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Original Research Article

An Analytical Study to Determine the Association between Iron Deficiency Anemia and Febrile Seizure

Pawan Kumar Yadav

Senior Resident, Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India

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Corresponding Author: Dr. Pawan Kumar Yadav
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Abstract

Aim: The aim of the present study was to determine the association between iron deficiency anemia and febrile seizure.

Methods: The study was a hospital-based case-control study which was conducted in the Department of Pediatrics in between the duration of 24 months. A total of 100 Children in the age group from 6 months to 5 years admitted with first episode of simple febrile seizure were taken as cases. The control group included 100 children in the same age group admitted with acute febrile illness without seizures.

Results: Majority of children were males (58% and 55% in case and control group respectively). Majority of children belonged to lower socioeconomic class in both the study groups (82% and 64% among cases and controls respectively). Majority of children in both the groups were exclusively breastfed (81% and 72% in cases and control respectively). Initiation of complementary feeding at 6 months of age was poor in children with febrile seizure group compared to controls (22% versus 52%). Mean Hb level among cases was 7.63 g/dl whereas in controls it was 11.68 g/dl, which was statistically significant (p-value<0.001). Mean MCV and MCH levels in the cases were 64.6 fl, 24.06 pg and in controls, these values were 76.82 fl, 31.32 pg, respectively which was statistically significant. Mean RDW among cases was 16.04% compared to controls 11.22% which was statistically significant. Mean serum iron level was found to be low among cases compared to controls (43.47 mg/dl and 119.52 mg/dl respectively). Mean TIBC was 476.4 microgram/dl in cases and 302.8 mcg/dl in control, which was statistically significant (p value<0.001). Transferrin saturation was less among case group (12.08%) compared to controls (36%), the difference was statistically significant. Mean serum ferritin level was 20.50 mcg/l in the cases and 71.65 mcg/l in controls which was statistically significant.

Conclusion: Iron deficiency anemia (IDA) was more frequent among children with febrile seizures. The result suggests that IDA may be a risk factor for febrile seizures. Early detection and timely correction of iron deficiency may be of help for prevention of recurrence of febrile seizures in children of this age group.

Keywords: Febrile seizures, Hemoglobin, IDA-iron deficiency anemia.

Introduction

Febrile seizures are the seizures which are associated with fever of above 38°C (100.4 F) which occur above 6 and below 60 months of age, in the absence of any central nervous infections, metabolic disturbances, and any prior afebrile seizures. [1] This condition occurs in 2-5% of the children who are neurologically healthy. [2] Febrile seizures are divided into simple/typical and complex/atypical febrile seizures. Simple febrile seizures are usually generalized tonic clonic type, lasting less than or equal to than 15 min and does not reoccur within 24 h in neurological and psychomotor normal children. [3,4] Complex febrile seizures last more than 15 min, reoccurs within 24 h, and can be focal or generalized with postictal neurological deficit like Todd's palsy or with prior neurological deficit. The precise cause of febrile seizure is not known, but several genetic and environmental factors have been implicated. [5]

The maximum age of febrile seizure occurrence is 14-18 months, which overlaps with the maximum prevalence of Iron Deficiency Anaemia (IDA). [6] IDA is the most common nutritional deficiency in the world. Iron is an important micronutrient which is used by roughly all the cells in the human body. Iron is used as cofactor for metabolism of many neurotransmitters, monoamine and aldehyde oxidase in the brain. The metabolism of these neurotransmitters, monoamine and aldehyde oxidase will be affected in the patient with iron deficiency leading to decrease in these neurotransmitters, which may decrease the threshold for seizure. Fever can worsen the

negative effects of low serum ferritin on the brain and trigger seizure. [7]

Some of the recent studies have reported that iron deficiency could be a risk factor for febrile seizure because the latter is more common in children under two years and iron deficiency anemia is also common in children of the same age. Due to the presence of iron in the hemoglobin structure, it plays a crucial role in the transport of oxygen to different tissues such as the brain. [8,9,10] Iron deficiency reduces the metabolism of some neurotransmitters. [11,12]Different factors have been considered for febrile seizures, including familial (genetic) factors, prenatal factors, present acute illness, the highest degree of fever and finally anemia. On the other hand, fever can exaggerate the negative effect of anemia on brain. [13]

Considering the age of prevalence of IDA and FS 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 aldehydase), a relationship between IDA and FS is probable. With respect to the high prevalence of febrile seizures and IDA in children and considering the fact that IDA is a probable risk factor for febrile seizure occurrence.

