±1.2	0.70
		MCV<70		73.4±9.5	0.89
		MCH<27		21.4±3.1	0.71
		Ferritin<30		31.9±31.0	0.003
5	Kamalammal et al[14]	Hemoglobin<11	50	11.04±1.03	0.2134
		MCV<73		68.84+12.68	0.007
		MCH<24		24.63+3.62	0.18
		MCHC<34		32.74+2.9617+5.115	0.19
		Serum ferritin<12		61.42+20.61	0.11
		Serum Iron		-	<0.001

Continued.

S. no.	Author	Parameters studied	Study sample size	Mean	P value
6	Present study	Hb<11	70	10.14±1.62	0.224
		MCV<70		68.90±7.85	0.01
		MCH<27		23.72±3.85	<0.01
		Ferritin<30		47.71±36.4	0.033

Similar observations were made in a study done by Vaswani et al.[12] The mean serum ferritin level was significantly low in children with first febrile seizures (31.9±31.0 mcg/l) as compared to controls (53.9±56.5 mcg/l) (p=0.003). In our study, there is no significant correlation of Hb (p=1.0), MCH (p=1.0) and serum ferritin (p=0.39) between first and recurrent febrile seizures. This is similar to studies done by Gupta et al.[6] As India is a developing country, a greater number of infants and children presents with anemia. This may be detected in infants and children when presents with first febrile seizures and they are treated with the nutritional supplements as it may be cause of anemia which inturn leads to decreased recurrence of febrile seizures.

Limitations

There are only few numbers of studies conducted to know the correlation of iron deficiency between first and recurrent febrile seizures. The study being a hospital-based study the prevalence of exposure and outcome variables may be different from a community setting.

CONCLUSION

We concluded from our study that there is significant association between iron deficiency and febrile seizures. Early detection and iron supplementation in children who are at risk of developing iron deficiency might prevent simple febrile seizures. These findings support the usefulness of the serum ferritin to establish an early diagnosis of iron deficiency anemia.

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