Hence this study was conducted to determine the association between iron deficiency anemia and febrile seizure.

Material & Methods

The study was a hospital-based case control study which was conducted in the Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India in between the duration of 24 months(March 2017 to February 2019)

CASE: A total of 100 Children in the age group from 6 months to 5 years admitted with first episode of simple febrile seizure were taken as cases.

CONTROL: The control group included 100 children in the same age group admitted with acute febrile illness without seizures.

Exclusion criteria

- Children with epilepsy and developmental delay were excluded from the study.
- Children on iron therapy.

Methodology

A detailed history was taken in cases regarding duration of fever, time-interval between onset of fever and convulsion, duration for which convulsion lasted, history of developmental delay and family history of epilepsy. Detailed examination was done in cases to rule out possible central nervous system infection, developmental delay and any other co-morbidities. Control group was also examined to rule out any associated significant co-morbidities. Complete haemogram, red cell indices, iron profile were done in both the groups. Other necessary investigations were carried out wherever it was necessary. Diagnosis of iron deficiency anemia was made in a child with low haemoglobin (<11gm/dl), peripheral smear findings of microcytic hypochromic anemia with reduced RBC count and increased red cell distribution width (RDW>15%).

Statistical Analysis

Data was analysed using appropriate descriptive and inferential statistics. The categorical type data was expressed in terms of frequencies and percentages whereas the numeric continuous data as mean±SD. All the bio-chemical markers were expressed as mean±SD. In order to compare the various markers in two groups, independent student's t-test was used. Odd ratio was calculated as a risk of iron level in cases with seizures to the group without seizures along with 95% CI. For all statistical evaluations, a p-value<0.05 was considered as statistically significant. Qualitative data was summarized using charts and diagrams. Data was analysed using statistical package SPSS-20.

Results

Table 1: Patient details

Parameters	Cases	Controls
Gender		
Male	58 (58)	55 (55)
Female	42 (42)	45 (45)
Socio-economic status		
Lower	82 (82)	64 (64)
Higher	18 (18)	36 (36)
Breast feeding	81 (81)	72 (72)
Complementary feeding	22 (22)	52 (52)

Majority of children were males (58% and 55% in case and control group respectively). Majority of children belonged to lower socioeconomic class in both the study groups (82% and 64% among cases and controls respectively). Majority of children in both the groups were exclusively breastfed (81%

and 72% in cases and control respectively). Initiation of complementary feeding at 6 months of age was poor in children with febrile seizure group compared to controls (22% versus 52%).

Table 2: Red cell indices and iron profile among study group

Lab parameters	Cases		Controls	SD	P- value
	Mean	SD	Mean		
Hemoglobin (gm/dl)	7.63	1.13	11.68	1.72	<0.001
MCV(fl)	64.6	4.34	76.82	4.26	<0.001
MCH (pg)	24.06	2.52	31.32	2.46	<0.001
RDW%	16.04	1.24	11.22	1.07	<0.001
TIBC (mcg/dl)	476.4	42.44	302.80	47.03	<0.001
S. Iron (mcg/dl))	43.47	2.64	119.52	28.06	<0.001
S. Transferrin (mg/dl)	274.06	28.52	266.24	42.16	0.2816
Transferrin saturation (%)	12.08	1.43	36.00	12.88	<0.001
Serum ferritin (microgram per litre)	20.50	1.07	71.65	5.4	<0.001

Mean Hb level among cases was 7.63 g/dl whereas in controls it was 11.68 g/dl, which was statistically significant (p-value<0.001). Mean MCV and MCH levels in the cases were 64.6 fl, 24.06 pg and in controls, these values were 76.82 fl, 31.32 pg, respectively which was statistically significant. Mean RDW among cases was 16.04% compared to controls 11.22% which was statistically significant. Mean serum iron level was found to be low among cases compared to controls (43.47 mg/dl and 119.52 mg/dl respectively). Mean TIBC was 476.4 microgram/dl in cases and 302.8 mcg/dl in control, which was statistically significant (p value<0.001). Transferrin saturation was less among case group (12.08%) compared to controls (36%), the difference was statistically significant. Mean serum ferritin level was 20.50 mcg/l in the cases and 71.65 mcg/l in controls which was statistically significant.

Discussion

Different factors have been considered for febrile seizures, including familial (genetic) factors, prenatal factors, present acute illness, the highest degree of fever and finally anemia. Iron deficiency anemia (IDA), as the most common type of anemia during infancy and childhood, occurs usually between 9-24 months of age and this period coincides with the peak incidence of FS. It has been determined that iron depletion has negative effect on neurocognitive functions of children and supplemental iron can reduce breath holding spells. On the other hand, fever can exaggerate the negative effect of anemia on brain. [13]

Majority of children were males (58% and 55% in case and control group respectively). Similar findings were observed in studies done by Leela Kumari P et al and Hartfield DS et al. [14,15] Majority of children belonged to lower socioeconomic class in both the study groups (82% and 64% among cases and controls respectively). Majority of children in both the groups were exclusively breastfed (81% and 72% in cases and control respectively). Initiation of complementary feeding at 6 months of age was poor in children with febrile seizure group compared to controls (22% versus 52%). Mean Hb level among cases was 7.63 g/dl whereas in controls it was 11.68 g/dl, which was statistically significant (p-value<0.001). Mean MCV and MCH levels in the cases were 64.6 fl, 24.06 pg and in controls, these values were 76.82 fl, 31.32 pg, respectively which was statistically significant. A Kenyan case-control study as well as the meta-analysis of eight case-control studies that have examined the relationship between febrile seizures or acute seizures and iron deficiency suggested that iron deficiency may be associated with an increased risk of febrile seizures in children. [16] Fever can worsen the effects of anemia or iron deficiency on the brain, and therefore cause convulsions. In addition, anemia can be associated with the degree of febrile disease, and patients with more severe symptoms may be affected by convulsions. But, febrile convulsion usually occurs at the onset of a febrile disease, before hemoglobin is reduced due to the infectious disease. [17] In a study conducted in Thailand, the rate of thalassemic children with febrile convulsion was reported as being 4.4 times less than the general population of children. The researchers suggested that it might be due to higher levels and the role of iron in brain metabolism, which leads to less occurrence of febrile convulsion in those children. [18]

Mean RDW among cases was 16.04% compared to controls 11.22% which was statistically significant. Mean serum iron level was found to be low among cases compared to controls (43.47 mg/dl and 119.52 mg/dl respectively). Mean TIBC was 476.4 microgram/dl in cases and 302.8 mcg/dl in control, which was statistically significant (p value<0.001). Transferrin saturation was less among case group (12.08%) compared to controls (36%), the difference was statistically significant. Mean serum ferritin level was 20.50 mcg/l in the cases and 71.65 mcg/l in controls which was statistically significant. There are many confounding factors, such as nutritional status, incidence of infection,

cultural factors, and genetic background. Richard et al. have reported that severe malnutrition (reduced concentrations of albumin and plasma protein, hypokalemia and hyponatremia, hypomagnesemia and hypocalcemia associated with vitamin D deficiency) can lower the seizure threshold and contribute to an increased prevalence of epilepsy in developing countries. By the time hypomagnesemia occurs tissue and CSF magnesium deficiency is usually severe because magnesium is primarily an intracellular ion and neurological function is already adversely affected. [19] Full-time day-care attendance (20 h per week or more) is nearly as important a risk factor as social history. Day-care attendance has been linked with an increased risk of infectious disease, particularly respiratory infections, and diarrhea. Children with a history of ear discharge, frequent sore throats, or pneumonia were more likely to have had a febrile seizure. [13]

Conclusion

Iron deficiency anemia was more frequent among children with febrile seizure. Strong association was found between various parameters of iron deficiency anemia and occurrence of febrile seizure. The result suggests that IDA may be a risk factor for febrile seizure. Screening for IDA should be considered in children with febrile seizure. Early detection and timely correction of iron deficiency may be of help for prevention of recurrence

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